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(54) **GRANULOCYTE SUBTYPE-SELECTIVE RECEPTORS AND ION CHANNELS AND USES THEREOF**

Related U.S. Application Data

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(76) Inventor: **Chaker N. Adra, Boston, MA (US)**

Publication Classification

Correspondence Address:
WOLF GREENFIELD & SACKS, P.C.
600 ATLANTIC AVENUE
BOSTON, MA 02210-2206

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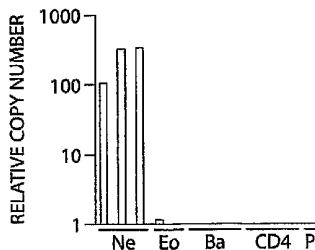
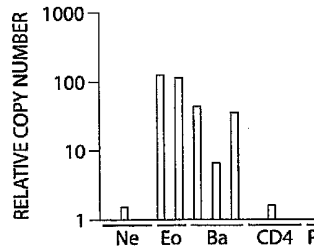
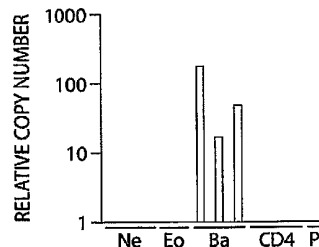
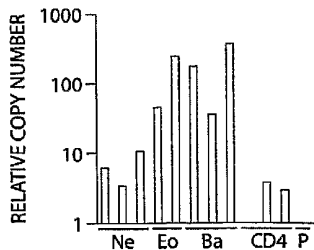
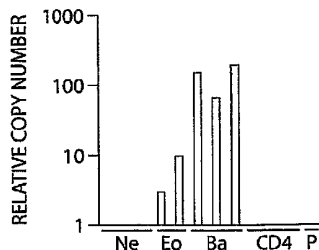
(57) **ABSTRACT**

(22) PCT Filed: **Mar. 3, 2005**

The invention relates, in part, to granulocyte type selective markers that are preferentially expressed in granulocytes and their use in drug screening assays. Additionally, the granulocyte type selective markers are useful in the diagnosis and treatment of granulocyte disorders and in the assessment of the efficacy of therapies of granulocyte disorders.

(86) PCT No.: **PCT/US2005/007519**

§ 371 (c)(1),
(2), (4) Date: **Nov. 16, 2007**



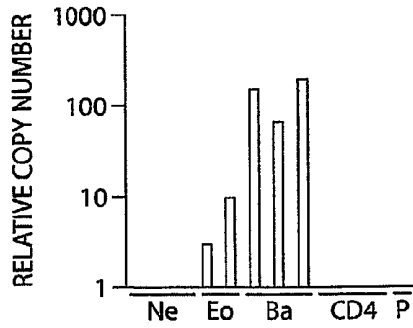


Fig. 1A

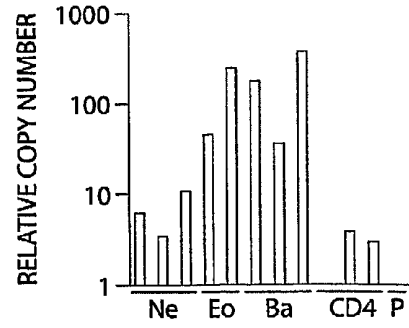


Fig. 1B

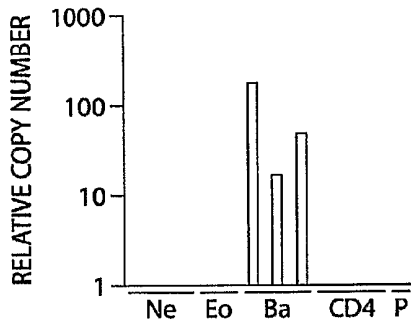


Fig. 1C

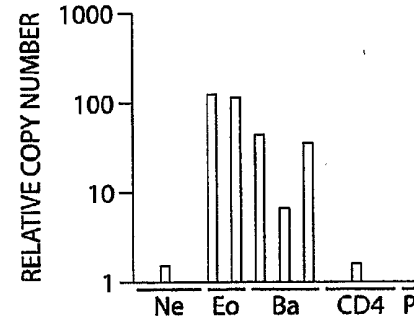


Fig. 1D

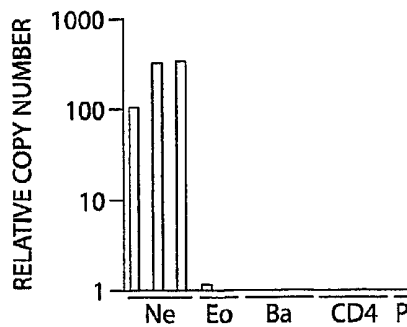


Fig. 1E

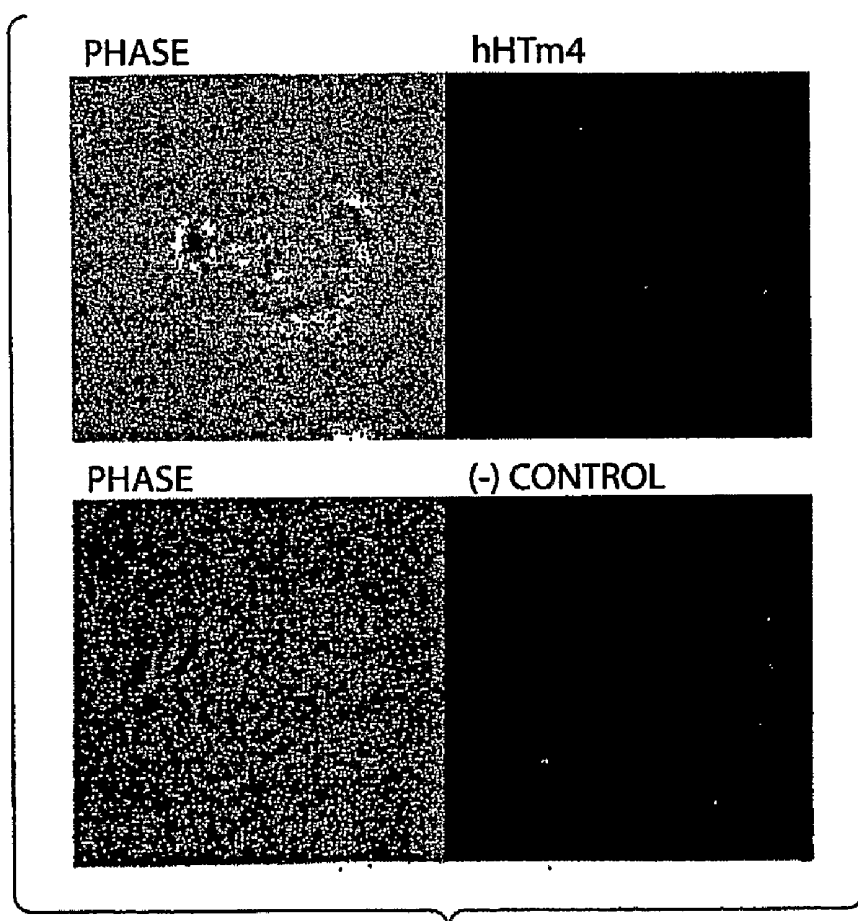


Fig. 2

Figure 3. Granulocyte subtype-specific transcripts for ion channels and receptors

<u>Ion Channels</u>	<u>Transcript (Accession #, GenBank)</u>	<u>Cell-type^a</u>	<u>MC</u>	<u>Ba</u>	<u>Eo</u>	<u>Ne</u>	<u>PI</u>	<u>CD4</u>	<u>CD8</u>	<u>CD14</u>	<u>CD19</u>	<u>Fb</u>	<u>TC^b</u>	<u>Gene Functions</u>
<u>Ca²⁺ channel type A1 D (BE550599)</u>		Ba, Eo	0.1	1.7	1.5	0.4	0.0	0.3	0.1	0.0	0.3	0.0	0	facilitates uptake of the metalloids arsenite and antimonite
<u>aquaporin 9 (NM_020980) 602914</u>		Ne	0.7	0.1	0.4	137.4	0.4	0.9	0.1	8.6	0.1	0.2	7	
<u>K⁺ channel Kir 1.3 (U73191) 600359</u>		Ne	0.9	0.2	0.4	99.5	0.7	0.2	0.0	0.8	0.0	0.0	5	Andersen syndrome (170390) and Bartter syndrome (241200)
<u>K⁺ channel Kir 2.1 (AF153820) 600681</u>		Ne	0.7	3.8	5.3	40.7	0.4	0.2	0.5	1.5	0.7	1.1	6	Andersen syndrome (170390) and Bartter syndrome (241200)
<u>GPCR</u>														
<u>histamine H₄ R (AF312230) 606792</u>		Ba	0.7	34.2	9.4	0.7	0.4	0.8	0.5	0.6	0.0	0.1	0	expression of HRH4 conferred sensitivity
<u>PGE₂ R type 3a2 (X83858) 176806</u>		Ba	0.8	10.3	0.1	0.7	0.6	0.3	0.2	0.2	0.5	1.7	0	signaling pathways
<u>C3a R (U62027) 605246</u>		Ba, Eo	11.8	55.7	39.4	2.0	1.6	1.6	1.5	3.0	0.6	0.5	3	anaphylatoxin receptor
<u>CCR3 (NM_001837) 601268</u>		Ba, Eo	0.6	117.4	90.9	24.9	0.2	0.5	0.4	0.2	0.2	0.4	0	importance for eosinophil responses
<u>CRTH2 (NM_004778) 604837</u>		Ba, Eo	1.1	26.0	38.2	2.0	0.8	1.4	1.0	1.2	0.9	0.5	0	mediate signals to the interior of the cell via activation of heterotrimeric G proteins
<u>EMR-1 (NM_001974) 600493</u>		Ba, Eo	0.8	33.5	90.9	4.2	3.4	1.7	0.8	7.1	1.6	0.5	1	Probably involved in cellular response to a hormone
<u>adenosine A₃ R (NM_000677) 600445</u>		Eo	2.6	2.9	15.4	2.3	1.2	1.6	0.5	2.0	0.5	0.5	0	cardioprotective function
<u>P2Y2 purinergic R (NM_002564) 600041</u>		Eo	0.1	0.1	5.5	0.1	0.2	0.1	0.3	1.2	0.2	0.1	0	P2RY2 may participate in control of the cell cycle of endometrial carcinoma cells
<u>GPR 105 purinergic R (NM_014879)</u>		Eo	2.6	2.9	15.4	2.3	1.2	1.6	0.5	2.0	0.5	0.5	2	GPR105 is a G-protein-coupled receptor identifying a quiescent, primitive population of hematopoietic cells restricted to bone marrow; GPR105 might play an important role in peripheral and neuroimmune function
<u>GPR, Edg-4 (AF011466) 605110</u>		Eo, Ne	1.3	2.8	15.9	24.2	0.1	3.6	5.0	3.8	1.9	0.9	2	edg-4 mRNA was expressed in mouse islets; edg-4 (lpa2) r is a distinctive functional marker for ovarian carcinoma, and is expressed both as the wild-type and a carboxyl-terminally extended gain-of-function mutant
<u>PART-like GPR43 (NM_005306)</u>		Eo, Ne	0.3	0.7	12.4	35.2	0.8	0.1	0.1	0.7	0.4	0.1	0	the highest levels of gpr43 were

Fig. 3A

<u>603823</u>																			found in immune cells; gpr43 is highly restricted in hematopoietic tissues
C5a R (NM_001736) 113995	Ne	2.3	21.6	13.6	92.6	2.3	1.2	0.5	25.6	1.0	0.4	5							receptor for the chemotactic and inflammatory peptide anaphylatoxin c5a. this receptor stimulates chemotaxis, granule enzyme release and superoxide anion production.
CXCR1 IL-8R (NM_000634) 146929	Ne	0.2	4.3	0.3	83.4	0.4	0.3	0.2	0.2	0.1	0.1	0							receptor to interleukin-8, which is a powerful neutrophils chemotactic factor. binding of il-8 to the receptor causes activation of neutrophils. this response is mediated via a g-protein that activate a phosphatidylinositol-calcium second messenger system. this receptor binds to il-8 with a high affinity and to mgsa (gro) with a low affinity.
CXCR2 IL-8R (NM_001557)	Ne	0.2	1.1	1.5	112.1	2.7	0.3	0.8	0.7	0.6	0.0	1							receptor to interleukin-8, which is a powerful neutrophils chemotactic factor. binding of il-8 to the receptor causes activation of neutrophils. this response is mediated via a g-protein that activate a phosphatidylinositol-calcium second messenger system. this receptor binds to il-8 with a high affinity and to gro/mgsa and nap-2 also with a high affinity.
formyl peptide R 1 (NM_002029) 136537	Ne	2.8	23.5	8.8	282.9	3.6	1.3	0.7	62.6	1.1	0.5	0							HIGH AFFINITY RECEPTOR FOR N-FORMYL-METHIONYL PEPTIDES WHICH ARE POWERFUL NEUTROPHILS CHEMOTACTIC FACTORS. BINDING OF FMLP TO THE RECEPTOR CAUSES ACTIVATION OF NEUTROPHILS. THIS RESPONSE IS MEDIATED

Fig. 3B

isoforms 2 to 6 block apoptosis (in vitro), does not induce apoptosis.

decoy R1, TRAILR3 (AF012536) 603613	Ne	0.1	1.5	7.7	78.7	0.5	0.2	0.1	0.7	0.1	0.6	0
Fcγ R IIc2 (U90939)	Ne	1.5	2.4	7.8	59.9	0.3	0.2	0.1	7.2	2.3	0.2	2
Fcγ R IIc3 (U90940)	Ne	2.4	10.7	10.0	84.3	3.0	1.4	0.6	14.0	7.2	1.0	5
Fcγ R III (J04162) 146740	Ne	0.7	1.6	1.9	199.6	6.6	1.3	1.3	2.2	2.6	0.1	4
G-CSF R (NM_000760) 138971	Ne	0.1	0.4	1.6	163.6	0.2	0.8	0.2	25.5	0.1	0.2	3
IL-13 R (U81379) 308385	Ne	0.3	0.2	2.0	14.1	0.4	0.4	0.3	2.9	1.3	1.3	0
IL-1R, type II (NM_004633) 147811	Ne	0.1	0.1	0.1	53.5	0.2	0.4	0.1	0.2	0.0	0.0	3
IGFR 1 (NM_000875) 147370	Ne	0.3	3.5	5.0	17.4	1.6	0.1	2.8	2.4	2.0	3.5	3
IGFR 2 (NM_000876) 147280	Ne	4.6	0.9	5.4	85.3	1.7	2.9	8.7	8.4	4.8	15	32
leukocyte immunoglobulin-like R A2 (NM_006866) 604812	Ne	0.5	5.8	4.3	41.2	1.8	0.0	0.1	11.6	0.5	0.1	2
Toll-like R 1 (AL050262) 601194	Ne	0.6	0.3	1.2	31.5	1.6	0.8	0.7	3.0	1.5	0.3	0
Toll-like R 2 (NM_003264) 603028	Ne	0.9	6.0	1.3	83.8	1.6	1.3	0.1	26.3	0.9	0.4	0
Toll-like R 6 (NM_006068)	Ne	0.5	1.0	0.9	8.8	0.1	0.9	0.9	2.1	1.2	0.6	0

a. Cell-type specificity was obtained by comparing the "normalized AD" levels of each gene in mast cells (MC; average of 2 experiments), basophils (Ba; average of 3 experiments), eosinophils (Eo; average of 4 experiments), neutrophils (Ne; average of 4 experiments), platelets (Pl), CD4⁺ cells (CD4), CD8⁺ cells (CD8), CD14⁺ cells (CD14), CD19⁺ cells (CD19) and nasal polyp-derived cultured fibroblasts (Fb).

Fig. 3E

	CB cultured MCs	Basophils	cultured basophils	Eosinophils	Neutrophils	platelets	Erythrocytes	CD4	CD8	CD14	CD19
Spink5	21	17	11	22	16	30	15	28	36	129	104
chymase human	1221	47	65	45	12	101	62	108	59	104	45
tryptase alpha	21179	212	40	33	25	184	139	104	17	52	39
tryptase beta	25414	195	113	49	28	152	10	122	113	93	6
tryptase delta	349	45	6	23	55	74	113	11	10	42	11
tryptase gamma	654	56	19	38	78	28	24	81	230	142	83
TRPV2	129	37	15	97	99	259	137	133	67	97	110
ANKTM1_	28	28	8	38	30	96	18	14	46	11	28
Cannabinoid receptor type 1	50	41	14	47	36	27	61	41	56	18	54
Cannabinoid receptor type 2	160	369	226	578	177	271	530	324	232	212	421

Fig. 4A

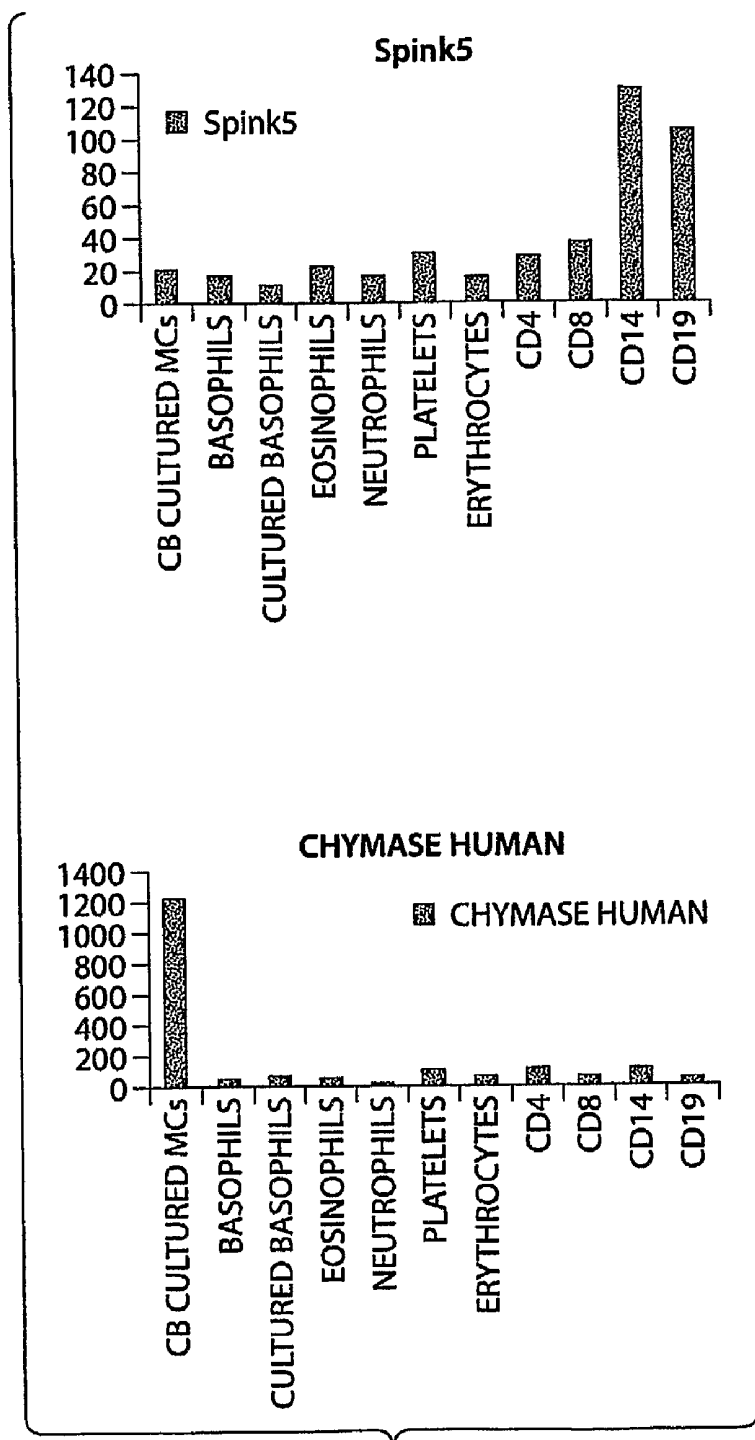


Fig. 4B

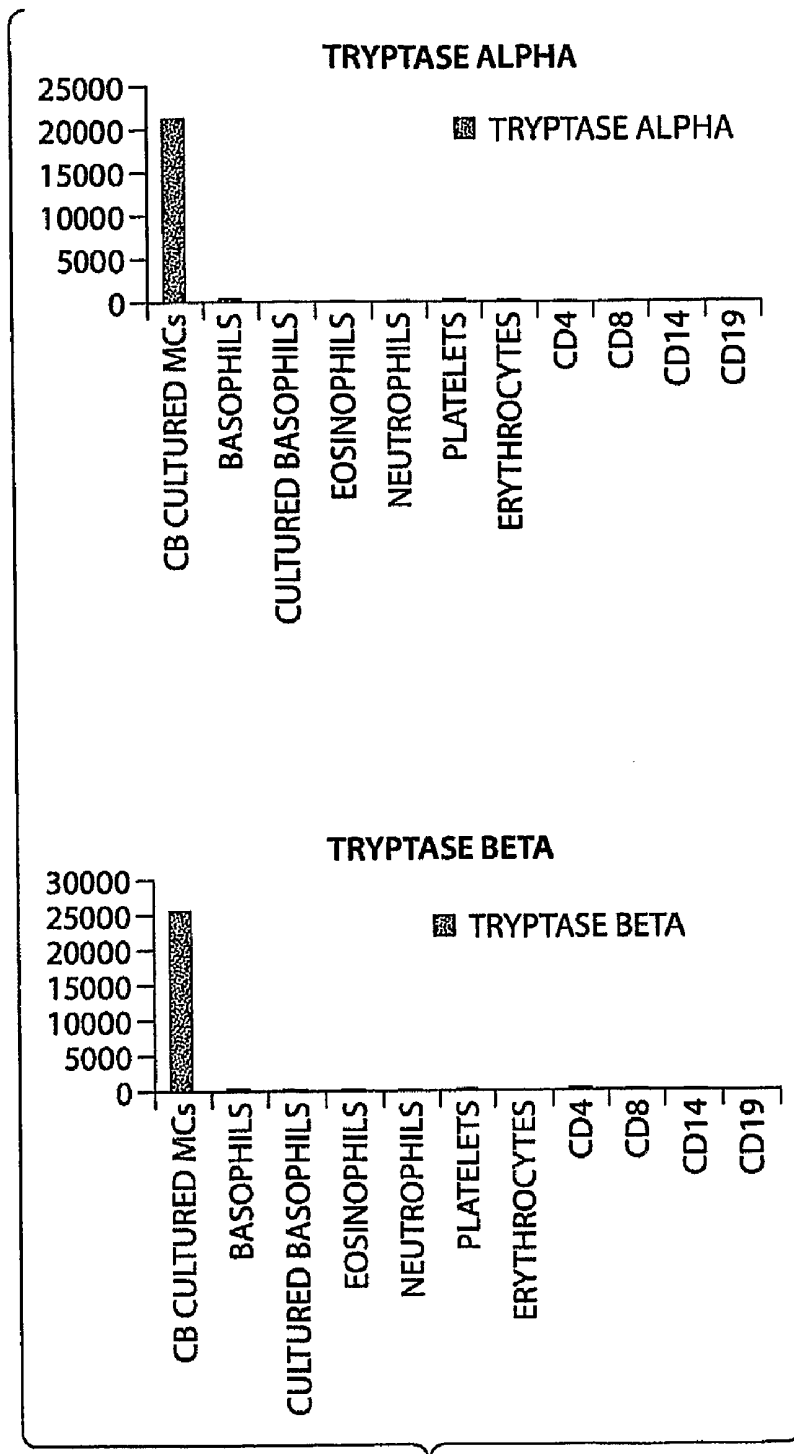


Fig. 4C

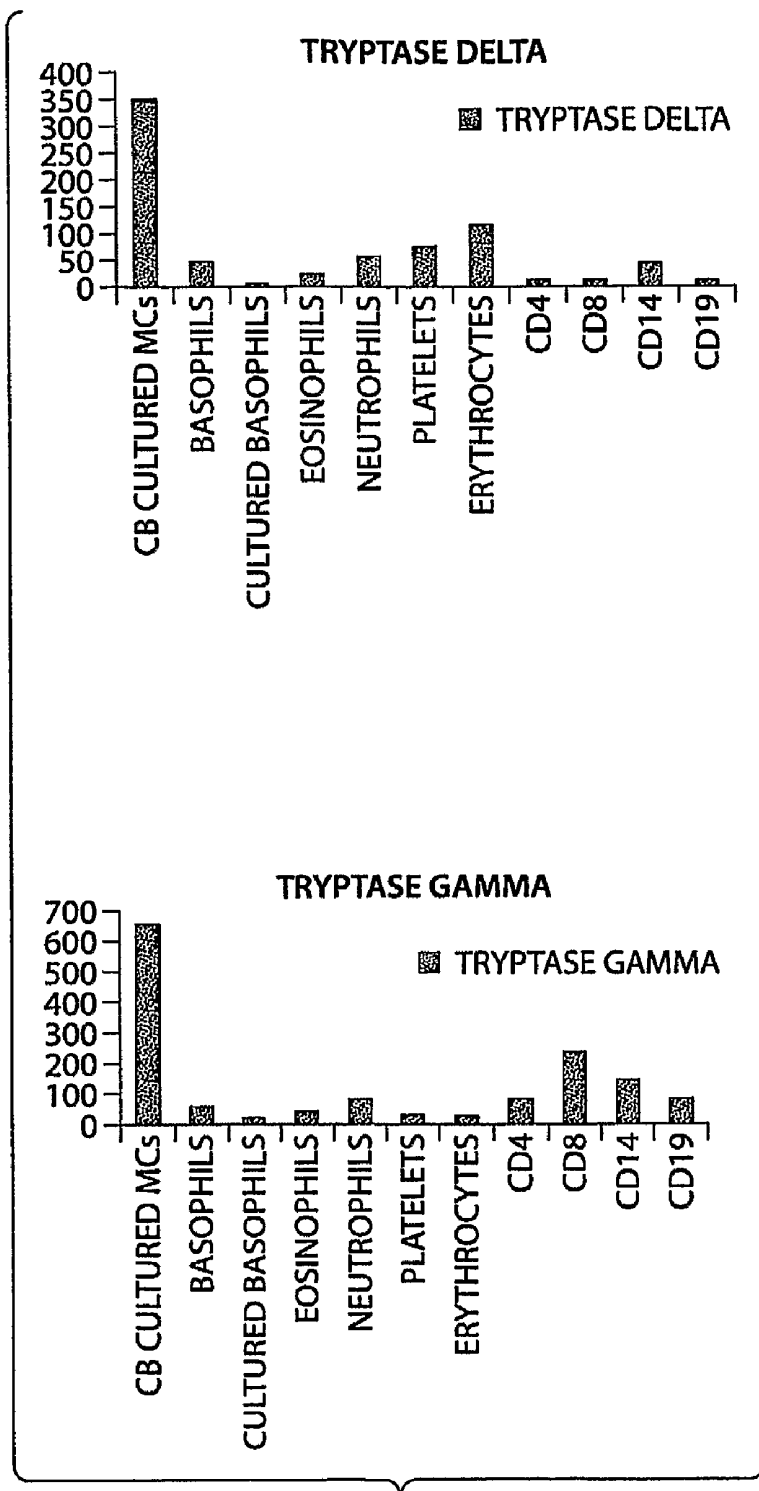


Fig. 4D

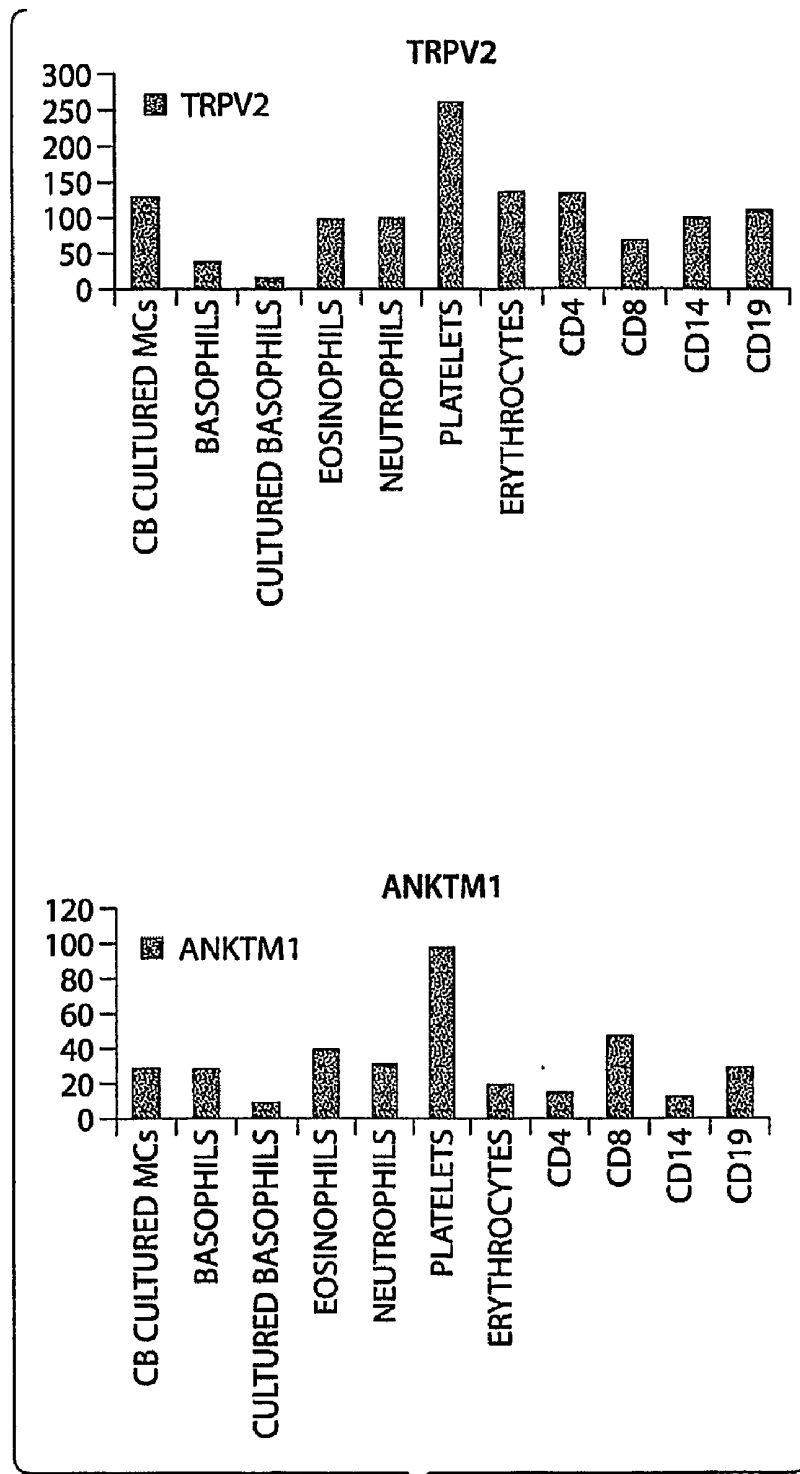


Fig. 4E

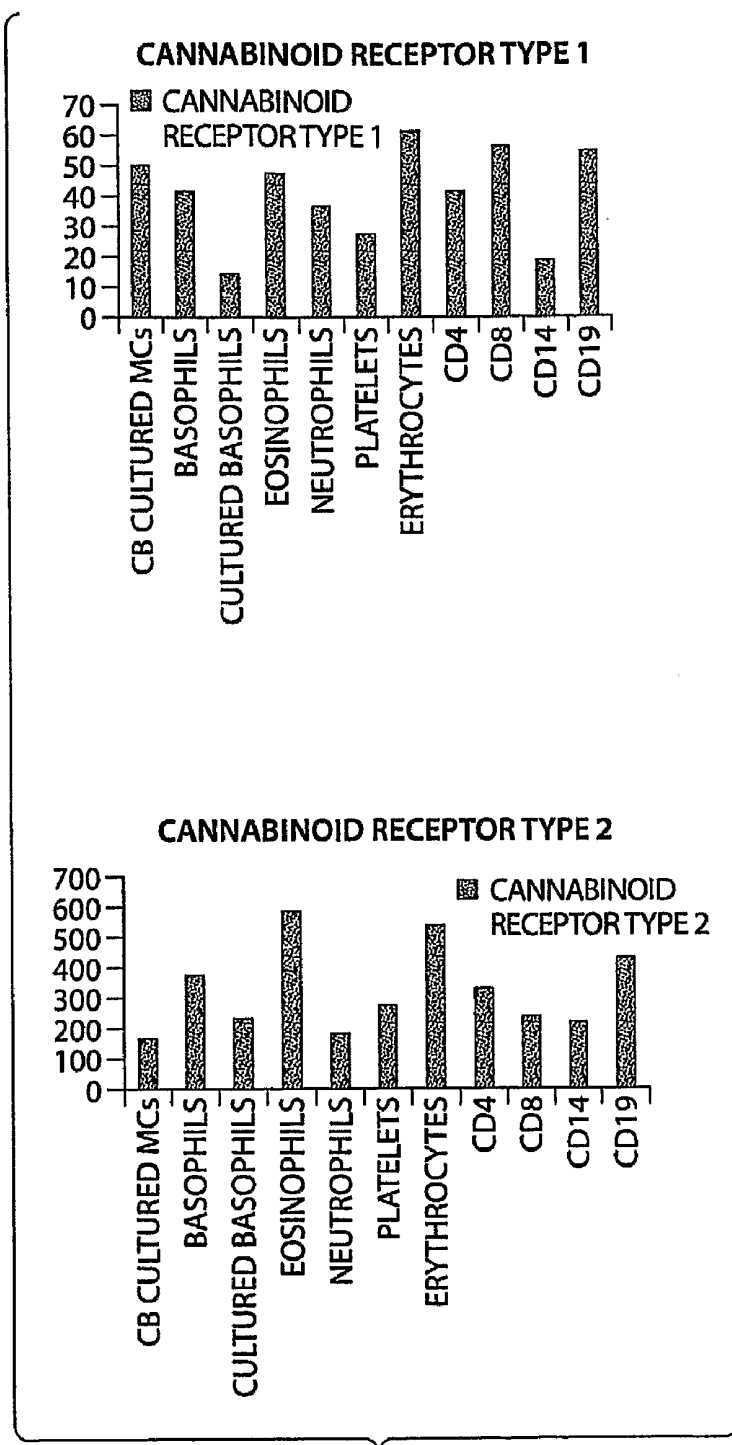


Fig. 4F

CB cultured MCs	Basophils	cultured basophils	Eosinophils	Neutrophils	platelets	Erythrocytes	CD4	CD8	CD14	CD19
86	28	39	26	37	125	46	103	95	85	28
4	45	1004	59	84	18	68	31	68	451	13
165	84	51	258	1261	31	42	13	18	1105	125
375	780	227	1755	4237	199	375	286	58	2963	214
49	614	384	461	3269	146	318	8	9	1247	52
28	50	45	154	389	120	148	127	35	539	86
7	58	34	18	23	13	106	14	286	68	204
22	17	21	27	28	35	11	28	110	88	111
30	54	134	66	61	149	95	39	247	147	271
35	138	81	88	93	191	132	57	257	21	267
24	31	23	21	21	53	27	33	135	19	173
139	140	85	157	144	280	210	35	239	152	196
11	45	41	50	41	88	15	19	72	77	85
41	43	31	20	52	31	121	96	163	26	193
27	83	24	41	49	61	239	92	323	56	72
68	89	41	51	95	75	97	76	169	36	196
144	621	83	1334	2386	107	146	145	52	2154	99
18	14	5	28	37	86	12	13	14	32	23

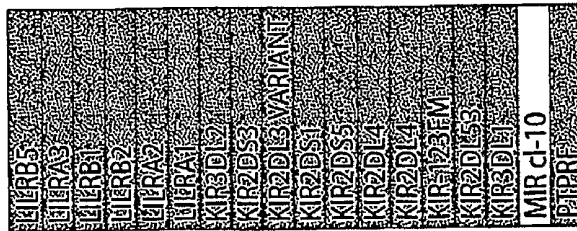


Fig. 5A

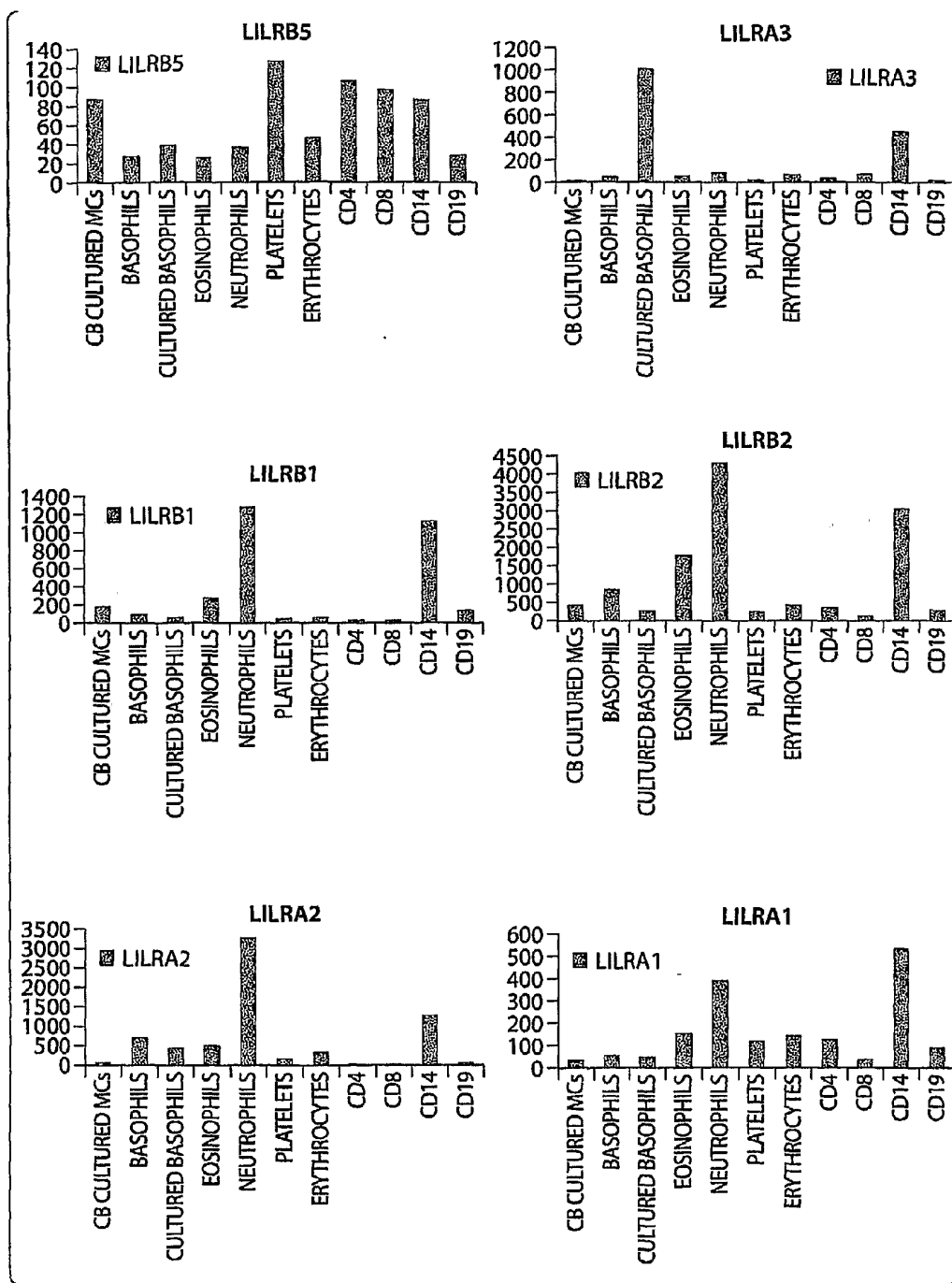


Fig. 5B

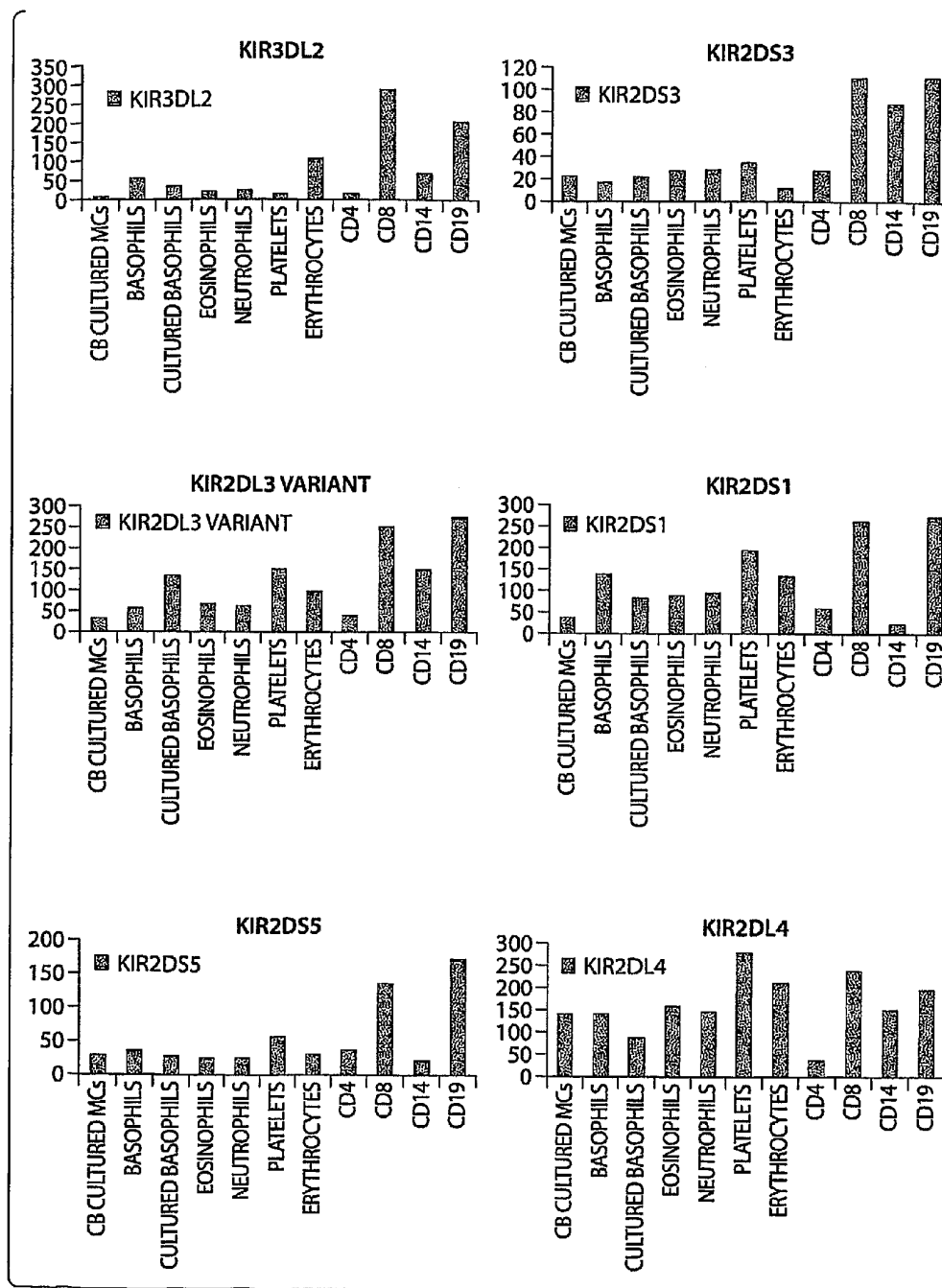


Fig. 5C

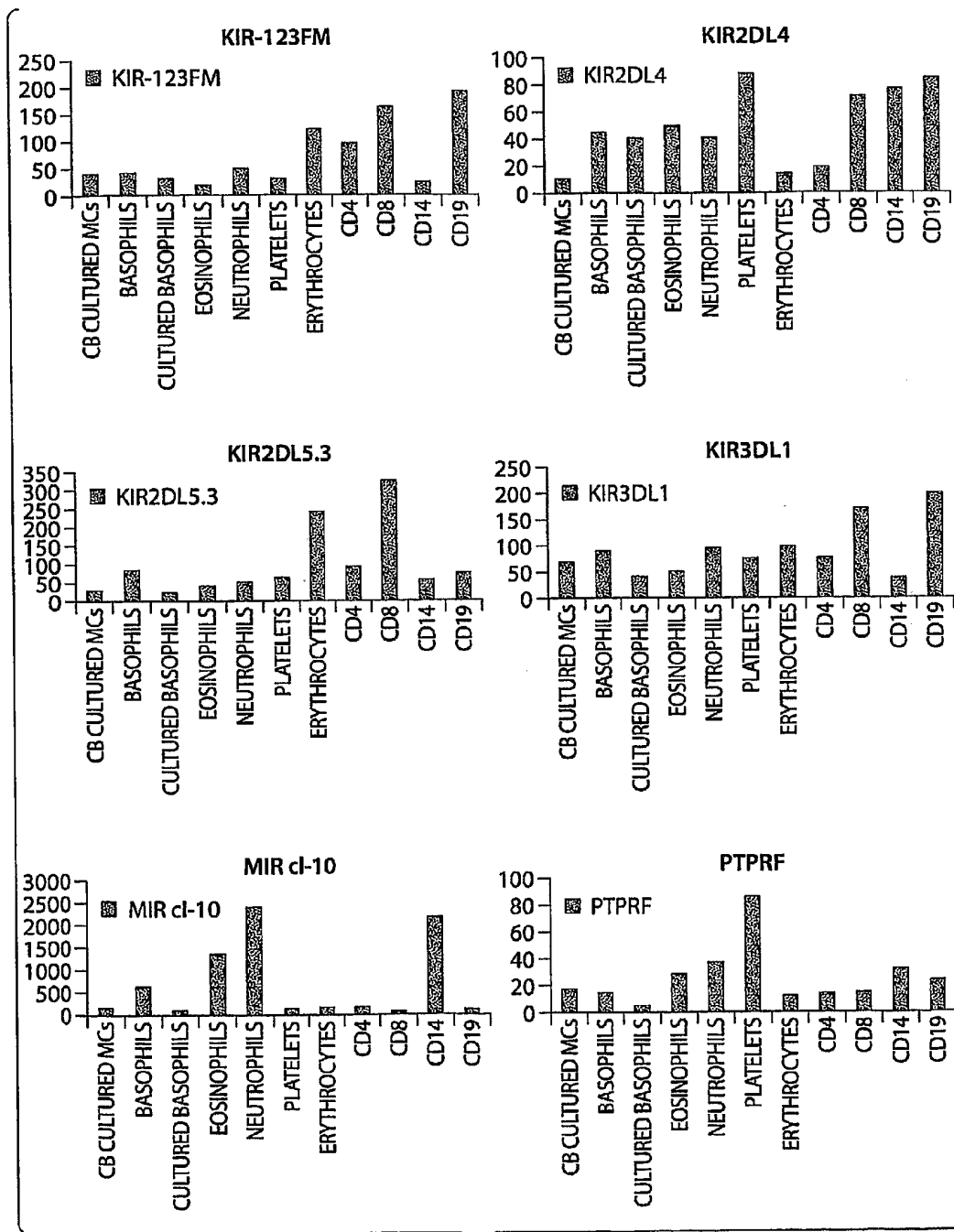


Fig. 5D

Table E1. The complete list of granulocyte subtype-selective transcripts. Selectivity index (S.I.) was calculated by comparing the "normalized AD⁺ level of a cell type or of two cell types with the maximal gene expression level of the other 8 or 9 cell types including platelets (Pl), CD4⁺ cells, CD8⁺ cells, CD14⁺ cells, CD19⁺ cells and nasal polyp-derived cultured fibroblasts (Fb). When the result was accompanied by presence call, it was shown as a bold numeral. *Italic numerals show that the raw AD levels were associated with absence call by the GeneChip analysis software. Transcripts having S.I. >3-fold were shown in A-H. Abbreviations used in the table through A-I were (small); the results obtained by the small sample protocol (see materials and methods), R; receptor, and ICN; ion channel.*

A. Basophil (Ba)-selective transcripts (1/2).

Probe.set	Accession #	Transcripts	MC		Eo3		Eo4		Ne3		Ne4		CD4	CD8	CD14	CD19	Fb	Ba.S.I.					
			cord	lung	1	2	1	2	1	2	1	2							1	2			
207539_s.at	NM_000589.1	IL-4	0.2	0.7	104	169	134	0.1	0.3	0.0	1.2	0.2	0.0	0.2	0.1	0.0	0.0	73.348					
210254_at	L35848.1	HTIm4	0.8	0.4	115.6	130.1	153.6	2.4	1.7	21.8	1.7	0.1	0.9	0.5	0.4	0.1	0.2	0.0	38.24				
205513_at	NM_001062.1	vitamin B12 binding protein	1.5	1.2	98.9	149.3	110.9	3.2	2.2	16.1	1.9	4.9	4.5	6.3	8.1	1.8	0.7	0.8	1.4	20.322			
206748_at	NM_002183.1	IL-3 R	1.0	0.1	6.2	80.2	71.3	1.7	1.7	1.8	2.9	0.3	0.4	0.2	1.9	0.2	0.3	0.2	0.7	0.1	16.62		
214920_at	R33964	FLJ11022 fs	0.1	1.1	4.9	13.1	15.4	0.1	0.2	0.7	0.5	1.0	0.4	0.5	0.7	0.1	0.1	0.2	0.1	0.3	0.1	16.049	
201825_s.at	AL572542	CGI-49	3.3	1.6	21.4	74.9	46.5	2.1	1.2	0.1	1.2	0.1	0.1	0.2	0.1	1.3	0.7	1.7	1.4	0.8	2.8	15.045	
213238_at	AI478147	ALPase, Class V, type 10D	1.2	2.9	39.9	76.3	118.9	2.3	1.7	3.1	1.9	2.1	1.4	2.3	6.8	0.7	0.9	0.9	2.5	5.0	4.1	14.398	
211734_s.at	BC005912.1	Fc epsilon R1 alpha	10.5	28.4	2100	2208	226.2	8.4	2.1	4.8	2.9	0.3	0.7	4.5	16.6	1.4	5.1	0.8	1.4	0.4	0.2	12.703	
213894_at	BF447246	KIAA0960	0.1	0.0	3.7	13.0	15.6	0.3	0.4	0.4	0.4	0.9	0.7	0.7	1.0	0.6	4.8	2.7	0.5	1.0	0.0	11.927	
206363_at	NM_005360.2	e-MAF	3.7	1.4	36.5	75.7	66.4	1.2	0.1	0.2	0.2	0.2	0.1	0.2	0.2	0.2	0.1	0.1	0.1	0.2	0.2	12.272	
203373_at	NM_003877.1	SOC52	2.1	3.9	21.7	85.0	112.2	4.6	4.7	9.4	6.5	0.7	1.2	0.3	2.5	1.6	3.2	3.5	0.8	0.9	3.6	9.8282	
207538_at	NM_000589.1	IL-4	0.3	0.1	11.1	9.8	9.2	0.4	0.4	0.0	0.3	0.1	0.0	0.4	0.7	0.8	0.4	0.3	0.1	0.0	0.1	9.8156	
213684_s.at	BF671400	LIM-protein	0.6	0.1	11.1	21.0	20.6	1.9	1.6	2.4	1.8	0.8	0.6	1.5	2.5	0.1	0.0	0.3	1.0	0.0	0.1	8.9245	
209360_s.at	D43968.1	AML1, l1b protein	10.4	2.4	53.2	131.1	90.5	8.5	7.0	13.8	11.3	0.5	0.5	0.5	4.2	1.3	4.1	5.9	1.3	2.5	3.1	8.7543	
220234_at	NM_004056.2	carbonic anhydrase VIII	0.4	0.1	11.7	10.2	6.0	1.2	0.1	0.2	0.4	0.8	0.9	0.1	0.5	0.5	1.1	0.1	0.1	0.1	0.8	0.0	8.1309
210643_at	AF053712.1	osteopontin ligand	0.1	0.3	1.8	3.4	6.0	0.7	0.4	0.3	0.2	0.4	0.1	0.3	0.1	0.1	0.3	0.4	0.3	0.2	0.2	7.6628	
209211_at	AF132818.1	colon Kruppel-like factor	0.1	0.0	1.8	10.2	8.8	0.3	0.5	1.5	0.8	1.1	0.7	0.8	0.5	0.2	0.2	0.4	0.2	0.1	0.3	7.239	
204309_at	NM_000781.1	CYP11A	0.3	0.1	2.6	6.1	5.6	0.1	0.3	0.5	0.5	1.0	0.1	0.1	0.9	0.3	0.3	0.1	0.0	0.3	0.7	6.8366	
203372_s.at	AB004903.1	SOC52	0.6	1.6	9.2	8.5	15.9	1.4	2.4	0.9	0.2	0.7	0.6	0.4	0.8	0.8	1.6	1.3	0.3	0.3	1.4	6.8271	
207463_x.at	NM_002771.1	seime protease 3 (trypsin 3) acid sphingomyelinase-like	1.0	1.0	4.8	10.0	10.9	0.4	1.0	1.0	1.2	1.2	0.9	1.8	0.4	0.6	0.4	0.4	0.3	0.7	1.2	6.7218	

Fig. 6A-1

ProbeSet	Accession #	Transcripts	MC	MC	Ba1	Ba2	Ba3	Eo	Eo	Eo3	Eo4	Ne	Ne	Ne3	Ne4	pl	CD4	CD8	CD14	CD19	Fb	Ba.SI.
			cord	lung	(small)	(small)	(small)	1	2	(small)	(small)	1	2	(small)	(small)							
213624_at	AA873600	phosphodiesterase	4.7	2.0	208	306	259	21	28	38	1.7	0.5	1.1	1.3	1.3	0.1	0.2	0.1	3.8	0.2	3.2	6.6846
214873_at	AL137651.1	clone DMFZp3400213	0.1	0.4	3.7	15.5	24.4	2.0	0.9	2.5	2.3	0.2	0.1	0.7	0.6	0.1	1.1	1.5	0.5	0.6	0.7	6.2585
204928_s_at	NM_019848.2	protein P3	2.3	1.5	9.8	49.0	34.3	3.7	3.3	4.8	4.2	1.6	1.0	1.9	2.2	4.1	1.8	3.0	0.8	2.0	2.6	6.2142
208935_s_at	L78132.1	prostate carcinoma tumor antigen (pcta-1)	2.2	1.2	9.9	19.1	16.6	2.3	1.5	3.6	2.5	1.1	1.1	1.9	0.9	1.8	1.8	2.0	2.0	1.4	0.8	6.2011
203201_at	NM_000303.1	phosphomannomutase 2 (PMM2)	1.8	0.3	10.7	15.9	6.5	0.9	0.6	1.2	0.9	0.8	0.4	1.1	1.3	1.0	1.3	1.2	1.2	1.1	1.7	6.1557
201826_s_at	NM_016002.1	CGI-49	1.8	3.1	11.0	27.5	15.1	1.6	1.1	1.4	2.1	1.1	1.4	1.3	1.8	1.6	1.1	1.1	1.1	0.6	2.9	5.6407
213471_x_at	NM_016002.1	serine protease 4 (trypsin 4)	1.8	1.7	5.9	12.5	11.4	1.0	0.5	1.2	0.5	1.2	1.7	1.2	1.2	0.9	1.0	1.2	1.0	0.4	1.7	5.4082
209348_s_at	AF055376.1	c-MAF, short form	6.4	4.9	29.6	47.7	42.3	0.8	0.3	0.4	0.6	0.3	0.0	0.9	1.4	1.0	7.3	3.1	0.9	0.7	1.4	5.3183
213343_s_at	AL041124	hypothetical protein PP1665	0.9	0.2	12.2	17.0	12.0	3.5	1.7	0.5	0.6	0.1	0.3	0.8	0.4	0.6	1.5	2.6	0.7	1.6	1.3	5.2721
202491_s_at	NM_003640.1	Kappa B-associated protein	1.6	3.8	23.9	51.9	43.5	4.6	4.0	7.1	7.3	1.6	2.1	2.5	2.3	1.7	3.7	7.4	3.2	4.7	4.2	5.107
221021_s_at	NM_030877.1	Bostaurus P14 protein	6.9	3.2	7.2	29.2	58.9	2.8	3.2	5.4	6.3	0.9	1.2	1.8	1.6	1.6	2.2	2.4	2.0	3.5	1.8	4.9129
213346_at	BE748563	hypothetical protein BC015148	2.7	1.8	17.5	38.8	25.8	4.0	6.7	6.2	4.8	1.4	0.9	0.8	1.1	0.2	1.2	1.5	0.6	1.1	1.9	4.8879
209764_at	AL022312	mannosyl (beta-1,4)-glycoprotein	0.0	0.9	4.1	6.1	5.8	0.8	1.4	0.9	1.4	0.6	0.1	0.5	0.2	1.0	0.4	0.2	0.2	0.4	0.3	4.855
207067_s_at	NM_002112.1	beta-1,4-N-acetylglucosaminyltransferase	64.1	14.7	105.2	164.9	165.7	3.4	1.4	4.1	2.8	2.1	1.2	4.6	14.0	2.4	0.8	0.9	1.1	0.7	0.2	4.6305
210375_at	X83658.1	histidine decarboxylase	7.0	0.6	2.4	11.5	17.0	0.3	0.1	0.1	0.0	0.4	0.7	0.9	0.7	0.6	0.3	0.2	0.2	0.5	1.7	4.6103
206306_at	NM_001056.1	prostaglandin E receptor, type 3a2	2.1	1.1	3.7	11.0	7.8	1.0	0.6	1.5	0.5	1.2	0.3	1.5	0.9	1.1	0.7	0.3	1.0	0.2	0.4	4.5552
210001_s_at	AB005043.1	ryanodine receptor 3 (RYR3)	5.2	0.2	3.0	24.1	29.9	2.1	3.0	3.2	3.4	0.3	1.0	0.8	1.3	0.8	0.8	0.8	0.0	0.8	0.9	4.5248
		SOC51																				
		serine (or cysteine) proteinase inhibitor, class B (ovalbumin), member 2 (SERPINB2)																				
204614_at	NM_002575.1	hepatocyte growth factor (HGF)	0.3	0.6	5.3	12.9	12.5	0.4	2.4	4.2	2.0	1.0	0.8	0.7	0.3	1.9	0.5	0.7	2.1	0.2	0.2	4.5061
209960_at	X16323.1	transcription factor BTEB2	0.4	0.0	2.3	7.3	5.5	0.5	0.4	0.6	0.5	0.1	0.1	1.0	0.6	0.7	0.1	0.0	1.0	0.0	0.5	4.4335
209212_s_at	AB030824.1		0.1	0.2	7.5	14.3	22.1	2.3	2.0	4.9	3.7	1.2	1.3	1.5	2.5	1.4	0.5	0.2	1.1	0.9	0.8	4.363

Fig. 6A-2

A. Basophil (Ba)-selective transcripts (2/2).

Probe-set	Accession #	Transcripts	MC cond	MC lung	Ba.1 (small)	Ba.2 (small)	Ba.3 (small)	Fo 1	Fo 2	Fo3 (small)	Fo4 (small)	Ne 1	Ne 2	Ne3 (small)	Ne4 (small)	CD4	CD8	CD14	CD19	Fb	Ba.SL
21451_s_at	U18133.1	Class 1 homeobox protein (HOXA9)	0.6	0.6	1.7	6.3	8.3	0.3	0.5	0.8	0.5	0.1	0.1	0.5	1.0	0.1	0.1	0.3	0.7	0.1	4.318
32502_at	AL041124	DKFZp434D0316_s1	1.6	1.9	14.6	22.5	17.4	0.4	2.1	0.7	1.4	1.1	1.0	0.4	0.4	2.3	2.5	4.1	2.5	2.3	4.354
203373_at	NM_004389.1	catenin (cadherin-associated protein)	0.2	0.1	1.1	3.9	3.2	0.6	0.1	0.1	0.1	0.1	0.1	0.2	0.1	0.1	0.6	0.2	0.2	0.2	4.2308
219676_at	NM_025231.1	FLJ22191	0.3	0.3	2.5	7.3	12.0	0.9	0.2	2.0	1.5	1.7	1.4	4.2	2.2	0.6	1.1	0.3	1.4	0.1	4.2135
213385_at	AK026415.1	beta-2-chimaerin	4.7	3.1	8.3	22.9	21.8	1.1	0.8	0.9	1.0	0.2	1.5	0.8	1.0	0.1	0.9	1.6	0.2	0.4	4.2131
214637_at	BG-437034	oncostatin M	0.4	0.0	0.9	5.4	4.4	0.2	0.7	0.1	0.7	0.5	1.8	0.2	1.1	0.4	0.1	0.2	0.1	0.0	4.1983
202490_at	AF153419.2	Reppin B-associated protein	0.2	0.2	1.3	3.6	2.2	0.4	0.4	0.5	0.1	0.3	0.0	0.2	0.0	0.3	0.5	0.2	0.2	0.4	0.41747
220416_at	NM_024837.1	FLJ21472	4.1	1.5	9.1	9.7	12.2	1.9	3.3	3.0	1.9	0.8	0.6	1.1	0.9	0.7	0.6	0.2	0.8	0.3	4.1718
218318_s_at	NM_016231.1	neuro-like kinase	1.4	1.3	6.2	7.0	7.1	0.8	0.9	0.8	0.6	0.5	1.0	0.1	0.1	1.6	1.3	0.9	1.2	1.1	4.1558
215201_at	NM_166925	FLJ14135 fig. clone MAMMA1002728	0.1	0.1	2.1	3.5	5.1	0.5	0.7	0.8	0.9	0.0	0.1	0.1	0.1	0.5	0.3	0.8	0.4	0.5	4.1491
222303_at	AV700891	ETS2 intronic transcript 1 mRNA	0.6	1.4	31.1	88.8	63.8	3.6	2.2	2.9	3.2	10.8	10.5	16.6	19.0	1.2	0.7	8.1	0.3	0.8	4.0555
201664_at	AL136871.1	DKFZp434F205	2.8	5.0	17.3	27.7	31.8	4.4	5.3	9.1	8.3	4.3	3.9	5.7	5.5	0.1	4.8	4.2	2.5	4.1	3.8471
210252_s_at	AB002356.1	MAP-kinase activating death domain	3.6	4.6	12.7	35.0	40.7	6.2	6.1	7.0	8.3	2.2	1.3	1.9	3.3	5.2	2.7	5.4	3.0	3.5	3.8424
201328_at	AL575509	vets avian erythroblastosis virus E26 oncogene homolog 2	1.7	0.1	18.4	34.7	50.7	2.8	1.6	1.7	1.8	6.4	9.9	8.7	8.9	0.5	0.9	1.0	4.4	0.1	3.8075
218392_x_at	NM_022754	FLJ12876	1.2	1.0	3.5	7.5	7.4	1.4	1.0	2.7	1.5	1.0	0.6	0.9	0.1	0.9	1.4	0.4	0.7	0.5	3.7693
205046_at	NM_001813.1	FLJ14150 fig. clone MAMMA1003026	0.0	0.3	1.5	8.1	13.1	1.7	0.5	1.9	1.2	0.5	1.3	1.0	0.9	1.1	1.5	0.9	1.0	0.4	3.7324
221170_at	AF12230.1	histamine H4 receptor	0.6	0.8	35.9	34.2	32.5	7.8	11.9	8.7	9.3	0.2	0.8	0.8	1.0	0.4	0.8	0.5	0.6	0.0	3.6719
201663_s_at	NM_005496.1	chromosome-associated polypeptide C (lectin, galactoside-binding, soluble, 8 gallectin 8)	2.2	4.3	17.6	15.1	18.1	3.4	6.6	4.9	4.2	4.0	3.7	2.2	2.7	1.7	4.1	2.9	1.7	3.7	3.6472
208933_s_at	AL659005	lectin, galactoside-binding, soluble, 8 gallectin 8	11.8	4.9	26.7	28.3	28.2	5.9	6.6	10.1	4.8	3.8	4.5	5.5	2.1	4.3	7.6	7.4	7.2	4.3	3.6311
209710_at	AL563460	GATA-binding protein 2	50.4	38.9	141.1	189.2	154.7	4.4	1.3	3.8	3.1	0.7	1.2	5.4	10.8	2.5	0.7	0.9	0.3	0.1	3.6251
205769_at	NM_003645.1	fatty-acyl-Coenzyme A ligase, very long-chain 1 (FACVL1)	3.3	2.5	7.0	16.2	9.2	0.3	0.3	0.3	0.5	0.1	0.4	0.2	0.2	0.4	0.4	0.7	0.1	0.3	3.5389
209409_at	D86462.1	KIAA0207	8.4	2.6	12.5	38.0	33.1	4.9	4.2	12.3	10.4	1.7	1.7	2.1	1.8	1.4	0.4	0.7	1.5	0.4	3.4907
38398_at	AB002356	KIAA0358	5.5	5.5	3.1	13.8	28.6	29.8	6.1	6.4	5.6	7.0	3.0	3.3	4.1	5.1	3.3	5.3	3.7	4.4	3.4534
205899_at	NM_003914.1	cyclin A1	5.6	3.6	16.2	20.6	10.5	0.1	0.6	0.9	0.7	1.6	0.7	0.8	0.4	1.9	0.7	0.1	0.1	0.3	3.8624
218150_at	NM_012097.1	ADP-ribosylation factor-like 5	8.2	5.3	37.6	56.6	54.6	9.1	8.6	14.0	12.1	3.9	5.0	7.7	9.6	3.8	8.3	8.1	14.5	9.9	3.3745
213097_s_at	AK338837	zuotin related factor 1	2.1	1.8	8.4	13.4	16.7	4.8	2.1	4.8	3.7	1.8	1.2	1.2	1.6	0.3	3.4	3.7	2.3	3.3	3.3672
208158_s_at	NM_018030.1	oxysterol-binding protein-related protein nasopharyngeal carcinoma associated gene protein 8	1.2	2.3	8.8	18.0	15.3	0.6	0.8	1.5	1.4	1.5	2.3	2.7	1.8	2.0	0.2	0.7	1.3	0.5	3.342
210109_at	AF191492.1	gene protein 8	1.2	0.7	3.6	5.4	4.2	1.2	1.5	1.0	0.3	0.6	1.1	1.7	0.6	0.2	1.3	0.5	1.4	0.6	3.2977
220918_at	NM_025143.1	FLJ0856	1.0	1.1	26.1	37.3	26.2	6.2	6.5	14.1	11.3	3.3	2.5	2.0	2.0	1.1	0.9	0.9	3.5	1.1	3.2902
209389_x_at	L34598.1	ami 1 (acute myeloid leukemia 1) oncogene	1.2	0.1	3.1	7.2	7.1	2.5	1.6	1.6	1.1	0.2	1.0	0.6	1.4	0.7	1.0	0.8	0.6	0.1	3.2789
208107_s_at	NM_030941.1	exonuclease NEF-sp	3.6	7.6	7.8	30.6	20.1	1.6	2.3	2.7	0.8	0.6	0.2	1.5	1.0	0.2	0.1	0.3	0.2	0.1	3.2356
212412_at	AV715767	DKFZp564A072	18.2	16.2	41.3	72.5	67.3	7.7	7.7	16.3	11.6	6.4	6.3	9.1	12.7	3.7	3.1	4.1	8.0	3.3	3.2017
215215_s_at	AC004381	chromosome 16 BAC clone	2.9	2.5	4.8	12.8	10.4	0.6	0.9	1.4	0.8	0.1	0.0	0.2	0.8	0.1	0.4	0.3	0.4	0.3	3.198
221509_at	AB014731.1	SMAP-3	7.6	5.4	13.2	48.5	32.4	5.2	5.7	18.1	10.7	3.5	3.8	11.4	8.1	2.8	5.6	6.0	4.1	7.5	8.0
218637_at	NM_018439.1	hypothetical protein IMPACT	1.3	2.4	2.5	10.7	9.3	1.5	1.5	2.7	2.1	0.6	0.7	0.6	0.6	1.2	0.8	0.7	0.9	1.1	3.1618
218357_at	NM_018191.1	hypothetical protein FLJ10716	0.8	0.5	4.9	13.7	8.7	2.3	1.7	3.4	3.9	1.0	2.0	2.8	3.6	0.8	2.3	2.0	1.7	2.2	3.1058
213035_at	A098184	KIAA0379	2.1	3.8	11.1	26.7	22.4	2.3	1.5	3.4	2.5	1.9	1.1	2.3	1.6	4.6	2.5	1.3	0.1	2.2	6.1
211160_x_at	D89788.1	ami 1 (acute myeloid leukemia 1) oncogene	1.5	0.2	3.1	9.4	7.5	2.0	2.5	1.7	1.7	1.0	1.4	0.3	1.1	0.4	0.6	1.1	0.7	0.2	3.0937
210731_s_at	AL136105	lectin, galactoside-binding, soluble, 8 gallectin 8	2.1	1.1	4.8	9.1	6.4	1.9	1.8	3.0	1.8	1.2	1.4	2.7	1.6	2.1	1.2	1.2	1.7	1.3	3.0876
203164_at	BE464756	acyl-Coenzyme A transporter	2.3	1.9	3.7	12.6	12.4	2.5	1.9	4.0	2.7	1.1	0.6	1.2	1.7	1.4	2.3	2.6	2.1	2.7	2.5
205768_s_at	NM_003645.1	long-chain 1 (FACVL1)	3.0	1.7	3.9	10.7	7.7	0.4	0.1	0.6	0.2	0.1	0.8	0.1	0.7	0.0	0.8	0.1	0.2	0.1	3.0353
210517_s_at	AB003476.1	A kinase (PRK) anchor protein (gravin) 12	25.1	4.9	44.0	69.5	59.6	1.5	0.4	0.6	0.8	0.1	0.2	1.0	3.0	0.9	0.8	0.5	0.1	0.2	3.0146
210647_x_at	AF102988.1	Ca ²⁺ -independent phospholipase A2 short isoform	2.3	1.1	18.7	13.2	9.1	3.4	3.3	4.0	4.5	3.3	5.0	4.2	3.6	1.8	3.5	4.4	1.8	2.8	2.2

Fig. 6B

C. Neutrophil (Ne)-selective transcripts (117).

Probe set	Accession #	Transcripts	MC	MC	Ba2	Ba3	Eo	Eo3	Eo4	Ne	Ne	Ne3	Ne4	p	CD4	CD8	CD14	CD19	Fb	NeS1
205403_at	NM_024633.1	Interleukin 1R, type II	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.2	0.4	0.1	0.2	0.0	0.0	12.86
216782_at	AK026679.1	FLJ22026.16	0.0	0.2	0.2	0.1	0.1	0.5	0.2	0.2	0.2	0.3	0.3	0.1	0.1	0.1	0.1	0.2	0.2	11.28
210119_at	U73191.1	KCNJ15 inward rectifier potassium channel Kir 1.3	0.7	1.1	0.1	0.1	0.1	0.9	0.6	0.6	0.6	1.29	0.88	0.7	0.2	0.0	0.8	0.0	0.0	107.47
209395_at	M80927.1	Chitinase 3-like 1 (cartilage glycoprotein-39)	1.5	0.2	0.9	0.1	0.1	8.1	0.1	0.1	28.9	70.7	40.7	0.1	0.0	0.1	0.1	0.1	0.0	79.595
203691_at	NM_002638.1	Protease inhibitor 3, skin-derived (SKALP)	0.2	0.1	0.1	0.1	0.8	0.5	0.2	0.4	0.1	16.9	36.7	2.7	0.1	0.1	0.1	0.1	0.5	51.901
211372_s_at	U64094.1	Interleukin 1R, type II	0.1	0.2	0.1	0.1	0.0	0.1	0.5	0.7	0.1	21.6	36.5	31.4	0.2	0.0	0.6	0.0	0.0	50.606
207008_at	NM_001557.1	CXCR2 Interleukin 8 receptor, beta	0.0	0.4	1.1	1.2	1.0	1.3	1.3	2.1	1.2	12.98	168.4	81.5	0.3	0.8	0.7	0.6	0.0	39.316
206515_at	NM_000896.1	Leucine B4-omega hydroxylase (CYP4F3)	0.3	0.1	1.1	0.7	1.2	0.5	0.8	5.9	1.7	56.8	40.3	57.2	0.2	0.9	0.0	0.7	0.3	34.919
204407_at	J04162.1	Fc gamma R1lb (CD16)	0.8	0.7	1.4	1.6	1.8	1.1	1.8	2.8	1.9	20.45	2.65	19.40	1.3	1.3	2.2	2.6	0.1	29.895
204470_at	NM_001511.1	Melanoma growth stimulating activity, alpha	1.2	0.0	0.7	0.9	0.1	0.6	0.5	1.2	0.7	19.1	23.0	26.3	0.1	0.2	1.0	0.1	0.2	28.189
206025_s_at	AW188198	Tumor necrosis factor, alpha-induced protein 6	0.1	0.3	0.1	0.6	0.4	0.6	0.1	0.2	0.1	19.0	29.9	17.2	0.1	0.2	0.8	0.3	0.6	26.336
209396_s_at	M80927.1	Chitinase 3-like 1 (cartilage glycoprotein-39)	1.8	0.2	1.6	0.4	0.5	0.8	0.5	5.6	0.9	37.9	32.2	52.8	1.4	0.0	0.0	0.1	0.4	25.669
211806_s_at	D87291.1	KCNJ15 inward rectifier potassium channel Kir 1.3	0.9	1.7	2.0	1.4	1.4	2.1	1.3	1.8	1.7	62.2	77.2	77.5	3.0	1.0	1.7	0.9	0.7	22.254
211920_s_at	B65776.1	Mitochondrial solute carrier, CACR1	0.4	0.8	6.9	0.0	0.2	2.4	1.5	2.2	1.5	59.0	43.2	57.4	2.5	0.7	0.3	1.8	1.1	20.163
207094_at	NM_000634.1	CXCR1 Interleukin 8 receptor, alpha	0.3	0.1	4.2	4.3	4.4	0.3	0.3	0.2	0.3	69.2	81.9	95.3	0.4	0.3	0.2	0.2	0.1	0.1
213589_s_at	AW468201	Z3614 mRNA sequence	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.2	0.1	5.5	2.7	5.1	0.1	0.1	0.2	0.1	0.0	18.973
218463_s_at	NM_015515.1	PAR2 protease activated receptor-2	0.0	0.0	0.1	0.5	0.3	0.1	1.1	2.8	2.8	2.0	46.3	32.5	31.3	0.3	0.3	0.1	0.1	0.1
213506_at	BE965369	PAR2 protease activated receptor-2	0.1	0.0	0.0	0.4	0.3	1.2	1.3	4.1	2.3	33.4	35.7	42.4	0.1	0.7	0.1	1.6	0.4	18.208
220187_at	NM_024636.1	FLJ23153	0.3	0.1	0.3	0.1	0.1	0.0	0.1	0.5	0.1	16.5	26.3	5.7	0.0	0.1	0.1	0.7	0.1	17.111
206026_s_at	NM_007151	Tumor necrosis factor, alpha-induced protein 6	0.1	0.8	0.4	0.8	0.6	1.1	0.5	0.9	0.1	18.2	23.3	20.0	0.6	1.0	1.1	1.1	1.0	17.051
41469_at	L10343	elafin	1.2	0.7	1.2	0.8	0.8	1.0	1.0	0.7	0.8	16.2	39.1	19.5	1.3	1.3	0.7	0.8	0.5	15.913
205568_at	NM_020880.2	aquaporin 9	0.5	0.9	0.1	0.1	0.1	0.3	0.1	1.0	0.1	133.3	136.7	168.0	0.4	0.9	0.1	8.6	0.1	15.805
210483_at	BC050483.1	deoxyreceptor 1, TRAILR3	0.1	0.1	0.4	0.9	0.7	1.0	0.9	1.3	1.2	25.8	23.2	9.7	0.2	0.4	0.3	0.2	0.1	13.337
215223_s_at	W46368	superoxide dismutase-2	4.4	1.9	1.7	4.9	8.7	5.8	3.3	6.0	8.3	12.46	15.31	14.24	1.0	1.6	1.1	7.3	2.2	13.008
210464_s_at	BC050483.1	deoxyreceptor 1, TRAILR3	0.9	0.9	0.9	0.2	0.1	2.2	4.8	0.8	0.6	60.1	86.3	4.7	0.5	0.6	0.4	0.9	0.4	12.748
205654_at	NM_000715.4	complement component 4-binding protein, alpha	0.5	1.1	1.3	0.7	0.7	1.5	1.0	7.3	1.4	2.1	20.7	43.6	1.2	0.3	1.3	1.2	0.9	12.161
210773_s_at	U81501.1	formyl peptide receptor 2	0.8	0.1	0.6	0.6	0.3	0.6	0.6	0.6	0.5	86.9	105.0	50.2	1.0	0.6	6.0	0.8	0.1	12.14
206222_at	NM_003841.1	deoxyreceptor 1, TRAILR3	1.5	0.8	1.9	0.7	0.7	3.6	13.7	3.4	3.9	121.0	137.1	37.5	0.0	0.1	1.8	0.5	0.7	12.034
202083_s_at	NM_003003.1	SEC14 (S. cerevisiae)-like 1	0.8	0.2	0.9	1.8	3.0	2.2	2.6	3.8	2.6	36.7	25.9	33.9	1.3	0.1	1.1	1.0	0.7	11.729
211163_s_at	AF012536.1	deoxyreceptor 1, TRAILR3	0.2	0.1	2.2	1.5	0.6	2.6	12.3	9.4	6.4	87.9	110.9	60.4	0.5	0.2	0.1	0.7	0.1	11.404
205931_s_at	NM_004904.1	cAMP response element-binding protein CREBpa	0.0	0.1	0.3	0.1	0.6	0.6	0.6	0.6	0.7	23.2	14.5	20.5	1.6	0.8	0.1	1.6	0.1	10.618
205972_at	NM_004665.1	veitin 2	0.1	0.0	1.2	2.6	3.9	1.0	0.2	1.9	0.3	11.45	11.46	17.41	0.1	1.4	4.0	1.38	1.7	0.0
210176_at	AL050262.1	Toll-like receptor 1	0.7	0.6	0.2	0.3	0.3	0.5	1.1	1.9	1.2	29.5	38.6	25.1	0.8	0.7	3.0	1.5	0.3	10.418
215977_x_at	X68285.1	glycerol kinase	1.9	0.9	0.8	0.7	1.0	0.3	0.6	0.9	1.0	15.8	19.8	9.7	0.2	0.2	0.2	0.2	0.3	10.203
215783_s_at	X14174.1	inver-type alkaline phosphatase	0.5	1.2	0.1	0.9	0.4	0.7	0.5	1.0	0.6	21.2	42.8	11.6	1.28	1.2	0.7	0.5	0.5	19.1067
217167_x_at	AJ252550	GK gene for glycerol kinase, exon 1	1.2	0.1	0.2	0.3	1.0	0.2	0.1	0.8	0.3	8.0	13.6	7.5	0.2	0.1	0.9	0.2	0.2	10.667
213349_at	AU934439	KUAA0779	0.9	0.7	0.9	1.4	1.0	1.9	1.4	2.3	2.1	15.6	15.3	19.5	0.1	1.4	1.5	1.6	1.2	9.7704

Fig. 6D

C. Neutrophil (Ne)-selective transcripts (2/77).

Probe set	Accession #	Transcripts	MC cond blood	MC Lung	Ba2 (small)	Ba3 (small)	EO 1 (small)	EO 2 (small)	EO3 (small)	EO4 (small)	NE 1 (small)	NE 2 (small)	NE3 (small)	NE4 (small)	pI	CD4	CD8	CD14	CD19	Fb	Ne.S1
210789_x_at	L00652.1	carcinoembryonic antigen (CEM1)	1.7	0.4	1.9	1.4	1.5	2.0	1.5	0.4	194	186	226	155	0.7	7.6	0.9	2.0	0.3	7.1	9.2/49
210772_at	M88107.1	formyl peptide receptor 2	0.1	0.2	0.4	0.7	0.7	0.3	0.8	0.7	51.4	67.7	44.8	46.4	0.5	0.5	0.5	5.6	0.1	0.1	9.2/61
218978_s_at	NM_018586.1	PRO1584	0.7	0.5	1.6	0.2	0.5	1.1	0.9	0.7	26.3	20.5	6.6	2.8	0.2	0.7	0.4	1.1	0.2	0.4	9.1/36
204006_s_at	NM_000570.1	Fc gamma R IIb (CD16)	0.7	0.2	1.2	0.7	0.6	0.7	0.8	0.0	230.7	278.8	47.6	45.9	4.2	1.9	6.9	12.0	3.9	0.1	9.0/79
207275_s_at	NM_001995.1	fatty acid-Coenzyme A ligase	4.3	2.6	5.1	11.5	19.4	5.3	5.1	3.7	95.8	127.8	92.8	69.1	0.7	1.0	1.1	8.3	0.9	1.7	8.9/65
203002_at	NM_005906.2	long-chain 1 (FACL1)	0.1	0.0	1.3	0.7	0.8	0.2	0.2	2.0	1.4	7.9	8.4	7.9	0.3	0.1	0.0	0.1	0.1	0.0	8.8/66
221803_s_at	A4883074	nuclear receptor binding factor-2	1.1	0.8	3.2	4.0	2.9	2.8	2.8	4.7	3.2	24.7	33.2	29.3	0.1	1.5	1.2	1.7	2.0	2.6	8.3/78
206765_at	AF153820.1	KCNJ2, inwardly-rectifying potassium channel Kir2.1	1.0	0.4	2.5	4.4	4.4	2.4	4.7	6.1	8.0	25.8	52.4	48.3	0.4	0.2	0.5	1.5	0.7	1.1	8.1/08
213351_s_at	A934469	K04A0779	0.0	0.1	0.9	2.0	1.6	0.8	0.6	2.3	2.7	7.9	20.1	20.1	0.2	0.5	0.2	0.1	0.2	1.2	7.9/05
214590_s_at	AL545760	ubiquitin-conjugating enzyme E2D1 leukotriene B4 omega hydroxylase (CY4FE3)	0.0	0.1	0.3	0.4	0.5	1.1	1.0	0.5	0.4	7.9	10.1	4.4	0.1	0.4	0.3	1.0	0.4	0.9	7.8/12
206572_at	NM_004668.1	Fc gamma receptor IIc2	0.0	0.0	0.8	1.8	1.0	3.0	5.4	11.7	9.4	46.0	56.9	43.0	0.1	0.0	0.0	0.6	0.6	0.1	7.5/73
210992_x_at	U90939.1	VNRS protein	1.9	1.0	1.7	2.1	3.3	8.1	16.1	2.8	4.2	70.9	95.6	42.8	0.3	0.2	0.1	7.2	2.3	0.2	7.5/29
20528_at	NM_018399.1	early development regulator 2	0.1	0.2	1.3	6.1	5.0	0.2	0.1	0.5	0.4	26.8	20.0	36.8	0.8	0.2	0.1	3.0	0.1	0.1	7.5/16
200919_at	NM_004427.1	glycero kinase	5.6	4.4	4.8	6.5	9.6	7.6	6.8	5.3	7.3	109.5	52.9	61.4	2.5	4.9	7.0	10.0	3.9	6.5	7.5/56
207387_s_at	X51757	heat shock protein HSP70B	2.1	1.5	1.0	1.5	1.6	1.1	1.4	1.6	1.4	14.3	10.7	10.3	0.9	0.6	0.3	1.7	0.6	0.6	7.4/63
117_at		glutathyl-peptide cyclotransferas	1.1	0.2	0.8	0.6	0.9	0.9	0.8	2.1	4.1	46.3	25.1	25.8	0.4	0.9	0.6	3.7	1.6	0.5	7.4/139
205174_s_at	NM_012413.2	triggering receptor expressed on myeloid cells 1	0.4	0.0	0.4	0.7	0.9	0.7	0.0	0.4	0.3	30.1	36.4	24.7	0.7	0.6	0.0	4.6	0.1	1.5	7.3/46
219434_at	NM_018643.1	thrombospondin 1	1.3	0.3	0.4	0.2	0.5	2.9	0.7	1.4	1.5	92.8	81.2	98.6	3.4	0.6	0.1	12.3	0.9	0.3	7.2/68
203887_s_at	NM_000361.1	orosomucoid 1 (ORM1)	1.7	0.1	0.4	0.4	0.1	0.2	1.0	1.4	1.1	16.8	13.4	1.3	0.7	0.6	0.4	1.1	0.4	0.2	7.1/28
205040_at	NM_000607.1	glycerol kinase	0.5	0.1	0.1	0.1	0.1	0.0	0.0	1.1	0.0	3.4	4.3	0.3	0.1	0.3	0.1	0.4	0.0	0.2	7.0/823
214681_at	A830490	FLJ20273	0.2	0.4	0.1	1.2	1.7	0.8	1.1	0.6	1.2	7.8	24.0	12.1	0.9	0.0	0.1	1.9	1.0	0.3	6.9/6
218095_s_at	NM_019027.1	GTPase regulator associated with the focal adhesion kinase pp125(FAK)	2.9	1.0	0.9	1.5	0.8	0.9	0.4	1.3	1.1	47.2	91.9	94.0	1.7	0.7	0.4	9.9	1.5	0.3	6.9/74
205068_s_at	B5671084	secretory leukocyte protease inhibitor (antileukoprotease) (SLPI)	1.2	1.4	3.5	5.9	5.1	6.5	5.1	8.5	7.1	43.7	45.2	56.0	0.7	1.3	2.9	5.1	0.8	1.2	6.8/94
203021_at	NM_003064.1	glycerol kinase pseudogene, chromosome 1	1.7	0.8	4.6	1.5	1.1	1.2	2.2	8.5	0.8	16.2	13.9	8.7	1.8	0.6	1.2	1.7	1.1	2.1	6.7/97
216316_x_at	X78713	carcinoembryonic antigen subdomains A and B	2.0	0.9	0.4	0.6	1.0	0.7	0.6	0.5	1.0	10.3	5.8	5.8	0.5	0.2	0.2	0.8	0.3	0.1	6.6/75
217209_at	X16454	FLJ21458	0.6	0.4	0.2	0.2	0.4	0.1	0.3	0.7	0.5	2.8	3.3	2.7	0.3	0.4	0.0	0.1	0.1	0.2	5.3/82
220421_at	NM_024850.1	putative lymphocyte G0G1 switch gene (GUS2)	0.3	0.6	0.1	0.1	0.3	0.8	0.4	0.4	0.3	8.9	9.1	7.0	1.2	0.6	0.0	0.1	0.1	0.2	6.4/87
213524_s_at	NM_015714.1	translocin-like enhancer of split 3	0.8	0.8	1.3	0.9	0.5	8.0	8.5	18.7	10.1	118.0	39.6	92.5	1.7	0.8	0.1	6.0	0.2	3.4	6.4/79
206472_s_at	NM_005078.1	KIAA1547	2.2	2.6	1.3	0.7	0.5	1.6	0.6	0.5	1.0	22.6	11.5	8.3	1.3	1.2	1.5	1.8	1.5	0.9	6.4/34
212769_at	AI567426	KIAA0329	1.4	1.5	0.5	1.3	2.3	1.1	1.0	2.2	1.9	17.9	15.1	12.8	2.4	0.8	1.1	1.3	1.2	0.5	6.4/271
204307_at	AB02295.1	granulocyte colony-stimulating factor receptor	0.7	0.0	0.1	2.6	2.1	1.8	1.5	2.4	2.0	10.3	15.4	12.8	1.9	0.1	0.5	0.2	0.1	0.5	6.3/478
203591_s_at	NM_000760.1	immunoglobulin superfamily member FMN78	0.1	0.0	1.0	0.1	0.2	2.3	0.6	2.4	1.0	220.3	134.9	112.1	0.2	0.8	0.2	25.5	0.1	0.2	6.2/51
210210_at	AF181660.1	FLJ11151	0.9	1.1	1.6	1.8	1.9	1.1	1.9	1.7	2.0	11.1	13.7	14.1	1.4	1.3	0.9	1.6	1.1	0.6	6.1/72
218610_s_at	NM_018340.1	Fc gamma receptor Ila (CD32)	1.5	1.2	1.2	1.2	1.8	3.3	3.2	2.6	1.8	25.2	17.9	21.8	0.5	0.6	0.4	3.6	0.4	0.6	6.1/12
203561_at	NM_021642.1	superoxide dismutase 2	4.7	1.2	0.9	1.2	2.4	1.9	2.8	19.4	21.4	104.3	153.0	123.9	4.0	0.7	0.7	16.3	2.2	0.2	6.1/15
216841_s_at	X15132.1		1.3	1.1	1.2	1.8	2.2	1.4	1.3	3.2	2.4	20.5	35.8	42.2	5.6	0.8	0.7	2.0	0.7	1.1	6.0/24

Fig. 6E

C. Neutrophil (Ne)-selective transcripts (3/7).

Probe set	Accession #	Transcripts	MC cond blood	MC lung	Ba 1 (small)	Ba 2 (small)	Ba 3 (small)	Eo 1	Eo 2	Eo 3 (small)	Eo 4 (small)	Ne 1	Ne 2	Ne 3 (small)	Ne 4 (small)	pl	CD4	CD8	CD14	CD19	Fb	Ne.SL	
207624_s_at	NM_000328.1	retinitis pigmentosa GTPase regulator (RPGR)	0.0	0.6	1.1	2.0	1.2	1.1	1.2	2.1	2.8	7.1	7.0	13.6	15.1	0.2	1.2	0.4	0.9	0.7	0.3	6.0348	
209850_s_at	BC005406.1	Cdc42 effector protein 2	0.2	0.2	1.3	0.2	1.0	0.2	0.4	0.5	0.4	1.32	0.6	6.7	8.7	0.2	0.2	0.2	0.6	0.4	1.6	5.9313	
203936_s_at	NM_004994.1	matrix metalloproteinase 9	4.7	0.6	1.6	1.9	1.4	1.2	2.4	13.5	1.5	36.5	35.1	36.8	21.9	1.7	2.0	1.4	1.9	1.3	1.4	5.9311	
215966_x_at	AA292874	glycerol kinase	1.2	0.2	0.6	0.1	1.2	0.2	1.0	1.2	1.2	6.6	10.2	7.3	7.4	0.2	0.1	0.2	1.3	0.5	0.0	5.9077	
206925_at	NM_005568.1	sialyltransferase 8	3.1	1.2	2.1	2.5	2.0	1.4	3.1	1.6	1.6	21.7	33.3	6.8	11.4	0.4	0.9	1.6	2.6	1.2	0.2	5.8688	
211764_s_at	BC005980.1	ubiquitin-conjugating enzyme E2D 1 (PITPN)	1.8	1.4	1.1	2.9	2.4	7.5	5.7	3.9	2.2	29.3	31.2	52.6	25.4	0.2	1.4	5.7	1.3	2.3	0.3	5.8143	
201192_s_at	NM_006224.1	placental taurine transporter	3.0	3.1	1.9	5.0	4.6	3.9	5.4	6.6	5.4	27.9	26.9	32.9	35.2	2.0	3.5	3.7	5.0	3.2	2.8	5.811	
205921_s_at	U16120.1	tubiquitin c-terminal hydrolase related polypeptide	1.2	0.7	0.5	0.2	0.4	0.3	1.6	0.5	0.9	14.8	17.2	2.8	2.6	0.0	0.1	0.3	1.1	0.3	0.4	5.7909	
209137_s_at	BC000263.1	carcinoembryonic antigen-related cell adhesion molecule 3 (CEACAM3)	3.6	4.1	2.0	2.6	1.9	1.5	0.9	2.7	0.9	25.0	24.5	37.6	29.7	3.5	5.0	2.5	3.5	2.7	3.0	5.7864	
208052_x_at	NM_001815.1	insulin-like growth factor 2 receptor FL10652	1.7	1.4	2.9	2.7	1.9	3.0	2.6	2.8	2.1	14.3	16.5	20.0	13.7	2.5	1.3	2.3	2.8	2.5	1.6	5.7572	
201393_s_at	NM_000876.1	SEC14 (S. cerevisiae)-like 1	6.4	2.8	0.2	0.8	1.8	4.1	5.4	6.8	5.4	82.4	105.9	80.1	71.7	1.7	2.9	8.7	8.4	4.8	14.8	5.7104	
218614_at	NM_018169.1	solute carrier family 22, member 4 (SLC22A4)	5.7	2.5	1.2	6.9	12.5	3.2	3.3	7.7	5.8	52.7	54.4	82.8	83.3	2.9	8.7	11.8	3.2	10.8	1.3	5.6442	
202084_s_at	NM_003003.1	MD-2 protein	1.2	1.0	0.9	1.3	1.2	2.0	1.8	3.5	2.9	13.0	12.9	13.5	17.9	1.9	4.1	3.5	11.5	7.7	11.8	5.6423	
32069_at	AB014515	CD10, membrane metallo-endopeptidase	2.8	1.5	2.1	3.6	5.5	4.6	3.7	5.9	6.9	23.9	20.9	35.1	40.5	1.0	3.4	3.3	2.6	2.1	1.5	5.6348	
205896_at	NM_003059.1	adiponectin	0.8	1.2	1.0	0.1	1.1	1.9	2.4	3.5	2.7	8.5	13.3	30.0	12.6	0.5	0.7	0.8	2.6	0.5	1.4	5.4612	
206560_at	NM_015364.1	MD-2 protein	7.4	1.1	2.0	3.9	1.8	1.0	0.4	0.6	0.5	43.9	62.3	87.8	56.0	1.3	3.5	1.0	1.1	3.5	9.4	5.4459	
202082_s_at	NM_003003.1	SEC14 (S. cerevisiae)-like 1	1.0	0.3	3.6	2.5	2.2	15.5	5.4	12.3	8.4	40.2	57.3	54.9	60.9	3.8	0.8	1.3	2.7	3.5	2.4	5.4472	
204308_s_at	NM_014844.1	KIAA0329	2.9	1.1	2.2	2.8	2.8	2.1	3.1	3.1	4.3	16.5	18.7	19.9	19.0	3.4	1.3	1.7	1.8	1.3	2.5	5.4369	
207500_at	NM_004347.1	caspase 5	0.3	1.1	0.1	0.0	0.1	0.1	0.3	0.2	0.5	4.2	6.2	4.6	2.9	0.3	0.3	0.4	0.8	0.1	0.3	5.379	
203435_s_at	NM_007287.7	metallo-endopeptidase	0.3	0.5	0.4	0.3	0.2	0.1	0.3	0.3	0.2	16.4	44.2	54.6	42.8	0.2	0.3	0.2	0.2	0.2	0.2	6.9	5.2591
205539_at	NM_006576.1	adiponectin	0.4	0.5	2.0	1.4	0.8	1.0	1.1	1.0	1.1	8.4	6.9	6.0	10.1	1.0	1.3	0.4	1.5	0.7	1.1	5.2541	
204601_at	NM_014664.1	KIAA0615	1.9	1.2	1.3	3.2	2.3	3.0	2.7	3.7	3.0	12.9	12.8	20.2	20.0	0.1	2.2	2.6	1.3	1.9	1.0	5.2381	
201963_at	NM_021122.2	fatty-acyl-Coenzyme A ligase, long-chain 1 (FACL1)	2.9	2.1	5.0	1.9	3.4	6.6	3.8	10.3	6.1	58.8	86.6	92.2	80.2	0.1	1.1	1.1	1.0	1.5	2.4	5.2374	
207064_s_at	NM_009590.1	CXCR1 interleukin 8 receptor, alpha	0.7	0.1	0.9	0.9	0.8	0.8	0.8	0.9	1.2	4.3	4.7	4.0	6.6	0.8	0.5	0.8	0.5	0.8	0.3	5.1905	
220005_at	NM_023914.1	P2YX purinergic receptor GPR86	0.6	0.0	0.1	0.5	0.1	19.7	9.6	25.1	17.3	76.5	77.1	100.7	98.6	1.9	0.1	0.2	12.3	0.6	0.0	5.1686	
211395_x_at	U90940.1	Fc gamma receptor IIc3	4.6	0.3	7.3	9.7	15.1	9.7	19.5	4.4	6.6	115.0	140.3	42.9	38.9	3.0	1.4	0.6	14.0	7.2	1.0	5.1401	
201780_s_at	NM_007282.1	ring finger protein 13 (RNF13)	4.4	2.8	3.5	9.2	6.6	6.8	6.2	8.9	7.1	27.1	36.6	52.5	35.7	0.8	4.1	3.7	7.2	7.2	4.6	5.1305	
208864_at	AB045118.1	GSK-3 binding protein FRAT2	2.8	1.3	4.4	9.2	8.0	13.4	16.9	27.3	22.6	95.2	97.2	100.6	104.2	1.3	1.9	2.9	10.2	2.5	1.0	5.1047	
218319_at	NM_020651.2	pellino (Drosophila) homolog 1 (PELL1)	3.4	2.9	5.9	17.5	33.5	17.7	11.7	12.6	15.1	64.9	88.3	73.0	80.2	2.4	6.3	2.9	13.8	12.6	1.1	5.0403	
206632_s_at	NM_004900.1	pherolin	0.6	1.1	1.0	1.2	1.6	1.3	0.8	3.9	0.5	19.5	11.1	30.8	0.5	1.5	0.2	0.4	0.4	1.0	1.2	5.0277	
220990_s_at	NM_030938.1	Dkk-Zps66133	11.7	6.2	4.6	18.5	12.5	5.0	3.5	8.2	4.9	115.5	117.2	125.3	122.5	2.6	5.3	4.2	24.1	4.4	8.3	4.9858	
221653_x_at	BC004395.1	apolipoprotein L	0.7	2.8	0.6	2.1	1.5	2.0	0.4	1.8	1.1	8.0	3.9	12.7	5.2	0.2	0.9	0.4	1.4	1.1	0.4	4.9332	
204748_at	NM_00963.1	synthase 2	6.5	16.2	0.6	2.4	2.0	4.5	2.3	3.4	3.4	35.8	44.1	44.6	91.8	0.4	0.6	0.2	4.3	0.3	0.5	4.9206	
210422_s_at	L3785.1	integral membrane protein	2.0	0.2	1.4	1.6	1.3	1.3	2.2	1.5	2.0	85.0	78.5	75.2	52.9	1.9	0.4	1.9	14.7	1.0	1.0	4.8845	
216429_at	NM_005242.2	PAR2 protease-activated receptor-2	0.8	0.8	0.9	1.2	0.9	0.9	1.1	0.5	0.8	11.8	15.1	4.1	4.1	1.3	1.5	0.2	1.5	0.3	0.7	4.8608	
213352_at	A934469	KIAA0779	0.6	0.9	1.2	1.5	1.2	1.2	1.1	1.2	2.2	8.4	6.0	8.7	7.7	7.6	0.9	1.5	1.0	1.0	0.8	4.6373	
201888_s_at	U81379.3	interleukin-13 receptor	0.1	0.6	0.3	0.2	0.0	1.7	2.7	1.7	2.0	8.6	19.0	15.0	13.9	0.4	0.4	0.4	0.3	2.9	1.3	4.746	

Fig. 6F

C. Neutrophil (Ne)-selective transcripts (4/7).

Probe set	Accession #	R	Transcripts	MC	CD95	Ba3	Eo	Eo	Eo3	Eo4	Ne	Ne	Ne3	Ne4	CD4	CD8	CD14	CD19	Fb	Ba.SI
204780_s_at	AA164751		CD95, Fas, APO-1	1.4	1.4	1.4	6.6	6.6	9.3	6.6	4.3	3.8	5.5	3.8	1.3	3.6	4.8	2.6	9.7	4.7254
209310_s_at	U225041		Ich-2 cysteine protease phosphatidylinositol glycan, class B (PIGB)	2.5	1.9	2.1	7.7	7.0	1.3	1.4	1.9	1.7	3.6	2.9	4.1	4.5	4.9	3.9	2.2	4.6817
205452_at	NM_004855.1		FLJ20950	2.3	2.7	2.3	6.4	7.7	3.0	3.0	1.6	1.7	2.2	1.7	2.0	2.9	2.8	3.5	2.2	4.6577
217396_s_at	NM_024932.1		swine vesicular disease virus chromosome 1 open reading frame	3.1	3.3	5.4	8.1	7.2	8.8	9.4	3.7	2.3	3.7	3.1	3.1	5.8	2.3	2.7	2.7	4.6558
221210_s_at	NM_030705.1		12 clone MGC12484	3.8	1.2	0.8	1.2	1.4	3.2	4.6	2.0	2.3	2.3	1.8	0.6	0.1	0.3	0.5	0.1	4.6378
221497_x_at	BC005369.1		ferritin, light polypeptide-like 1	3.0	2.4	4.3	5.7	5.9	3.3	5.4	2.9	3.2	2.4	1.5	1.4	1.3	2.9	2.9	1.9	4.6333
204668_at	AL031670		guanine nucleotide binding protein 10 (GNGL1)	0.8	0.5	1.8	1.0	1.2	0.3	0.9	0.8	0.8	0.7	0.5	1.8	1.0	1.0	0.5	0.1	4.614
201921_at	NM_004125.1		peroxisomal acyl-coenzyme A oxidase	7.1	5.4	2.6	6.7	6.5	11.7	15.3	4.5	8.7	8.1	0.8	2.7	3.0	8.4	3.2	12.4	4.5644
209600_s_at	S59189.1		formyl peptide receptor 1	2.9	1.7	2.8	5.3	4.7	1.4	1.3	1.5	1.7	2.1	0.4	1.0	0.8	2.1	0.7	1.5	4.5552
205119_s_at	NM_020292.1	GPR	pre-B-cell colony-enhancing factor	4.1	1.4	1.2	2.6	3.2	1.0	6.0	2.8	3.1	2.4	3.6	1.3	0.7	6.6	1.1	0.5	4.505
217738_at	BF575514		DKF Z0564M2422	5.7	0.9	7.4	2.4	3.9	7.5	3.9	7.3	8.0	8.9	2.2	1.7	1.6	10.1	1.7	2.3	4.4839
215078_at	AL050388.1		rumba (Drosophila) homolog	0.0	0.1	0.0	0.1	0.4	0.9	0.3	0.1	0.1	0.5	0.1	0.5	0.5	1.6	0.1	0.1	4.4943
207545_s_at	NM_003744.1		heat shock 70 kD protein 6 (HSP70B)	0.7	1.4	1.1	1.5	2.4	2.7	1.2	1.2	1.2	1.0	0.8	0.8	0.5	1.7	1.1	1.2	4.3728
213418_at	NM_002155.1		putative nuclear protein (LOC51307)	1.1	0.4	0.7	1.5	1.6	2.3	1.0	1.0	1.6	1.0	0.8	0.5	0.5	1.2	1.1	0.5	4.3655
218023_s_at	NM_016605.1		Shintaronexin 1	5.7	3.8	6.6	13.0	12.6	8.5	10.9	4.0	3.7	7.0	3.0	4.4	5.9	7.0	6.0	6.8	4.3383
210386_s_at	BC001490.1		CD120b, TNF- β p55	6.2	1.9	2.7	5.4	4.0	1.4	2.2	1.8	1.8	2.3	2.2	3.6	2.6	4.1	2.6	4.7	4.3318
207643_s_at	NM_001065.1		B-cell CLL/lymphoma 6 (BCL6)	7.8	1.6	0.9	1.3	1.4	6.3	7.4	8.5	8.1	11.5	1.3	2.2	5.9	17.4	0.6	16.0	4.2796
203140_at	NM_001706.1		ubiquitin 1	6.2	2.9	9.1	13.5	19.8	23.5	16.7	28.7	33.1	115.8	101.1	2.3	3.4	23.4	6.7	6.5	4.2767
207253_s_at	NM_016936.1		pre-B-cell leukemia transcription factor 2	3.2	2.8	2.9	4.4	5.0	3.8	3.6	1.6	2.0	1.4	2.3	2.5	2.5	2.2	2.4	1.8	4.2556
202875_s_at	BE39715		factor 2	2.0	1.4	0.1	0.1	0.2	2.5	1.5	1.6	1.5	6.8	0.8	1.7	1.9	1.1	1.3	0.7	4.2425
218791_s_at	NM_024713.1		FLJ22557	1.2	0.7	2.5	2.7	1.8	0.9	1.0	0.9	0.7	1.3	1.2	1.4	1.0	0.5	1.3	0.8	4.2114
211862_x_at	AF015451.1		Usurpin-beta	3.5	2.6	1.6	9.7	10.1	5.6	7.1	6.5	6.7	3.6	3.1	6.8	8.7	10.1	6.9	2.0	4.2001
217986_s_at	NM_013448.1		zinc finger domain adjacent to zinc finger domain, 1A	3.5	3.0	3.5	9.2	8.4	6.1	13.1	3.0	3.5	4.3	5.1	5.9	6.5	7.0	5.0	1.7	4.1976
217986_s_at	NM_022083.1		myb	4.1	1.9	6.4	7.4	9.0	24.2	11.8	5.1	10.5	7.6	8.0	3.3	3.8	3.2	2.0	8.2	4.1888
212602_at	AB06395		KIAA0993	2.3	3.5	0.4	0.9	1.1	0.8	0.8	1.7	1.8	1.2	1.9	0.5	0.3	3.6	0.8	2.8	4.1806
208485_x_at	NM_003879.1		CASP8 and FADD-like apoptosis regulator (FLAR)	3.2	2.5	1.9	9.8	9.9	6.2	8.3	7.0	6.9	3.8	4.1	6.4	8.4	11.5	6.6	2.0	4.1719
201942_s_at	D85390.1		gp 180-carboxypeptidase D-like enzyme	0.6	1.7	0.6	1.3	1.7	1.6	2.6	1.5	2.3	6.8	0.5	0.8	1.3	2.5	0.5	2.6	4.1525
220933_s_at	NM_024617.1		glycerol-3-phosphate dehydrogenase	2.1	2.0	9.6	14.2	14.0	7.1	12.5	3.8	3.7	8.1	1.9	3.1	4.8	6.2	3.8	3.0	4.1025
221764_at	AL574186		Toll-like receptor 6	6.3	4.4	16.5	18.6	15.0	10.4	22.7	8.0	9.2	4.6	6.3	8.9	9.4	5.7	9.4	2.5	4.0745
207446_at	NM_006068.1		chromosome 6 open reading frame 76	0.5	0.5	0.7	1.5	0.8	0.8	0.8	0.9	1.2	7.2	8.7	0.7	0.9	2.1	1.2	0.6	4.0697
219748_at	NM_024807.1			0.2	0.3	0.3	0.4	0.6	1.9	1.6	0.9	0.9	6.7	6.4	0.2	0.3	0.6	1.1	0.0	4.0619
220945_x_at	NM_018050.1		FLJ10298	1.0	1.4	0.5	0.7	0.7	1.1	1.0	0.8	1.3	1.6	1.1	0.5	0.3	0.9	0.6	2.6	4.057
211577_at	A48687.4		KIAA0650	1.9	1.3	6.4	8.0	9.9	10.1	9.4	7.4	9.8	4.2	4.4	10.8	9.5	7.5	16.0	3.7	4.0417
221732_at	AK026161.1		RIKEN cDNA 583042C20	2.8	0.7	3.4	10.5	8.8	5.0	16.9	2.6	3.1	3.0	3.4	0.3	0.4	1.8	1.6	4.6	4.041
205986_at	NM_004920.1		apoptosis-associated tyrosine kinase	1.6	1.3	0.7	1.0	0.5	0.3	1.4	1.0	1.0	1.3	3.2	1.0	0.5	3.4	0.9	0.4	4.0322
213501_at	TC2985		acyl-Coenzyme A oxidase 1, palmitoyl	1.3	1.1	2.0	2.6	2.8	1.3	0.6	8.5	11.5	12.4	0.1	1.1	0.3	1.8	0.5	1.1	4.0194
204542_at	NM_006456.1		sialyltransferase (ST6M)	0.4	0.2	1.5	0.3	0.2	3.4	3.2	1.3	1.3	2.1	0.7	0.7	0.3	1.4	0.3	0.6	4.016

Fig. 6G

C. Neutrophil (Ne)-selective transcripts (5/7).

Probe-set	Accession.#	Transcripts	MC	cord blood	MC	Ba1	Ba2	Ba3	Eo	Eo2	Eo3	Eo4	Ne	Ne2	Ne3	Ne4	CD4	CD8	CD14	CD19	Fb	Ne.51	
			lung	MC	Ba1	Ba2	Ba3	Eo	Eo2	Eo3	Eo4	Ne	Ne2	Ne3	Ne4	CD4	CD8	CD14	CD19	Fb	Ne.51		
			14	14	1.6	1.1	3.0	2.9	3.7	2.3	2.6	2.2	10.5	12.8	8.0	11.9	1.5	2.2	2.2	1.4	2.2	2.1	4.0148
204071_s_at	NM_005802.1	tumor protein p53-binding protein	1.2	0.5	0.6	1.5	1.2	0.1	0.4	0.8	0.8	1.9	15.3	13.9	7.1	10.9	0.5	0.2	0.6	1.0	0.7	2.8	3.9778
210594_x_at	AF239756.1	myelin protein zero-like 1	0.7	0.4	0.4	3.3	3.0	4.0	6.0	6.1	10.0	33.1	22.2	29.6	31.8	0.3	2.9	1.2	7.3	1.5	1.8	3.9764	
203063_at	NM_014634.1	protein phosphatase 1F (PP2C domain containing)	15	0.7	0.1	0.0	0.0	2.6	3.0	1.9	1.5	51.1	59.1	12.8	15.0	1.7	4.0	3.8	2.2	7.0	2.2	3.9602	
201943_s_at	BC031974	insulin-like growth factor 2 receptor	2.9	1.4	3.4	4.3	9.0	4.2	4.2	4.2	4.2	56.8	63.6	36.1	46.6	7.9	3.2	1.2	12.6	2.7	2.1	3.9562	
221477_s_at	BF575213	MGC55618																					
206756_at	NM_019886.1	carboxylate (N-acetylglucosamine 6-O)sulfontransferase 7	0.2	0.1	0.1	0.0	0.1	0.1	0.1	0.1	0.1	0.1	5.0	3.9	3.5	10.5	0.1	1.3	1.0	1.0	0.2	0.5	3.9516
204994_at	NM_002463.1	mixovirus (influenza) resistance 2 (MX2)	1.3	2.3	5.4	7.8	8.2	9.2	11.6	15.2	12.3	49.8	46.6	77.6	80.8	2.4	7.5	6.0	15.6	4.8	1.8	3.9478	
201943_s_at	NM_001304.2	carboxypeptidase D	0.9	0.9	0.5	2.1	3.6	1.7	7.6	7.2	4.6	16.4	21.3	18.7	15.2	0.7	7.0	1.7	3.3	0.4	3.8	3.8926	
216252_x_at	Z70519.1	CD95, Fas, APO-1	0.3	0.8	4.3	2.5	1.1	1.8	4.7	1.8	1.7	18.5	31.2	10.3	8.4	2.2	3.8	2.4	1.9	1.4	3.9	3.8691	
203066_at	NM_014863.1	B cell RAG associated protein (BRAG)	1.3	3.9	0.9	1.2	1.0	10.6	10.2	13.1	20.2	57.0	65.9	95.2	86.9	1.9	0.1	0.0	19.3	4.2	5.9	3.8667	
212479_s_at	AL050159.1	FLJ13910	1.7	1.6	2.1	2.5	2.6	2.4	2.5	3.5	1.7	9.0	10.1	8.8	9.8	1.1	2.3	2.4	2.2	1.9	0.9	3.8422	
209571_at	U03644.1	receptin	0.7	0.2	1.6	3.3	2.7	2.2	1.3	2.6	2.7	6.8	7.8	12.8	10.9	0.8	7.0	1.1	7.2	1.5	1.1	3.8367	
211317_s_at	AF041461.1	CASP8 and FADD-like apoptosis regulator	1.6	1.8	9.5	3.6	4.0	3.7	6.8	3.2	2.8	33.1	44.8	15.2	17.6	2.4	4.7	6.5	5.7	4.9	1.1	3.8332	
209732_at	BC005254.1	C-type (Calcium dependent, carbohydrate-recognition domain) lectin, sialin family member 2	8.1	5.9	10.0	18.6	23.6	9.0	10.0	8.9	7.3	72.9	77.0	99.7	75.5	4.1	14.4	21.2	10.2	16.4	1.3	3.8003	
201779_s_at	AF070558.1	clone 24450 RING zinc finger protein RZF	14.8	5.9	13.0	13.3	13.9	21.8	27.0	25.3	13.1	88.2	108.1	116.5	81.8	6.0	9.6	11.3	25.7	15.7	8.5	3.7993	
212441_at	D86985.2	KIAA0232	5.4	2.9	3.5	9.8	10.3	8.0	6.9	11.5	11.3	31.9	30.1	30.8	49.8	2.5	2.0	4.0	5.9	2.1	4.9	3.7668	
205920_at	NM_003043.1	solute carrier family 6, member 6 (SLC6A6)	1.2	1.4	0.9	0.2	0.2	1.1	5.2	0.7	1.4	33.1	26.7	2.7	4.0	0.3	0.1	0.4	2.6	0.1	0.5	3.7836	
213596_at	AL050391.1	DKFZ6586A181	0.7	0.7	2.3	3.6	3.0	1.2	1.2	1.1	1.2	10.6	10.9	12.5	9.9	2.2	1.1	2.0	1.5	0.7	0.3	3.7615	
209508_x_at	AF00574.1	caspase-like apoptosis regulatory protein (Carp)	1.7	2.7	10.8	7.6	11.5	4.9	6.3	6.0	8.4	37.0	34.8	34.7	40.8	2.7	4.0	5.1	6.3	3.4	1.3	3.7451	
218115_at	NM_018154.1	FLJ10694	0.9	2.2	2.4	1.5	0.9	1.8	2.1	1.3	1.1	10.5	9.1	6.7	7.7	1.1	1.2	2.2	2.1	1.7	1.5	3.7435	
215652_at	AK024382.1	FLJ14320	0.2	0.1	2.0	0.3	1.6	0.3	0.3	1.2	0.7	5.5	4.5	3.4	2.5	0.1	0.5	1.0	0.9	0.2	0.6	3.7149	
212561_at	AA349595	RAB6 interacting protein 1	10.0	6.1	10.2	12.4	11.4	18.7	14.9	12.1	10.0	66.3	60.0	47.6	37.1	4.0	8.7	9.9	13.9	5.9	10.2	3.6962	
204166_at	NM_014963.1	KIAA0963	3.6	0.4	1.1	0.0	0.1	1.0	1.3	0.1	0.8	11.8	12.5	4.0	2.9	0.3	0.9	1.7	1.7	7.2	0.2	3.6908	
221876_at	AB037451.1	KIAA1324	0.3	0.3	0.7	1.1	0.3	0.8	0.8	0.7	0.5	9.1	5.1	5.1	1.2	0.9	1.1	0.7	0.5	0.6	0.4	3.6808	
217207_s_at	AK025267.1	butyrophilin like receptor	1.2	1.1	1.4	2.1	1.7	1.2	1.9	0.6	2.4	10.9	3.4	7.2	6.1	1.5	1.7	1.6	0.9	1.5	1.3	3.6795	
212579_at	AA868754	KP4A0050	1.3	1.6	5.3	9.8	15.5	7.3	7.8	11.3	8.3	32.8	42.9	40.0	39.7	2.0	5.4	5.7	3.1	10.5	2.2	3.6784	
212657_s_at	AW083357	IL-1 receptor antagonist IL-1Ra (IL-1RN)	48.8	2.3	0.9	0.5	0.6	2.1	0.9	1.5	1.3	35.2	37.0	48.2	35.5	0.6	0.8	0.3	9.3	0.4	0.6	3.6759	
202397_s_at	NM_014338.1	phosphatidylserine decarboxylase arginase (ARG1)	3.4	2.7	6.2	11.7	6.8	3.4	4.7	5.4	4.7	32.8	31.0	22.0	32.3	0.8	1.6	1.4	4.2	1.4	1.2	3.6753	
206177_s_at	NM_000045.2	LPS-induced TNF-alpha factor (LPS-IND)	0.5	1.3	2.2	0.4	0.6	0.9	0.8	7.2	0.7	3.9	4.3	8.1	5.0	1.1	0.1	0.4	0.6	0.7	0.0	3.6722	
200706_s_at	NM_004862.1	FLJ13910	31.2	39.0	20.7	64.6	62.5	15.6	13.4	31.8	21.7	173.2	148.5	172.0	150.2	8.5	13.3	42.7	14.3	16.7	18.2	3.6696	
212478_at	AL050159.1	FLJ13910	0.1	0.1	0.2	2.3	3.5	1.4	0.8	1.5	1.0	3.7	3.0	4.8	6.5	0.1	0.3	1.1	0.6	0.4	0.5	3.6683	
218660_at	NM_003494.1	cystein	2.9	0.5	1.5	0.2	0.2	1.7	0.2	2.6	1.1	48.5	51.8	44.5	20.4	3.3	1.2	1.7	10.6	0.2	1.3	3.6616	
211982_x_at	AL546600	exportin 6	9.8	6.7	14.9	31.8	27.8	24.6	24.0	34.0	24.0	107.2	101.1	86.6	90.2	6.6	17.5	17.4	9.6	11.5	7.7	3.6408	
202748_at	NM_004120.2	guanylate binding protein 2, interferon-inducible (GBP2)	2.4	5.3	3.7	9.0	7.4	3.3	2.1	3.0	3.3	28.1	35.2	45.0	24.8	4.2	7.3	9.0	6.3	1.9	3.7	3.6111	
220086_at	NM_001736.1	Csa receptor	2.2	2.3	15.4	24.6	24.8	17.1	15.6	9.8	12.0	90.5	104.5	84.4	91.1	2.3	1.2	0.5	2.56	1.0	0.4	3.6036	
202890_at	U03644.1	microtubule-associated protein 7	0.9	0.1	0.7	1.4	1.1	0.1	0.0	0.2	0.1	2.5	3.1	3.2	7.1	0.0	0.1	0.4	0.1	0.1	0.0	3.6032	
220987_s_at	NM_003095.2	DKFZ1434037	1.4	0.3	3.9	4.9	4.7	9.6	9.3	14.1	11.7	43.0	35.6	57.8	57.6	5.3	4.7	4.8	11.1	13.3	2.0	3.5748	

Fig. 6H

C. Neutrophil (Ne)-selective transcripts (6/7).

Probe-set	Accession #	Transcripts	HC cond blood	MC lung	Ba 1 small	Ba 2 small	Ba 3 small	EO 1	EO 2	EO 3 small	EO4 small	Ne 1	Ne 2	Ne3 small	Ne4 small	pl	CD4	CD8	CD14	CD19	Pb	Ne.S1
207072_at	NM_008853.1	Interleukin 18 receptor accessory protein (IL18RAP)	59	09	22	34	41	72	16	28	17	134	97	209	56	24	28	31	04	16	03	35722
215719_x_at	X83493.1	CD95, Fas, APO-1	10	06	31	27	16	22	52	18	17	190	319	114	94	10	45	22	16	1.1	44	35657
218404_at	NM_013322.1	sorting nexin 10	49	1.2	26	50	37	07	07	21	07	285	318	348	338	03	1.2	19	90	65	03	3563
219394_at	NM_024419.1	phosphatidyglycerophosphate synthase (PGS1)	34	3.0	17	42	35	24	38	61	92	172	169	175	163	10	21	26	24	15	17	35544
216913_s_at	AK071460.1	KiRA0690	01	0.3	01	07	01	19	25	23	28	89	83	75	109	01	01	02	25	01	00	35402
205178_at	M60626.1	formylpeptide receptor 1	01	0.2	08	01	11	01	04	06	01	39	70	32	78	02	01	01	14	01	00	35295
210364_x_at	AF009619.1	PLA2G1F-related	14	1.5	53	66	70	43	42	59	35	212	303	184	196	21	29	40	46	30	18	35148
213607_x_at	BE551347	KiRA0134	13	1.3	29	20	17	87	158	08	43	427	425	111	153	06	13	19	62	17	09	3514
203888_at	NM_000361.1	thrombomodulin	09	0.6	01	01	03	02	04	08	43	427	425	111	153	06	13	19	62	17	09	3514
210233_at	AF167343.1	interleukin-1 receptor accessory protein (IL1RAP)	05	0.1	00	01	06	08	04	06	07	18	30	20	23	06	00	00	00	00	03	35023
204959_at	NM_002432.1	myeloid cell nuclear differentiation antigen	12	0.6	242	500	262	175	179	498	223	2498	2902	1860	2170	34	16	06	66.6	25	00	34903
217967_s_at	AF288391.1	riban	63	37	163	424	359	279	295	430	309	1074	1153	1179	1103	26	75	99	4.9	34	204	34897
221763_at	A1694023	thyroid hormone receptor-interactor 8 leukocyte immunoglobulin-like receptor subfamily A (with TM domain) member 2 (LILRA2)	08	1.5	19	46	55	55	69	99	90	283	329	340	427	17	37	41	5.1	9.8	30	34777
207857_at	NM_006866.1	solute carrier family 12 member 6 (SLC12A6)	04	0.5	36	85	53	45	49	16	63	335	343	462	508	18	00	01	11.6	05	01	34773
220740_s_at	NM_005135.1	pre-B-cell colony-enhancing factor	16	1.0	25	33	34	35	56	32	32	126	190	107	144	40	29	22	29	35	08	34722
217739_s_at	NM_005746.1	orosomucoid 1 (ORM1)	71	1.7	99	460	610	189	139	129	93	1124	1205	908	934	12	23	14	17.6	2.1	3.1	34242
205041_s_at	NM_000607.1	expartin 6	03	1.0	04	01	01	00	07	10	01	26	36	27	04	01	02	01	05	00	01	34189
214784_x_at	BE956299	homodomain adjacent to zinc finger domain, 1A	74	5.0	100	237	239	130	167	233	205	603	678	572	608	29	87	78	66	59	54	34155
217985_s_at	AA102574	KiRA0993	15	1.4	18	26	38	74	51	73	47	169	192	221	242	27	25	23	35	24	09	33999
212598_at	A1806395	FLJ20847	07	0.7	01	01	01	01	07	01	01	55	73	31	32	02	01	00	10	01	13	33933
219053_s_at	NM_017966.1	PAC clone RP3-515N1	26	2.0	19	23	23	26	21	30	28	113	76	222	341	16	05	09	47	13	29	35686
217475_s_at	AC002073	Ca2+-dependent endoplasmic reticulum nucleoside diphosphatase	06	0.5	06	02	04	13	13	05	12	59	98	16	14	07	03	01	05	07	02	33448
46323_at	AI120741	KiRA0625	44	32	42	83	72	53	67	114	79	200	215	339	263	25	28	36	43	34	50	33028
201965_s_at	NM_015046.1	IL1M-like growth factor 1 receptor	27	3.1	35	85	83	49	58	74	75	195	165	187	278	22	39	34	46	56	26	35019
203628_at	NM_000875.2	IL1M domain kinase 2 (LIMK2)	05	0.1	37	30	40	68	49	27	58	188	234	68	206	16	01	28	24	20	35	32989
202193_at	NM_005569.2	transcript variant 2a	18	1.5	19	56	56	64	48	113	89	170	205	365	282	01	1.3	1.1	0.6	05	08	32887
203042_at	NM_002294.1	lysosomal-associated membrane protein 2 (LAMP2)	24	3.1	11	17	13	59	64	124	107	213	270	441	354	08	06	05	32	08	94	3282
220326_s_at	NM_018071.1	FLJ10337	51	4.5	19	12	19	63	89	52	85	253	261	192	210	09	01	07	64	01	41	32759
212470_at	AB011088.1	sperm associated antigen 9 clone 6 immunoglobulin-like transcript 5	40	2.9	33	63	72	45	40	47	49	132	170	181	240	12	25	22	3.9	3.0	54	32688
211133_x_at	AF009643.1	DNAZ434C0328	19	1.4	08	15	13	31	27	38	21	421	422	270	251	27	09	05	10.2	04	02	32526
219313_at	NM_017577.1	G protein-coupled receptor GRP77	00	0.8	02	00	04	02	01	01	00	38	37	31	56	02	01	01	00	12	01	32404
221149_at	NM_018485.1	5,10-methylenetetrahydrofolate synthetase	02	0.1	08	07	12	07	09	09	06	33	32	42	29	00	03	02	1.0	01	03	32282
203433_at	NM_006441.1	FADD-like apoptosis regulator	14	1.8	15	25	16	31	42	35	31	158	114	96	90	16	18	19	29	17	15	32181
214486_x_at	AF041459.1	FADD-like apoptosis regulator	19	2.1	107	50	65	42	53	43	60	263	162	253	242	24	37	50	5.3	2.9	23	32114

Fig. 61

C. Neutrophil (Ne)-selective transcripts (7/7).

Probe set	Accession #	Transcripts	MC cord blood	MC lung	Ba1 (small)	Ba2 (small)	Ba3 (small)	Eo1	Eo2	Eo3 (small)	Eo4 (small)	Ne1	Ne2	Ne3 (small)	Ne4 (small)	pl	CD4	CD8	CD14	CD19	Fb	Ba.S1	
209222_s_at	BC000795.1	oxysterol binding protein-like 2	1.3	0.2	2.7	8.8	8.0	5.4	5.4	7.7	7.3	17.2	18.4	22.3	23.9	0.9	2.3	3.4	2.8	2.5	4.9	4.6	3.1877
202334_s_at	A487765	ubiquitin-conjugating enzyme E2B	3.3	3.4	4.8	15.5	12.1	5.3	7.2	14.7	12.8	20.9	25.6	43.6	38.1	4.0	4.5	3.9	2.5	2.5	2.8	4.9	3.1871
203266_s_at	NM_003010.1	mitogen-activated protein kinase kinase 4	3.7	2.4	4.9	8.2	6.3	5.5	4.8	6.8	5.0	14.7	15.2	27.4	26.9	2.8	2.4	2.6	2.7	2.3	2.7	3.1804	
58780_s_at	R42449	FLJ10557	4.5	5.4	1.5	3.9	3.0	7.8	9.6	12.8	16.4	28.0	27.6	46.7	44.1	1.2	0.6	0.1	6.5	0.2	5.7	3.1803	
210582_s_at	AL117466.1	LIM domain kinase 2	3.8	1.9	4.3	5.1	4.8	8.7	10.3	10.8	9.4	33.9	36.5	30.8	23.8	1.3	1.7	1.8	1.9	0.9	1.4	3.1609	
214766_s_at	AL080144.1	ELKS transcription factor-like protein TIMPS6Z	1.3	0.2	2.0	3.1	4.2	1.9	1.4	2.1	2.4	9.4	9.5	9.9	11.3	3.2	1.3	0.8	0.5	1.0	1.3	3.1414	
202266_at	NM_016614.1	TRAF and TNF receptor-associated protein (AD022)	9.8	6.2	9.4	23.7	20.9	8.6	9.9	16.5	14.0	36.1	56.5	64.5	57.5	4.5	7.7	9.4	5.3	8.2	6.3	3.1402	
203278_s_at	NM_016621.1	BRAF35/HDAC2 complex (80 kDa) transmembrane	2.1	2.8	2.7	14.8	11.0	5.7	5.0	7.4	4.9	21.0	16.6	31.0	30.6	0.1	3.0	4.5	3.1	2.7	3.0	3.1382	
207291_at	NM_024081.1	gamma-carboxyl glutamic acid protein 4	0.1	1.2	1.3	1.4	1.1	0.9	0.2	0.4	0.2	3.8	7.9	4.5	8.5	0.2	0.8	0.1	1.9	1.1	0.4	3.1336	
213229_at	BF590131	Dicer1, Dcr-1 homolog (Drosophila)	8.5	4.5	19.5	12.9	15.4	15.9	6.7	19.1	16.0	35.2	39.0	61.4	69.4	6.2	5.9	7.3	15.2	12.2	5.0	3.1306	
204204_at	NM_001860.1	soluble carrier family 31	1.7	1.7	1.3	0.3	0.8	1.7	0.9	2.3	1.2	22.6	23.8	31.3	36.0	2.0	1.2	1.2	8.9	0.2	0.4	3.1262	
201364_s_at	AF242521.1	ornithine decarboxylase antizyme clone 17.6 immunoglobulin-like transcript	8.3	7.3	4.4	2.2	1.9	1.5	21.9	8.0	7.7	61.9	59.1	21.0	27.7	2.2	5.1	6.3	12.2	6.2	9.6	3.1253	
210784_x_at	AF009634.1	v-yes-1 Yamauchi-sarcoma viral related oncogene homolog (LYN)	1.4	0.1	2.1	1.2	2.4	2.5	2.2	2.8	2.1	52.1	48.8	31.8	36.3	0.8	0.2	0.2	13.3	0.3	0.2	3.1236	
202625_at	A135641.2	hypothetical protein MGC76706	6.9	6.9	5.0	18.2	14.9	20.7	21.7	27.7	28.6	74.7	76.3	77.5	75.7	7.5	1.7	0.9	17.1	23.6	0.5	3.1131	
221895_at	AW469184	major histocompatibility complex, class I, B	2.2	0.5	5.4	5.2	5.8	5.2	3.4	7.6	5.1	14.8	12.0	24.6	19.2	2.0	2.4	2.1	5.2	1.5	1.6	3.111	
37384_at	D13640	retinitis pigmentosa GTPase regulator 1	2.5	3.0	3.4	3.8	3.8	6.7	6.6	7.6	6.6	25.2	17.9	21.3	29.4	2.6	2.5	2.5	7.4	1.8	2.8	3.0885	
205608_s_at	NM_020366.1	retinitis pigmentosa GTPase regulator 1	1.1	1.4	1.2	0.8	1.0	1.1	1.0	0.5	1.4	6.1	3.4	5.3	4.7	1.5	0.9	0.8	1.3	0.5	0.7	3.091	
204694_at	NM_003364.1	cell-surface receptor 2	1.8	0.1	2.1	8.2	7.8	2.8	0.4	0.8	1.4	5.9	88.0	94.4	99.8	1.2	1.3	1.3	26.3	0.9	0.4	3.0899	
204761_s_at	NM_000048.1	CD25, low affinity PO-1	7.0	1.1	5.0	11.0	8.9	5.4	4.4	6.8	7.0	20.6	27.1	27.0	29.8	0.3	5.2	3.3	4.0	2.0	3.8	3.0877	
212616_at	A1806395	KLAF1993	3.0	2.0	0.0	0.7	0.6	0.7	0.0	0.7	0.1	18.0	14.3	25.0	24.9	0.1	0.2	0.2	6.9	0.0	3.4	3.0797	
213116_x_at	AF009515.1	FLAME-1	3.1	2.9	2.9	1.4	31.9	11.6	11.9	20.8	15.1	58.8	74.1	72.9	81.9	4.1	0.6	0.7	10.3	5.5	2.6	3.0752	
203045_at	NM_004148.1	ninjulin 1	4.4	2.5	3.2	6.4	4.8	10.7	9.7	18.5	12.1	29.3	94.1	44.7	46.1	0.5	1.2	1.7	8.5	0.2	2.9	3.0746	
204949_at	NM_002162.2	intercellular adhesion molecule 3 (ICAM3)	3.0	3.7	5.7	4.63	34.5	38.9	51.6	94.5	93.7	161.1	168.3	239.1	241.1	4.5	13.6	21.0	17.6	19.9	1.3	3.0617	
206208_at	NM_000717.2	carboxymethyltransferase metallophosphoesterase	0.2	0.6	0.1	0.1	0.1	1.1	0.7	1.0	0.8	5.6	5.2	2.8	2.4	1.2	0.1	0.1	0.1	0.1	0.1	3.0572	
213727_x_at	A1743654	v-yes-1 Yamauchi sarcoma viral immunoglobulin superfamily, member 5 (GSF6)	2.1	1.7	3.0	15.0	12.1	8.9	13.7	25.4	23.9	49.9	28.3	59.9	75.8	0.7	4.5	6.6	5.7	5.4	3.7	3.0554	
202626_s_at	NM_002350.1	immunoglobulin superfamily, protein kinase C and casein kinase substrate in neurons 2 (PACSIN2)	15.5	9.5	12.1	12.7	14.8	32.6	31.6	54.0	41.0	110.1	115.1	122.7	127.2	18.4	2.1	1.5	36.8	33.0	0.6	3.0541	
206420_at	NM_005849.1	protein kinase C and casein kinase substrate in neurons 2 (PACSIN2)	1.1	0.3	0.2	0.4	0.7	1.9	1.2	1.1	1.0	17.5	24.2	30.6	33.3	1.4	0.4	0.4	8.4	0.3	0.3	3.0442	
201651_s_at	NM_007229.1	zinc finger protein 267	21.4	17.4	4.6	24.8	20.1	13.3	19.5	33.9	35.3	61.3	72.5	76.1	94.4	24.7	4.9	4.4	8.6	6.1	8.0	3.0391	
219540_at	AU150728	v-rfl-1 murine leukemia viral oncogene homolog 1 (RAF1)	2.0	1.0	1.3	3.7	3.6	2.0	1.5	4.4	3.7	6.7	6.9	9.2	9.9	1.0	2.1	1.3	1.0	1.6	0.1	3.0361	
201244_s_at	NM_002880.1	mitogen-activated protein kinase kinase 4	6.0	5.4	12.4	32.8	33.1	14.9	19.0	27.3	25.7	60.4	58.2	89.2	86.2	2.2	6.6	11.3	12.8	7.6	7.3	3.0329	
203265_s_at	A4810268	JAR receptor-like protein-tyrosine phosphatase	1.4	1.2	2.8	6.4	4.5	1.7	2.6	3.5	3.1	12.8	12.8	10.4	16.8	1.4	1.4	1.3	1.3	2.5	1.5	3.028	
203030_s_at	AF007555.1	zinc finger protein 217	0.0	0.0	1.6	1.2	8.4	0.1	0.1	0.1	0.1	0.1	3.0	1.1	2.8	0.1	0.1	0.9	0.1	0.9	0.0	3.0269	
203739_at	NM_006526.1	interferon-induced protein with tetrapeptide repeats 4 (IFIT4)	1.9	2.8	3.0	18.4	8.4	7.6	8.0	14.7	14.9	37.3	45.1	24.4	27.0	1.2	4.6	5.3	6.1	5.5	3.6	3.0158	
204747_at	NM_001549.1	carbonic anhydrase IV (CA4)	2.0	3.0	4.9	6.0	3.5	4.3	12.4	4.4	3.0	24.2	27.0	15.4	12.0	0.3	1.0	1.5	6.2	1.4	2.6	3.0143	
206209_s_at	NM_000717.2	carbonic anhydrase IV (CA4)	0.7	1.0	0.8	0.6	0.6	2.2	2.1	1.5	2.1	13.8	7.4	4.7	3.5	2.1	1.0	0.5	0.9	1.0	0.5	3.0112	

Fig. 6J

D. Mast cell (MC)-selective transcripts (1/2).

Probe set	Accession #	Transcripts	MC cond blood	MC	Ba2 (small)	Ba3 (small)	EO 1 (small)	EO 2 (small)	EO3 (small)	EO4 (small)	Ne 1 (small)	Ne 2 (small)	Ne3 (small)	Ne4 (small)	CD4	CD8	CD14	CD19	Fb	MCSL	
217023_x_at	AF059143	tryptase beta	1694	187	1.1	0.4	0.1	0.1	0.5	0.1	0.2	0.1	0.6	0.4	0.7	0.1	0.2	0.1	0.2	202148	
215382_x_at	AF206666.1	tryptase beta	1681	1084	1.7	0.7	0.4	0.2	0.2	0.2	0.1	0.3	0.1	0.1	0.7	0.1	0.1	0.1	0.1	172668	
204041_at	NM_000898.1	monoamine oxidase B	235	469	0.2	0.7	0.1	0.2	0.6	0.3	0.3	0.1	0.2	0.1	0.2	0.1	0.2	0.2	0.1	136311	
210094_x_at	AF206665.1	tryptase alpha	1311	923	0.7	1.2	1.2	0.2	0.1	0.1	0.1	0.1	0.1	0.1	0.6	0.1	0.0	0.1	0.1	112376	
216474_x_at	AF206667.1	tryptase beta	2100	1209	2.4	2.0	1.4	1.2	0.4	0.2	0.1	0.2	1.1	0.1	1.8	0.8	0.9	0.1	0.1	843375	
205683_x_at	NM_003294.2	tryptase beta	1955	953	2.4	2.7	0.3	0.2	0.2	0.6	0.6	0.4	0.1	0.4	1.0	2.0	0.7	0.2	0.3	672617	
207741_x_at	NM_003293.2	tryptase alpha	1750	997	2.2	2.2	1.8	0.5	0.2	0.3	0.2	0.6	0.2	0.3	0.3	2.2	0.7	0.1	0.5	591015	
207134_x_at	NM_024164.2	tryptase beta	2146	1123	3.1	3.8	1.7	1.2	0.3	0.8	0.6	0.3	0.8	0.4	0.1	0.5	0.2	1.1	0.4	571834	
205653_at	NM_001911.1	cathexin G	912	570	2.7	1.1	0.9	0.9	0.4	3.1	0.8	0.3	1.4	1.6	0.6	0.7	0.2	0.4	1.3	0.3	514749
205766_at	NM_007309.2	leukemia inhibitory factor	170	98	0.2	0.2	0.3	0.1	0.2	0.2	0.2	0.1	0.2	0.4	0.7	0.1	0.2	0.1	0.1	443659	
210324_at	M17265.1	complement protein C8 gamma	29	69	0.1	0.1	0.0	0.0	0.0	0.1	0.1	0.3	0.1	0.1	0.1	0.1	0.0	0.0	0.0	33306	
211743_s_at	BC005929.1	major basic protein	743	707	1.0	4.7	2.7	0.1	0.7	0.8	0.6	0.2	0.3	0.7	0.2	0.1	0.2	0.2	0.3	315959	
206726_at	L63296.1	15-hydroxyprostaglandin	483	483	2.1	7.5	1.4	1.5	1.3	0.8	0.9	0.1	0.1	0.2	0.1	1.1	0.5	0.8	0.5	248454	
211549_s_at	NM_014485.1	prostaglandin D2 synthase	1190	940	5.0	2.8	5.7	0.7	0.1	1.0	0.5	0.2	0.2	0.2	0.6	1.3	0.7	0.3	1.2	17432	
205011_at	NM_014622.1	loss of heterozygosity, 11,	761	709	3.0	6.8	4.5	2.3	1.0	1.4	1.9	0.2	1.1	1.2	1.8	2.9	2.2	1.3	1.7	2026	
205408_s_at	NM_001740.2	chromosomal region 2, gene A	167	634	1.3	0.7	0.9	0.4	1.6	0.7	1.3	1.8	1.6	3.6	1.5	1.7	0.2	1.1	1.3	0.6	
219255_at	NM_024554.1	calbindin 2	100	92	0.7	0.1	0.1	0.2	0.1	0.6	0.6	0.1	0.6	0.1	0.2	0.1	0.6	0.1	0.6	161631	
204468_s_at	NM_005424.1	tyrosine kinase with immunoglobulin and epidermal growth factor homology domains	36	28	0.5	0.3	0.1	0.0	0.1	0.2	0.0	0.0	0.0	0.1	0.1	0.0	0.0	0.0	0.1	0.0	
208343_s_at	AF146343.1	CYP7A promoter binding factor	15	09	0.0	0.0	0.3	0.1	0.0	0.1	0.0	0.1	0.0	0.2	0.4	0.1	0.0	0.0	0.0	144259	
205051_s_at	NM_000222.1	CD117 c-KIT	921	858	6.2	8.1	7.3	2.3	5.2	6.5	2.7	0.7	2.1	0.8	1.1	0.8	0.2	0.5	0.1	138025	
210102_at	BC001234.1	loss of heterozygosity, 11,	409	411	2.8	3.7	4.5	0.3	0.4	0.3	0.6	0.7	0.9	0.2	0.6	1.8	0.8	0.7	1.2	113619	
210796_x_at	D86359.1	chromosomal region 2, gene A	178	260	1.5	1.0	1.1	1.2	1.5	1.3	1.4	1.4	2.3	1.7	1.3	2.0	1.4	1.5	1.8	105998	
206519_x_at	D86358.1	sigma acid binding b-like tectin, sigtec6	34	79	0.0	0.3	0.4	0.0	0.0	0.0	0.1	0.0	0.1	0.5	0.2	0.5	0.0	0.0	0.0	10.13	
206480_at	NM_000897.1	leukotiene C4 synthase	88	160	0.3	0.2	0.6	2.4	1.6	0.5	0.1	0.2	1.1	0.1	0.1	1.3	0.1	0.3	0.1	927381	
206517_s_at	NM_002910.4	retin-binding protein	106	62	1.2	0.1	0.4	2.8	1.6	0.5	0.1	0.6	2.1	0.1	0.1	0.9	0.2	0.7	0.3	918529	
208089_s_at	NM_030794.1	tudor domain containing 3	60	134	0.8	0.6	0.2	0.5	0.7	0.5	0.5	0.1	0.6	0.3	0.0	0.7	0.7	1.1	0.8	816897	
205466_s_at	NM_005114.1	heparan sulfate 3-D-sulfotransferase ADAMTS3 a disintegrin-like and metalloprotease (reprolysin type) with thrombospondin type 1 motif, 3	181	72	0.7	0.4	0.1	0.7	0.1	0.3	0.2	0.4	0.1	0.8	0.4	0.1	0.0	0.0	0.2	1400	
214913_at	AB002364.1	metalloprotease (reprolysin type) with thrombospondin type 1 motif, 3	68	43	0.5	0.7	0.8	0.5	0.7	0.6	0.4	0.5	0.4	0.7	1.2	0.7	0.6	0.5	0.4	72214	
201860_s_at	NM_000930.1	tissue-plasminogen activator	222	297	0.2	0.4	0.1	0.1	0.3	0.5	0.5	0.1	0.1	1.3	0.4	1.6	0.1	0.2	0.6	710135	
206520_x_at	NM_001245.1	sigma acid binding b-like tectin, sigtec6	190	227	2.4	1.1	0.8	1.1	1.5	1.3	1.0	2.0	2.0	0.4	1.4	2.9	2.1	2.3	1.9	710132	
220532_s_at	NM_014020.1	L88 protein	524	182	0.8	0.8	1.0	6.4	2.9	1.5	1.2	0.4	0.3	1.4	0.6	2.2	0.6	0.2	5.0	0.1	
218169_at	NM_018052.1	FLJ10305	62	146	0.3	0.2	0.4	0.4	0.3	0.3	0.4	0.6	0.5	0.1	0.1	0.5	0.2	1.4	1.6	604597	
211728_x_at	AK025198.1	nuclear receptor subfamily 1, group 1, member 3	56	55	0.6	0.9	1.0	0.4	3.6	0.9	0.8	0.7	0.6	1.4	0.9	0.9	0.8	0.7	0.7	0.8	
214028_x_at	AU15698	tudor domain containing 3	32	119	0.9	0.0	0.4	0.8	0.3	0.4	0.7	0.6	0.6	0.1	0.1	0.8	1.2	1.1	0.1	5.70228	
221552_at	BC001698.1	lipase	106	34	0.9	1.8	1.1	0.9	1.1	1.0	0.9	0.2	0.2	0.7	0.1	0.1	0.2	0.7	0.9	5.10738	
203367_at	NM_007026.1	MMP-1 like protein lysozyme phosphatase (MMP-L)	150	454	1.2	0.9	0.8	0.9	0.9	0.8	0.1	0.2	0.7	0.4	2.0	0.9	1.0	2.7	0.5	1.4	
206997_s_at	NM_004807.1	heparan sulfate 6-O-sulfotransferase	42	38	0.2	0.1	0.1	0.4	0.4	0.1	0.3	0.3	0.4	0.3	0.7	0.3	0.2	0.6	0.3	4.81127	

Fig. 6K

D. Mast cell (MC)-selective transcripts (2/2).

Probe set	Accession #	Transcripts	MC																			
			cord blood	lung	MC	Ba1	Ba2	Ba3	Eo	Ba3	Eo	Eo3	Eo4	Ne	Ne3	Ne4	CD14	CD19	Fb	MCS.L		
207480_s_at	NM_020149.1	TALE homeobox protein Meis2e	14.0	14.9	1.9	3.6	4.0	1.7	1.9	5.3	3.8	0.3	0.6	1.0	0.3	0.5	0.8	0.4	0.6	0.4	0.8	4.72642
45288_at	AA209239	lipase	10.9	3.0	0.2	2.1	0.8	0.5	0.5	1.3	0.9	0.1	0.1	0.2	0.1	0.4	0.5	1.3	1.0	0.9	0.9	4.52869
207093_at	NM_000077.1	cyclin-dependent kinase inhibitor 2A (melanoma, p16, inhibits CDK4)	7.5	3.6	0.7	0.7	0.1	0.6	0.4	0.3	0.5	0.1	1.2	0.6	1.1	0.1	0.9	0.5	0.8	0.1	1.2	4.35629
201650_at	NM_002276.1	keratin 19	6.2	12.0	0.0	0.0	0.3	0.1	0.0	0.0	0.0	0.1	0.1	0.1	0.1	0.1	0.0	0.1	0.1	0.0	2.0	4.35547
214533_at	NM_001836.1	chymase	10.1	2.7	0.4	0.2	0.8	0.1	0.1	0.8	0.6	0.1	0.1	0.2	0.2	1.2	0.7	0.5	1.0	0.4	0.3	4.27984
218211_s_at	NM_024101.1	melanophilin	24.8	29.6	2.7	2.5	1.8	3.0	2.5	1.9	2.2	4.6	4.1	3.3	4.1	6.4	4.0	3.2	2.4	3.4	2.7	4.24499
203916_at	NM_003635.1	N-acetylcysteine-S-lyltransferase	17.9	26.7	3.2	6.5	6.8	2.5	2.7	3.6	3.1	4.2	3.4	5.5	5.2	0.9	3.1	4.9	3.3	2.7	2.4	4.20693
212336_at	AB002336.1	erythrocyte membrane protein band 4.1-like 1	3.8	6.4	0.1	0.2	0.1	0.5	0.1	0.2	0.4	0.1	0.1	0.1	0.5	0.1	0.4	0.2	0.4	0.4	1.2	4.12758
200766_at	NM_001909.1	cathepsin D	42.6	39.5	2.5	5.3	4.3	4.3	4.8	3.4	2.7	4.0	6.7	3.1	1.9	2.6	1.6	2.5	10.0	1.6	5.9	4.1037
202218_s_at	NM_004265.1	delta-6 fatty acid desaturase (FADS6)	18.8	24.5	0.4	0.2	1.0	0.3	0.1	0.8	0.5	0.2	0.1	0.1	0.1	1.6	0.1	0.6	0.1	0.6	0.5	4.08548
204066_s_at	NM_014914.1	centaurin, gamma 2	5.3	7.9	0.4	0.4	0.7	0.2	0.2	0.6	0.6	0.3	0.5	0.4	0.4	0.8	0.6	1.6	0.6	1.0	1.6	4.06712
209644_x_at	U38945.1	cyclin-dependent kinase inhibitor 2A (melanoma, p16, inhibits CDK4)	14.0	6.4	1.0	1.4	0.7	1.2	1.3	1.7	1.5	1.0	1.6	1.5	2.1	2.3	1.8	1.5	0.9	0.3	2.4	3.88459
221679_s_at	AF225418.1	lipase	2.8	1.9	0.4	0.9	0.1	0.3	0.4	0.4	0.1	0.1	0.5	0.0	0.5	0.5	0.1	0.6	0.6	0.5	0.2	3.83039
211538_s_at	U56725.1	heat shock protein 70kD	4.4	7.4	0.3	0.6	0.4	0.6	0.3	0.3	0.9	1.4	0.4	1.0	0.8	1.5	0.5	0.5	0.1	0.5	0.7	3.80423
211548_s_at	J05594.1	15-hydroxyprostaglandin dehydrogenase	82.6	60.0	19.4	26.0	16.3	3.2	2.9	1.8	1.7	0.8	0.5	0.9	0.2	4.1	1.2	0.9	0.1	0.6	0.2	3.49258
210174_at	AF228413.1	nuclear receptor subfamily 5, group A, member 2	2.9	3.4	0.5	0.5	0.6	0.8	1.1	0.7	1.2	1.1	0.4	0.1	0.4	0.9	0.7	0.2	0.2	0.6	0.3	3.47124
219412_at	NM_022337.1	RAB38, member RAS oncogene	3.9	4.0	0.1	0.4	0.3	0.7	0.1	0.2	0.3	0.2	0.2	1.1	0.1	1.2	0.1	0.8	0.4	0.1	0.5	3.32805
201850_at	NM_001747.1	gelsolin-like capping protein (actin filament)	70.5	64.5	9.6	30.8	28.8	8.1	7.8	11.5	9.9	2.6	3.6	3.0	2.4	1.6	1.1	1.0	1.7	5.8	5.3	3.29919
205888_s_at	A1962693	KIAA0555	5.4	4.6	0.7	1.6	1.2	0.8	0.7	0.1	1.0	1.3	0.3	0.2	0.6	1.2	0.3	1.5	0.7	1.2	0.4	3.25197
221750_at	BG035985	3-hydroxy-3-methylglutaryl-Coenzyme A synthase 1	5.0	3.8	0.9	1.5	1.1	1.1	1.2	1.3	1.0	1.3	0.5	0.7	1.2	0.7	0.5	1.1	0.7	1.4	1.2	3.1926
214218_s_at	AV699347	nuclear receptor subfamily 1, group I, member 3	3.5	3.5	0.7	0.6	0.7	0.5	2.2	0.5	0.5	0.7	1.2	0.6	0.1	1.1	0.9	0.3	0.6	0.8	0.4	3.15254
218788_s_at	NM_022743.1	FLJ21080	16.1	23.7	0.5	2.3	2.5	0.9	1.1	2.7	2.1	1.1	1.0	0.8	0.9	2.3	2.1	2.9	0.6	2.0	6.3	3.07851
218087_s_at	NM_015385.1	SH3-domain protein 5 (ponsin)	1.4	1.9	0.4	0.9	0.4	0.5	0.0	0.0	0.1	0.0	0.1	0.1	0.2	0.1	0.0	0.2	0.2	0.2	0.1	3.07366
221577_x_at	AF003954.1	prostate differentiation factor	7.8	5.5	0.6	0.3	0.5	0.6	0.1	0.2	0.6	0.0	0.2	0.3	0.1	0.1	0.2	0.0	0.1	0.4	2.1	3.05552
35820_at	X62078	GIM2 activator protein	21.8	17.6	1.4	3.3	1.3	0.3	0.3	0.2	0.5	0.5	0.8	1.9	0.3	0.4	0.2	0.2	6.5	5.0	2.7	3.01647
208744_x_at	BG403660	heat shock 105kD	7.3	4.8	0.5	0.2	0.2	0.9	0.1	0.4	0.6	0.1	0.1	0.3	0.1	0.8	1.7	2.0	0.9	0.9	2.0	3.00671

Fig. 6L

E. Basophil and eosinophil-selective transcripts (1/1).

Probe set	Accession #	Transcripts	MC	MC	Ba1	Ba2	Ba3	Eo	Eo	Eo3	Eo4	Ne	Ne	Ne2	Ne3	Ne4	pl	CD4	CD8	CD14	CD19	Fb	Bat-FoSi	
211517_s_at	M96651.1	IL-5R intermediate 5 receptor alpha	0.0	0.0	11.8	28.2	17.9	16.4	25.3	32.6	29.5	0.0	0.7	0.0	0.0	1.0	0.0	0.4	0.2	0.0	0.2	0.0	0.0	61.9%
210744_s_at	M75914.1	CRTH2 chemotractant receptor-1 homolog molecule expressed on TH2 cells	0.2	1.6	15.4	30.8	15.3	18.7	40.2	29.7	33.0	0.3	0.2	0.2	0.5	0.5	0.1	0.1	0.1	0.1	0.1	0.2	0.1	42.811
206361_at	NM_004778.1	Charcot-Leyden crystal protein	1.8	0.3	22.0	40.5	15.3	33.7	37.9	38.9	42.3	1.0	2.6	2.2	2.2	2.1	0.8	1.4	1.0	1.2	0.9	0.5	16.642	
206307_at	NM_001828.3	egf-like module containing mucin-like hormone receptor-like sequence 1 (EMR-1)	1.1	0.1	270.0	219.1	203.6	226.8	233.8	197.7	163.1	2.1	19.4	19.1	19.1	49.3	2.8	1.0	1.4	0.9	0.7	0.4	15.164	
203638_s_at	NM_002969.1	histamine receptor H4	0.2	0.1	7.3	43.5	33.0	4.1	8.8	12.3	23.3	0.1	0.1	0.3	0.3	0.1	0.1	0.2	0.1	0.1	0.1	1.0	13.357	
207111_at	NM_001974.1	secreted fibroblast growth factor receptor (K-sam, Ilj)	1.5	0.1	16.4	49.5	34.5	85.9	93.1	91.2	93.5	2.7	3.7	5.4	5.4	3.4	1.7	0.8	0.8	7.1	1.6	0.5	80.092	
215248_at	AU145003	dactylorhizin (Drosophila) homolog	0.7	0.3	5.7	4.7	5.2	4.5	2.1	2.8	2.1	1.0	0.7	0.7	0.7	0.1	0.2	0.1	0.1	0.1	0.1	0.2	7.2618	
205471_s_at	AW772082	histamine receptor H4	0.1	0.6	5.1	4.1	3.7	6.4	8.3	9.0	7.6	0.8	0.9	1.0	0.8	0.1	0.1	0.3	0.5	0.5	0.0	0.1	6.8198	
218857_s_at	NM_025080.1	entropin	1.0	7.0	18.0	35.3	18.6	13.7	12.5	16.3	15.4	1.3	1.7	0.9	1.9	0.3	0.5	0.4	2.4	2.4	0.2	0.2	6.5045	
221169_s_at	NM_011624.1	CD244 natural killer cell receptor 2B4	0.2	0.2	0.5	4.5	8.9	1.9	2.6	4.2	2.9	0.5	0.6	1.1	0.6	0.4	0.7	0.5	0.7	0.7	0.0	0.3	5.9783	
201769_at	NM_014666.1	calcium channel, voltage-dependent, L-type, alpha 1D subunit (PLN1)	7.8	9.1	41.7	101.5	76.0	26.8	34.1	40.5	35.7	3.0	2.9	3.6	4.2	4.5	6.3	6.9	8.0	8.0	9.0	7.9	5.1015	
208228_s_at	M87771.1	inositol polyphosphate-1-phosphatase (INPP1)	0.3	1.4	3.7	10.2	8.3	3.9	8.9	4.5	8.3	0.8	1.4	1.1	0.5	1.3	0.4	0.7	0.3	0.3	0.5	1.1	4.9922	
213605_s_at	AL049987.1	hypothetical protein, MNCb-4779	0.8	0.0	10.8	46.8	44.7	6.7	6.1	25.8	20.6	1.3	1.4	4.5	4.2	2.9	1.1	2.1	3.7	2.0	0.3	0.3	4.7426	
205382_s_at	NM_001928.1	adipon	3.5	0.1	62.0	206.0	176.5	60.4	48.1	60.5	44.8	7.1	32.5	20.5	16.3	0.1	0.6	0.1	1.5	1.5	0.1	3.8	4.7202	
49452_at	AU57637	CD244 natural killer cell receptor 2B4	0.6	0.2	5.2	7.7	6.6	0.9	5.9	10.2	12.7	1.1	0.2	0.3	1.3	0.1	1.6	1.6	0.5	0.5	1.3	0.8	4.7183	
220307_at	NM_016382.1	calcium channel, voltage-dependent, L-type, alpha 1D subunit (PLN1)	0.5	0.1	15.7	87.0	65.4	9.9	10.8	26.6	18.5	0.3	0.4	1.2	3.0	0.1	0.4	3.5	5.2	1.1	0.1	0.1	4.6297	
210108_at	BE550599	protein kinase-related oncogene	0.2	0.1	1.0	1.7	2.4	0.9	0.8	2.4	1.8	0.0	0.6	0.5	0.5	0.0	0.3	0.1	0.0	0.0	0.3	0.0	4.5958	
209193_at	M24779.1	inositol polyphosphate-1-phosphatase (INPP1)	6.8	7.1	61.3	110.3	100.1	47.0	79.7	91.6	79.5	19.2	18.8	21.1	16.1	4.1	12.7	13.9	4.6	4.0	1.2	1.2	4.1983	
202794_at	NM_002194.2	CCR3 chemokine (C-C motif) receptor 3	5.7	6.2	7.1	25.8	20.5	17.9	24.8	53.6	57.8	2.8	2.7	2.6	4.0	1.9	1.8	2.6	4.8	1.9	4.8	1.9	4.1158	
208304_at	NM_001837.1	eosinophil-derived neurotoxin	0.2	1.1	10.72	142.9	102.2	46.4	91.7	118.1	107.5	28.3	26.0	26.3	25.1	0.2	0.5	0.4	0.2	0.2	0.4	0.4	3.9525	
206111_at	NM_002934.1	hypothetical protein LOC83945	2.2	2.0	33.7	71.4	38.4	104.7	80.8	47.7	45.1	2.0	2.3	3.1	2.8	1.4	0.7	0.4	1.4	0.7	0.5	0.5	3.7641	
43427_at	A970898	inositol polyphosphate-5-phosphatase, 75kD	0.8	0.7	2.1	4.8	4.3	5.1	4.6	8.0	6.4	1.0	0.8	0.7	0.8	1.1	1.0	1.3	0.6	1.1	1.1	1.1	3.7554	
213804_at	A1039084	Gsa receptor	0.6	1.2	4.3	8.0	6.8	8.6	5.6	6.3	9.7	0.7	0.5	2.2	1.7	1.4	1.2	1.4	1.0	1.0	1.9	1.3	3.6088	
209906_at	U62027.1	ATP-binding cassette, sub-family C (CFTR/MRP) member 1	12.4	11.2	44.1	72.3	50.5	18.8	38.8	70.3	29.9	1.2	1.2	1.8	3.8	1.6	1.6	1.5	3.0	0.6	0.5	0.5	3.6099	
202804_at	A1539710	cholinephosphotransferase 1 beta	8.5	7.0	24.2	56.2	48.9	14.2	20.0	30.1	20.7	3.0	3.6	4.3	6.0	3.8	3.5	5.4	5.1	5.5	5.3	5.3	3.5673	
221675_s_at	AF195624.1	sorbitol dehydrogenase (SORB)	7.0	6.8	31.6	79.7	55.8	26.9	32.6	43.8	41.8	5.2	7.5	5.9	9.6	2.4	3.1	3.3	7.7	11.8	5.7	5.7	3.5626	
201562_s_at	NM_003104.1	FLJ23438 fs, clone HRC13275	2.0	1.5	7.9	4.2	4.1	7.4	1.6	8.3	11.2	1.7	2.5	1.5	1.3	1.3	1.4	1.8	1.2	1.8	1.1	1.1	3.5088	
210230_at	BC003629.1	FLJ10928	1.1	0.1	6.3	11.0	13.3	2.4	5.1	5.1	4.1	0.1	0.5	0.2	0.7	0.3	0.2	0.6	0.8	1.9	0.5	0.5	3.2532	
219919_s_at	NM_018276.1	KIAA0711	0.1	0.2	3.1	1.8	2.5	1.7	4.3	1.7	2.1	0.1	0.5	0.4	0.3	0.1	0.1	0.1	0.1	0.1	0.1	0.7	3.2497	
204301_at	NM_014867.1	Grb-10- and Grb-IR-related splice variant 1	0.6	0.1	3.8	14.3	10.7	5.3	6.8	12.6	10.5	1.2	0.6	1.6	1.6	1.0	0.8	1.2	2.6	0.8	0.7	0.7	3.2398	
210999_s_at	U66065.1	RacGef2 guanine exchange factor (GEF) 6	3.6	1.7	8.4	13.6	11.8	7.3	4.6	4.8	6.4	2.2	1.7	1.9	2.0	1.9	1.2	1.2	1.6	0.4	1.6	1.6	3.1044	
209539_at	D25304.1	soybean (SRI)	13.1	24.8	28.8	74.7	73.0	53.8	35.5	97.9	59.6	9.2	6.1	18.5	13.7	3.1	10.8	12.9	7.1	7.8	1.0	1.0	3.0943	
20892_s_at	L12387.1	biofunctional ATP sulfurylaseadenosine	19.2	11.4	20.2	88.6	67.0	37.4	42.4	86.3	85.4	6.9	8.9	17.8	21.5	2.6	11.1	12.7	8.4	8.6	17.8	17.8	3.0628	
209043_at	AF033026.1	5-phosphosulfate kinase	19.9	16.1	39.0	87.1	75.2	66.4	68.7	89.4	71.4	13.8	20.0	46.5	8.9	6.3	6.7	4.4	10.6	11.0	22.7	22.7	3.0385	

Fig. 6M

E. Eosinophil and neutrophil-selective transcripts (1/1).

Probe set	Accession #	Transcripts	MC																		
			cord blood	MC lung	MC	Ba2	Ba3	Eo	Eo3	Eo4	Ne	Ne3	Ne4	Fb	Eo+Ne-SL						
221345_at	NM_005306.1	GPR43 PARI-like	0.1	0.4	0.9	0.6	0.7	16.6	15.4	10.5	49.7	45.7	22.5	23.0	0.8	0.1	0.7	0.4	0.1	21.742	
212860_at	BG168720	zinc finger, DHHC domain containing 18	2.2	0.8	4.1	3.9	4.0	16.0	14.8	16.7	59.2	53.9	30.9	39.8	1.1	2.4	3.8	2.6	1.5	1.3	65842
211576_s_at	BC003068.1	solute carrier family 19 member 1	1.4	0.1	0.7	1.4	0.7	5.1	11.5	12.4	19.8	18.7	27.1	28.1	1.8	0.9	0.4	2.7	0.5	0.8	4.99
214321_at	BF440025	neuroblastoma overexpressed gene ARF-GAP, RHO-GAP, ankyrin repeat and plekstrin homology domains-containing protein 3	1.3	1.0	0.8	0.2	0.7	6.2	17.0	13.7	4.5	7.6	10.7	11.3	0.1	0.1	0.0	0.1	0.1	1.8	49823
218950_at	NM_022481.1		1.4	3.1	2.4	3.7	2.1	15.5	18.3	15.5	28.0	24.3	15.9	20.6	0.7	0.2	0.8	3.9	0.9	1.0	4829
205681_at	NM_004049.1	BC12-related protein A1	0.5	1.9	1.0	3.2	2.4	32.4	35.9	30.5	46.5	49.2	35.5	33.5	1.5	2.2	1.9	8.3	4.3	0.2	4.782
203765_at	NM_012198.1	granulinh	2.0	1.8	4.5	11.7	8.3	27.5	46.7	34.8	71.6	85.2	80.5	77.9	1.0	1.0	1.2	12.1	3.1	0.5	4.403
213241_at	AF035307.1	CDNA FLJ36416 fs, clone	5.0	2.4	1.6	1.0	1.0	33.2	68.7	40.6	63.2	77.8	89.2	80.9	3.0	3.0	2.8	13.5	4.1	7.8	4.2603
221815_at	BE671816	hypothetical protein PRO2831 homolog of yeast long chain polyunsaturated fatty acid elongation enzyme 2	1.2	1.4	1.3	0.5	1.6	10.1	11.2	6.4	5.0	6.2	4.0	3.8	1.6	0.8	0.2	1.4	0.9	0.6	4.1325
214153_at	BE467941	KIAA0599	1.0	0.6	1.0	2.0	3.1	9.1	18.2	16.6	9.7	9.7	14.5	15.2	0.8	0.9	1.2	0.7	2.3	0.1	4.0797
212821_at	AU147160	Edg4, endothelial differentiation lysophosphatidic acid	0.1	0.1	0.4	1.2	0.9	4.6	4.7	3.4	4.4	3.5	6.0	7.9	0.4	0.2	0.4	0.3	0.0	0.2	3.727
206723_s_at	AF011466.1	G-protein-coupled receptor 4	1.2	1.4	2.1	3.6	2.6	13.7	19.6	22.3	24.6	17.0	26.1	29.1	0.1	3.6	5.0	3.8	1.9	0.9	3.7119
212360_at	A1916249	adenosine monophosphate deaminase 2 (isoform 1)	1.0	2.0	2.6	5.9	4.6	26.6	30.2	31.9	78.7	63.1	79.5	91.3	3.4	5.8	6.1	12.6	3.7	5.8	3.5888
218308_at	NM_006342.1	transforming, acidic coiled-coil containing protein 3 (TACC3)	0.4	0.4	4.8	8.3	9.5	3.3	3.3	4.7	17.6	14.8	23.5	22.8	2.4	2.3	1.6	3.6	1.0	0.7	3.4769
212629_s_at	AK023692.1	protein kinase C-like 2	1.9	0.6	3.1	3.7	5.1	11.8	17.7	13.8	16.7	23.6	27.0	28.4	1.1	2.1	2.2	4.2	4.2	2.9	3.2963
201739_at	NM_005627.1	serum glucocorticoid regulated kinase (SGK)	30.2	25.2	1.9	18.5	25.4	114.1	150.9	164.8	60.2	77.1	105.8	156.3	1.1	3.7	0.7	34.6	1.6	18.9	3.2456
209473_at	AV717590	ectonucleoside triphosphate diphosphohydrolase 1	1.4	0.6	2.1	1.6	2.0	15.9	39.5	29.1	14.1	13.7	23.7	13.8	2.6	2.6	1.3	6.5	4.8	0.6	3.0752
209304_x_at	AF087853.1	growth arrest and DNA damage inducible protein beta (GADD45B)	2.0	0.3	2.7	4.5	3.6	15.5	16.3	34.4	7.0	12.0	13.5	9.4	0.4	3.1	4.2	4.1	3.7	0.6	3.0295
210666_at	AF050145.1	iduronate 2-sulfatase	0.1	0.3	1.3	0.5	1.7	7.1	3.3	3.8	6.1	5.1	5.2	10.8	0.4	0.1	0.9	0.7	0.4	0.1	3.0005

Fig. 6N

G. Basophil and neutrophil-selective transcripts (1/1).

Probe set	Accession #	Transcripts	MC	Ba2	Ba3	Eo	Eo3	Eo4	Ne	Ne3	Ne4	CD14	CD19	Fb	Ba+Ne+SJ							
			cord blood	(small)	(small)	1	2	(small)	1	(small)	(small)	pl										
218739_at	NM_016006.1	CGI-58 protein	1.8	7.2	16.3	17.3	2.6	3.3	3.2	2.5	20.7	23.6	21.4	19.3	1.3	1.2	0.7	2.9	0.7	1.5	5.81398	
219242_at	NM_025180.1	FLJ13386	1.0	0.3	10.1	23.5	18.8	2.4	3.7	4.5	4.2	13.7	14.0	26.1	27.7	0.1	0.5	1.6	1.0	0.6	2.5	4.97025
219157_at	NM_007246.1	kelch (Drosophila)-like 2	2.4	1.7	4.2	16.2	19.2	3.8	3.8	15.5	24.4	24.5	22.5	0.7	2.0	1.5	3.0	3.0	2.2	1.7	4.61523	
206643_at	NM_002108.2	histidine ammonia-lyase	0.1	1.4	8.5	13.7	25.4	0.6	3.1	3.2	6.7	37.0	1.6	0.5	0.1	5.6	0.6	0.5	0.5	0.8	4.57355	
213935_at	AF007132.1	clone 23551 mRNA	0.8	0.1	5.0	26.2	26.4	2.4	1.7	2.9	1.2	4.5	6.7	11.2	9.0	0.1	0.1	0.2	2.3	0.5	0.8	4.33664
222151_s_at	AK023738.1	FLJ13676 fs	1.0	0.9	4.5	5.5	4.7	1.8	1.7	1.4	1.6	8.4	10.2	8.4	7.6	0.5	0.8	1.3	0.8	1.0	1.3	4.14372
207907_at	NM_003807.1	tumor necrosis factor (ligand)	0.1	0.1	3.9	10.4	6.3	1.2	1.5	4.0	4.1	15.8	7.3	15.8	11.5	0.2	0.4	0.1	0.6	0.0	0.1	3.89177
202530_at	NM_001315.1	superfamily member 14 (TNFSF14)	5.0	3.0	28.8	82.2	70.8	4.0	7.1	13.9	11.1	13.6	23.0	25.7	22.3	5.3	2.9	3.5	7.3	2.6	4.5	3.8469
217521_at	N54942	mitogen-activated protein kinase 14	0.1	0.1	5.5	18.9	20.9	0.3	0.3	1.6	0.1	19.6	14.5	29.9	18.4	0.4	0.8	0.9	4.3	1.0	0.3	3.84207
203693_s_at	NM_001949.2	Hs.276590 ESTs	2.5	1.7	4.3	16.2	13.2	2.1	1.9	5.7	3.3	8.8	11.7	13.3	15.4	1.5	1.4	2.5	2.3	1.1	1.2	3.7116
203420_at	NM_016255.1	E2F transcription factor 3	2.4	3.3	15.6	31.5	32.4	7.3	6.6	14.3	11.0	37.2	37.2	48.5	50.0	6.1	5.0	9.8	4.5	3.3	9.8	3.48188
218308_at	NM_006342.1	autosomal highly conserved protein (AHCP)	0.4	0.4	4.8	8.3	9.5	3.3	2.4	3.3	4.7	17.6	14.8	23.5	22.8	2.4	2.3	1.6	3.6	1.0	0.7	3.4769
203080_s_at	NM_013450.1	transforming acidic coiled-coil containing protein 3	2.2	2.4	10.4	22.8	22.9	4.9	6.6	10.0	9.5	29.5	30.7	33.5	40.6	1.1	1.7	1.9	4.6	2.3	1.5	3.401
219999_at	NM_018621.1	bromodomain adjacent to zinc finger domain, 2B	0.4	0.6	3.9	7.6	8.0	2.0	1.5	3.9	2.7	9.8	6.5	11.7	12.3	0.2	1.3	1.8	2.4	1.7	0.9	3.31991
213805_at	A1692428	hypothetical protein PRO2198	0.3	0.1	13.8	11.0	8.7	3.2	3.0	1.4	1.4	19.7	16.7	5.3	7.0	0.7	0.2	0.8	3.3	0.4	0.7	3.29317
204669_s_at	NM_007219.2	clone 23551 mRNA	0.9	0.2	4.4	27.9	34.3	2.1	5.9	16.1	14.5	18.8	14.4	60.7	56.1	0.5	0.1	0.1	0.1	0.1	0.8	3.18834
215555_at	AK023774.1	ring finger protein 24	0.0	0.4	5.0	4.3	5.8	1.5	1.9	1.5	1.5	7.6	8.2	3.3	3.2	0.9	1.0	1.5	1.5	1.0	0.1	3.1591
		FLJ13712 fs																				

Fig. 60

H. Mast cell and basophil-selective transcripts (1/1).

Probe set	Accession #	Transcripts	MC														MC-Hb-SL					
			cord blood	MC lung	Ba1 (small)	Ba2 (small)	Ba3 (small)	EO 1	EO 2	EO 3 (small)	EO 4 (small)	Ne 1	Ne 2 (small)	Ne 3 (small)	Ne 4 (small)	pI		CD4	CD8	CD14	CD19	Fb
205624_at	NM_0018701	carboxypeptidase A3	137.1	91.0	107.6	139.0	173.1	2.5	1.6	2.8	1.9	0.1	1.4	2.0	12.4	0.2	1.2	0.2	0.2	0.5	0.5	59.1989
208605_s_at	NM_0025292	R TRK neurotrophin receptor regulator of G protein signaling (RGS13)	80	1.2	4.6	9.3	8.1	0.2	0.2	0.0	0.1	0.2	0.0	0.1	0.1	0.1	0.1	0.1	0.1	0.0	0.0	34.7309
210258_at	AF030107.1	F-epsilon R1/beta	6.2	8.4	5.6	7.1	10.9	0.3	0.1	0.4	0.5	0.5	0.0	0.1	0.3	0.1	0.0	0.0	0.2	0.3	0.0	21.7762
207496_at	NM_000139.1	R solite carrier family 18	19.9	24.7	35.4	51.9	45.6	0.9	0.1	0.5	0.3	0.1	0.1	0.5	1.8	1.6	0.5	0.2	0.0	0.3	0.1	21.1783
208857_at	A1269290	GATA-binding protein 2	24.3	27.1	8.1	22.3	25.0	1.3	1.0	0.8	0.9	1.3	0.9	0.5	0.7	0.9	0.4	0.3	0.2	0.3	0.3	20.3301
210358_x_at	BC002557.1	F-epsilon R1/beta	18.4	12.8	55.0	31.7	24.7	2.0	1.6	1.9	1.7	0.9	1.9	1.3	3.7	2.6	0.8	0.8	0.9	0.4	2.7	9.46893
207497_s_at	D10583.1	15-hydroxyprostaglandin dehydrogenase (PDGF)	10.7	28.6	34.9	12.6	6.8	1.5	1.0	0.8	0.8	1.9	0.9	1.7	1.5	1.7	0.7	0.7	0.1	0.3	0.5	9.39967
203914_x_at	NM_000860.1	chromosome 11 open reading frame 14	63.9	51.4	24.8	36.0	23.3	4.1	4.6	4.6	2.6	1.3	0.9	1.3	1.2	6.0	1.4	1.5	0.4	0.8	0.4	6.14285
219557_s_at	NM_020645.1	protein kinase X-linked	7.4	4.2	4.4	7.4	6.6	1.2	1.6	2.0	2.4	0.9	1.9	1.1	2.1	1.1	1.4	1.4	1.5	0.4	1.6	3.38029
204061_at	NM_005044.1	low density lipoprotein receptor	6.2	5.2	5.2	12.8	16.9	2.3	2.7	2.5	2.4	0.8	0.4	0.7	1.2	1.9	1.5	2.1	2.5	2.0	0.8	3.26062
202068_s_at	NM_000527.2	R	24.6	16.8	19.3	28.5	13.5	1.6	1.0	1.6	0.9	0.8	2.4	1.5	2.5	2.3	2.1	3.4	3.5	0.8	6.3	3.1679

Fig. 6P

I. Specific transcripts markers for non-granulocytes.

Probe set	Accession #	Transcripts	MC	Ba 1	Ba 2	Ba 3	Eo 1	Eo 2	Eo 3	Eo 4	Ne 1	Ne 2	Ne 3	Ne 4	pI	CD4	CD8	CD14	CD19	Fb
203547_at	U47924	cord blood	4.7	2.2	1.1	1.2	2.0	1.6	0.4	0.9	0.7	1.1	0.7	0.8	3.5	15.0	0.3	17.6	7.2	0.4
205758_at	AW006735		1.7	2.6	2.3	3.2	1.3	1.1	2.2	1.7	0.3	0.5	1.8	0.3	4.2	3.0	76.1	0.8	0.6	0.4
206398_s_at	NM_001770.1		0.7	0.7	0.4	0.7	0.8	0.5	0.5	0.2	0.6	1.5	1.1	0.7	4.0	0.0	0.1	0.1	19.1	0.4
211644_x_at	L14458.1	IgGVJ region	0.2	0.1	0.1	0.2	0.2	0.2	0.2	0.3	0.1	0.3	0.2	0.2	3.8	0.1	0.2	0.1	70.9	0.1
201743_at	NM_000591.1	CD14	18.4	2.4	0.1	0.6	8.8	0.6	1.1	3.2	40.7	49.6	58.7	68.2	2.9	0.4	0.0	97.2	1.1	0.9
203104_at	NM_005211.1	v-fms M-CSF receptor	3.8	0.2	0.6	0.3	3.0	1.1	1.7	1.5	8.8	8.7	6.3	6.4	5.2	2.8	0.7	42.1	1.4	0.9
209968_s_at	U63041.1	CD56	0.1	0.1	0.1	0.1	0.1	0.1	0.2	0.1	0.1	0.1	0.2	0.1	0.1	0.1	0.1	0.2	0.1	0.0
204627_s_at	M35999.1	CD61 glycoprotein IIIa	1.7	9.4	0.2	0.3	0.1	0.1	0.1	0.1	0.1	0.4	0.1	0.2	48.3	0.1	0.3	0.1	0.2	0.5
216442_x_at	AK026737.1	fibronectin	0.3	1.5	0.3	0.2	0.1	1.0	0.3	0.6	0.1	0.1	0.2	0.1	0.3	0.1	1.0	0.3	0.1	92.6

Fig. 6Q

J. Raw AD levels for the median values used to normalize the raw AD levels, and the housekeeping genes.

Probe set	Accession #	Transcripts	MC		Ba 2		Ba 3		Eo 3		Eo 4		Ne 3		Ne 4		CD4	CD8	CD14	CD19	FB
			cord	lung	blood	MC	Ba 1	Ba 2	Ba 3	Eo 1	Eo 2	Eo 3	Eo 4	Ne 1	Ne 2	Ne 3					
AFX-HSAC07/X00351_3_at	X00351	beta-actin	18534	19383	14638	20922	19151	22019	18638	21153	18568	19406	22302	16589	17569	18295	18782	20805	20661	17542	20395
AFX-HSAC07/X00351_M_at	X00351	beta-actin	22898	21777	12940	11533	7608	22560	18785	14861	13431	23106	23373	6861	8019	19368	20362	22761	22294	19087	22757
AFX-HSAC07/X00351_5_at	X00351	beta-actin	15642	15838	9516	2927	2066	17186	21061	4861	3771	18772	19768	2165	2193	14887	16381	18218	17583	15063	16795
AFX-HUMGAPDH/M33197_3_at	M33197	GAPDH	14906	13632	3640	10477	9332	2649	2844	5498	2605	2549	3186	3586	3538	5929	6429	6098	9756	5180	19674
AFX-HUMGAPDH/M33197_M_at	M33197	GAPDH	15891	16852	3218	7587	6963	2382	2565	3720	1838	2194	2796	2312	2154	6182	5931	5921	11464	4344	17013
AFX-HUMGAPDH/M33197_5_at	M33197	GAPDH	16298	16701	3479	4559	5110	1827	3121	2127	1168	2492	3476	1636	1355	4655	6826	6260	9905	5636	23350
The median value of 2283 transcripts			121	1693	853	1122	1109	93.7	102.1	127.3	114	62.7	73.1	87.4	87.3	82.3	152.5	121.3	107.1	114.1	183.8

Abbreviations used in the table A-1 were (small); the results obtained by the small sample protocol (see materials and methods), R; receptor, and ICN; ion channel.

Fig. 6R

**GRANULOCYTE SUBTYPE-SELECTIVE
RECEPTORS AND ION CHANNELS AND
USES THEREOF**

FIELD OF THE INVENTION

[0001] The present invention relates to the identification of granulocyte-selective markers that can be used as targets for drug discovery.

BACKGROUND OF THE INVENTION

[0002] Three types of human blood granulocytes, eosinophils, basophils and neutrophils, play roles in protecting against microbial infection by releasing cell type-specific mediators and proteases. Specifically, eosinophils and basophils evoke allergic reactions as well as damage nematodes.^{1,2} As well as killing bacteria, neutrophils sometimes induce systemic vasculitis or multiple organ damage under certain conditions.^{3,4} Thus, targeting granulocyte type-selective functions is considered an important strategy for drug discovery.

[0003] Activation of blood granulocytes and tissue mast cells is generally characterized by an influx of extracellular calcium (Ca^{2+}), which is essential for subsequent release of granule-derived mediators, newly generated lipid mediators and cytokines.⁵ The mechanism by which granulocyte mediator secretion is sustained is therefore likely to include modulation of various types of ion channels. Flow of ions including K^+ and Cl^- may play an important role during granulocyte responses because they regulate cell membrane potential and thus influence Ca^{2+} influx.⁶ Treatment of mast cells and basophils with pertussis toxin inactivates the G_i -type of G-proteins and abolishes degranulation induced by non-immunological ligands such as thrombin and N-formylpeptide; however, it fails to inhibit the influx of Ca^{2+} .⁷ Thus, Ca^{2+} -independent stimulation of G_i is also involved in granulocyte degranulation. The thrombin (protease) activated receptors and formylpeptide receptors are classified as G protein-coupled receptors (GPR), having an extracellular N-terminal segment, a seven transmembrane region, which forms the transmembrane core; three exoloops, three cytoleups, and a C-terminal segment.⁸ Thus, ion channels and GPR both play essential roles in degranulation as well as other cellular function important for granulocytes. As a result, both ion channels and GPR are targets of drug development.⁹

[0004] As the human genome project nears completion, the identification of potential drug targets using gene expression profiles from specific cell types is becoming practical and important for drug discovery.^{10,11} The sequencing of the human genome is offering an unprecedented opportunity for the pharmaceutical development of drugs. Receptor genes and ion channel genes are found only in 5% and 1.3% of all genes present in the human genome,¹⁰ respectively. However, receptors and ion channels are respectively found in 45% and 5% of the molecular targets of all known drugs.^{9,12,13} Thus, receptors including GPR and ion channels are now considered as the most important drug targets.

[0005] Until recently, it has been impractical to analyze genome-wide expression of leukocytes. Newly developed technology, the microarray or high density oligonucleotide probe array (GeneChip) is one of the latest breakthroughs in experimental molecular biology, which allows approximately 39,000 transcripts derived from a cells transcriptome to be simultaneously monitored. Using this technology, we previously reported the transcriptome profiling of various types of

mast cells and eosinophils.¹⁴⁻¹⁶ However, there is still a need in the art to identify drug targets that are selectively, or preferentially, expressed in specific cell types such that efforts required for pharmaceutical development are minimized.

SUMMARY OF THE INVENTION

[0006] In the present study, we used GeneChip (version U133A containing approximately 22,000 gene probes) to examine the granulocyte type-selective transcriptome expression of 7 types of leukocytes (basophils, eosinophils, neutrophils, $CD4^+$ cells, $CD8^+$ cells, $CD14^+$ cells and $CD19^+$ cells), platelets, mast cells and fibroblasts by focusing on the expression of granulocyte-selective genes for ion channels, GPR and other receptors. We identified many novel granulocyte subtype-selective transcripts (markers) that are useful for drug development.

[0007] Granulocyte subtype selective transcripts were chosen based on several conditions such as the transcript having 5-fold or greater expression level compared to the maximum level of other leukocytes. Fifty-one transcripts were chosen to be preferentially expressed by each granulocyte subtype. Seventeen out of the 51 transcripts have not been previously reported as granulocyte subtype-selective. Among the 17 receptors and ion channels, six were basophil- and/or eosinophil-selective and were not highly expressed by other organs, indicating that they may be potential targets for anti-allergic drugs, for example.

[0008] Utilization of this database of potential granulocyte type-selective drug targets will minimize the efforts required for pharmaceutical development of drugs for treatment of diseases of the immune system, cancer, cardiac diseases, as well as other diseases.

[0009] Accordingly, the invention provides methods and compositions that are useful for drug discovery, disease diagnosis and/or prognosis, granulocyte type detection and/or selection and/or manipulation, and/or therapeutic applications.

[0010] Accordingly, in one aspect, methods of the invention include diagnosing a granulocyte disorder by detecting, in a biological sample obtained from a subject, a level of expression of one or more granulocyte-selective markers, and comparing the level of expression of each of the one or more granulocyte-selective markers with a reference level of expression. A statistically significant difference between the level of expression of at least one granulocyte-selective marker and an expected level of expression for the at least one granulocyte-selective marker is indicative of a granulocyte disorder in the subject. The reference level of expression for a granulocyte-selective marker may be, for example, a normal level of expression of the granulocyte-selective marker in a normal granulocyte. A higher level of expression of at least one of the one or more granulocyte-selective markers in the biological sample compared to the expected level of expression for the at least one granulocyte-selective marker may be indicative of the granulocyte disorder. A lower level of expression of at least one of the one or more granulocyte-selective markers in the biological sample compared to the expected level of expression for the at least one granulocyte-selective marker also may be indicative of the granulocyte disorder. In one embodiment, the granulocyte disorder may be an abnormally high number of one or more types of granulocyte in the biological sample. In another embodiment, the granulocyte disorder may be an abnormally low number of one or more types of granulocyte in the biological sample. In

yet another embodiment, the granulocyte may be an abnormal pattern of expression of one or more granulocyte selective markers in one or more types of granulocyte in the biological sample.

[0011] In another aspect, methods of the invention include diagnosing a non-neutrophil granulocyte disorder or mast cell disorder by detecting, in a biological sample from a subject, a level of expression of one or more non-neutrophil granulocyte or mast cell selective markers, and comparing the level of expression of each of the one or more non-neutrophil granulocyte or mast cell selective markers with a reference level of expression. A statistically significant difference between the level of expression of at least one non-neutrophil granulocyte or mast cell selective marker and an expected level of expression for the at least one non-neutrophil granulocyte or mast cell selective marker may be indicative of a non-neutrophil granulocyte disorder or mast cell disorder in the subject. In one embodiment, the non-neutrophil granulocyte disorder may be a basophil disorder. The basophil disorder may be one or more of the diseases described herein, including a tumor or cancer. In another embodiment, the non-neutrophil granulocyte disorder may be an eosinophil disorder. The eosinophil disorder may be one or more of the diseases described herein, including a tumor or cancer. In other embodiments, a mast cell disorder may be one or more of the diseases described herein, including a tumor or cancer.

[0012] A higher level of expression of one or more non-neutrophil granulocyte or mast cell-selective marker in the biological sample compared with the control level of expression of the one or more non-neutrophil granulocyte or mast cell-selective marker may be diagnostic of the non-neutrophil granulocyte disorder or mast cell disorder. Alternatively, a lower level of expression of one or more non-neutrophil granulocyte or mast cell-selective marker in the biological sample compared with the control level of expression of the one or more non-neutrophil granulocyte or mast cell-selective marker also may be diagnostic of the non-neutrophil granulocyte disorder or mast cell disorder.

[0013] In another aspect, methods of the invention include determining onset, progression, or regression, of a granulocyte disorder in a subject, by i) detecting in a first biological sample from a subject a first level of expression of one or more granulocyte-selective markers, ii) detecting in a second biological sample comprising blood and obtained from the subject at a time later than the first biological sample, a second level of expression of the one or more granulocyte-selective markers, and iii) comparing the first level of expression with the second level of expression. A statistically significant difference between the first and second levels may be an indication of onset, progression, or regression of the granulocyte disorder.

[0014] In another aspect, methods of the invention include selecting a course of treatment for a subject having or suspected of having a granulocyte disorder by i) detecting in a biological sample from a subject a level of expression of one or more granulocyte-selective markers, ii) comparing the level of expression of the one or more granulocyte-selective markers to a reference level of expression, iii) determining the status of the granulocyte disorder of the subject based on the difference in the level of expression of one or more granulocyte-selective marker in the sample compared to the reference level of expression, and iv) selecting a course of treatment for the subject appropriate to the status of the granulocyte disorder of the subject.

[0015] In another aspect, methods of the invention includes monitoring responses to treatment in a subject with a granulocyte disorder by i) detecting in a biological sample from a subject that has received treatment for the granulocyte disorder, a level of expression of one or more granulocyte-selective markers, and ii) comparing the level of expression of the one or more granulocyte-selective marker with a reference level of expression. A statistically significant change in the level of expression of one or more of the granulocyte-selective markers in the biological sample relative to the reference level of expression may indicate that the subject is responding to the treatment for the granulocyte disorder.

[0016] In another aspect, methods of the invention include identifying a compound that alters at least one physiological property of a granulocyte by i) contacting a granulocyte with a candidate compound that interacts with a granulocyte-selective marker, ii) determining at least one physiological property of the granulocyte after contact with the candidate compound, and iii) comparing the at least one physiological property to one at least one reference property to determine whether the candidate compound alters at least one physiological property of the granulocyte. In one embodiment, the effect of the candidate compound on a granulocyte may be compared to its effect on a second cell type to determine whether the candidate compound has a cell-type selective effect on the granulocyte. The second cell type may be another granulocyte cell type. Alternatively, the second cell type may be a non-granulocyte cell type (including a mast cell or other leukocyte). In one embodiment, a physiological property may be an expression level of one or more granulocyte-selective markers. In another embodiment, a physiological property may be the growth rate and/or proliferation rate of the granulocyte. In one embodiment, the candidate compound may be cytostatic or cytotoxic (e.g., it may kill the granulocyte). It should be appreciated that the candidate compound may have cell type selective effects (e.g., cell type selective cytotoxic and/or cytostatic effects).

[0017] In another aspect, methods of the invention include treating a granulocyte-associated disease, by administering to a subject having a granulocyte-associated disease a compound that interacts with a granulocyte-selective marker in an amount sufficient to treat the granulocyte-associated disease. Similarly, the invention provides methods for treating a mast cell-associated disease by administering to a subject having a mast cell-associated disease a compound that interacts with a mast cell-selective marker in an amount sufficient to treat the mast cell-associated disease. In some embodiments, a plurality (e.g., any whole number between 1 and 50, for example 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or more) of granulocyte-selective or mast cell-selective compounds may be administered. Compounds may be administered in physiologically acceptable (e.g., biologically compatible) solutions or carrier. Therapeutic preparations of the invention may be sterilized using any appropriate technique including filtration, heat treatment, radiation, chemical treatment, and/or other suitable techniques.

[0018] In another aspect, methods of the invention include treating a granulocyte-associated disease by modulating the activity or expression of a granulocyte-selective marker to an extent that is sufficient to treat the granulocyte-associated disease. Similarly, the invention also provides methods of treating a mast cell-associated disease by modulating the activity or expression of a mast cell-selective marker thereby to treat the mast cell-associated disease. Modulating the

activity or expression of a marker may involve activating or inactivating and/or increasing or decreasing the expression levels.

[0019] In any of the therapeutic methods described herein, one or more therapeutic compounds may be identified as described herein by screening for one or more compounds that alter at least one physiological property of a granulocyte and/or a mast cell.

[0020] In another aspect, the invention provides compounds that alter a physiological property of a granulocyte and/or a mast cell. One or more compounds may be identified as described herein by screening compounds that are known to interact (e.g., specifically, selectively, etc.) with a granulocyte-selective marker and/or a mast cell-selective marker. Compounds of the invention may be formulated in a physiologically acceptable preparation.

[0021] In any of the aspects described herein, the level of expression of each of the one or more granulocyte-selective markers (including neutrophil-selective markers, basophil-selective markers, eosinophil-selective markers, or a combination thereof) may be determined by determining an amount of an mRNA in the biological sample corresponding to each of the one or more granulocyte-selective markers. The amount of mRNA may be determined by reverse transcription polymerase chain reaction (RT-PCR) amplification or any other suitable method including microarray analysis or other hybridization or primer extension assays (e.g., using labeled probes and/or nucleotides). In other embodiments, the level of expression of each of the one or more granulocyte-selective markers may be determined by determining an amount of a protein in the biological sample corresponding to each of the one or more granulocyte-selective markers (e.g., using antibody binding assays with labeled antibodies, including ELISA assays or other antibody binding assays). Other suitable methods of determining expression levels of granulocyte-selective markers may be used (including activity levels). Similarly, expression levels of non-neutrophil granulocyte or mast cell-selective markers may be determined by determining mRNA and/or protein levels or using any other appropriate assay (including functional assays).

[0022] In any of the aspects described herein, the biological sample may be a blood sample, a tissue sample, or any other suitable biological sample.

[0023] In any of the aspects described herein, the subject may be human.

[0024] In any of the aspects described herein, a granulocyte may be a neutrophil, a basophil, or an eosinophil. It should be appreciated that aspects of the invention described herein in the context of granulocytes may be applied to non-neutrophil granulocytes and/or mast cells. Similarly, aspects of the invention described herein in the context of granulocytes or mast cells may be applied to other leukocytes including those described in the examples and for which cell-type selective expression is shown in the experiments including the Figures attached hereto.

[0025] According to aspects of the invention, one or more methods described herein may involve a combination of two or more markers. In one embodiment, markers that are more selective as described herein may be used. In some embodiments, a combination of two or more (e.g., 3, 4, 5, 6, 7, 8, 9, or 10 or more) markers may be used to increase the cell-selectivity of a screening or diagnostic method. It should be appreciated that different combinations of markers disclosed herein may be used (e.g., panels of two or more markers).

Accordingly, compositions of the invention may include compounds that interact with two or more markers (e.g., a single compound that interacts with two or more markers, or two or more compounds each of which interacts with a single marker, or any combination thereof).

[0026] Methods and compositions described herein may include or involve nucleic acids that hybridize to one or more nucleic acids that encode a granulocyte or mast cell-selective marker (e.g., DNA or RNA). The nucleic acids may be oligonucleotides (e.g., synthetic oligodeoxynucleotides). The oligonucleotides may be between 10 and 100 nucleotides in length (e.g., between about 20 and about 50). The oligonucleotides may include sequences that are complementary to sequences of one or more markers described herein (or the complement thereof). In some embodiments, nucleic acids may be antisense or siRNA nucleic acids that are useful to decrease the expression of one or more granulocyte or mast cell-selective markers. Similarly, methods and compositions described herein may include or involve agents that bind or interact with one or more proteins that are granulocyte or mast cell-selective markers. Binding agents may be antibodies or fragments thereof (including single chain antibodies, synthetic antibodies, humanized antibodies), aptamers, and/or other molecules including naturally occurring or synthetic molecules (e.g., low molecular weight molecules), that bind to one or more peptide epitopes of one or more granulocyte and/or mast cell-selective marker. Examples of nucleic acid and peptide sequences for certain granulocyte and/or mast cell-selective markers are provided in the sequence listing. These and others are described in the examples, tables, and figures. In the sequence listing, the nucleic acid sequences are presented as cDNA sequences. The following list of sequences in the sequence listing includes the description of the molecule and the genbank accession number is indicated in parentheses.

SEQ ID NO: 1	Ca ²⁺ channel type A1 D (BE550599) cDNA
SEQ ID NO: 2	K ⁺ channel Kir1.3 (U73191.1) cDNA
SEQ ID NO: 3	K ⁺ channel Kir1.3 (U73191.1) translation
SEQ ID NO: 4	K ⁺ channel Kir2.1 (AF153820.1) cDNA
SEQ ID NO: 5	K ⁺ channel Kir2.1 (AF153820.1) translation
SEQ ID NO: 6	PGE R type 3a2 (X83858.1) cDNA
SEQ ID NO: 7	PGE R type 3a2 (X83858.1) translation
SEQ ID NO: 8	EMR-1 (NM_001974.1) cDNA
SEQ ID NO: 9	EMR-1 (NM_001974.1) translation
SEQ ID NO: 10	GPR105 purinergic R (NM_014879.1) cDNA
SEQ ID NO: 11	GPR105 purinergic R (NM_014879.1) translation
SEQ ID NO: 12	GPR, Edg-4 (AF011466.1) cDNA
SEQ ID NO: 13	GPR, Edg-4 (AF011466.1) translation
SEQ ID NO: 14	PAR1-like GPR43 (NM_005306.1) cDNA
SEQ ID NO: 15	PAR1-like GPR43 (NM_005306.1) translation
SEQ ID NO: 16	GPR77 (018485.1) cDNA
SEQ ID NO: 17	GPR77 (018485.1) translation
SEQ ID NO: 18	GPR86 purinergic R (NM_023914.1) cDNA
SEQ ID NO: 19	GPR86 purinergic R (NM_023914.1) translation
SEQ ID NO: 20	PAR2 (BE965369) cDNA
SEQ ID NO: 21	HTm4 (L35848.1) cDNA
SEQ ID NO: 22	HTm4 (L35848.1) translation
SEQ ID NO: 23	CD244 NK cell R (NM_016382.1) cDNA
SEQ ID NO: 24	CD244 NK cell R (NM_016382.1) translation
SEQ ID NO: 25	Fibroblast growth factor R 2 (NM_022969.1) cDNA
SEQ ID NO: 26	Fibroblast growth factor R 2 (NM_022969.1) translation
SEQ ID NO: 27	Low-density lipoprotein R (NM_000527.2) cDNA
SEQ ID NO: 28	Low-density lipoprotein R (NM_000527.2) translation
SEQ ID NO: 29	Butyrophilin-like R (AK025267.1) cDNA

-continued

SEQ ID NO: 30	Leukocyte Ig-like R A2 (NM_006866.1) cDNA
SEQ ID NO: 31	Leukocyte Ig-like R A2 (NM_006866.1) translation

BRIEF DESCRIPTION OF THE DRAWINGS

[0027] FIG. 1 shows Real-time quantitative PCR analysis of granulocyte-selective gene expression. The relative mRNA expression level by each cell type against PBMNC was shown after normalization of mRNA levels for A. HTm4 (0.42 per 100 GAPDH), B. Ca²⁺ receptor alpha 1D subunit (0.003), C. prostaglandin E receptor type 3a2 (0.12), D. EMR-1 (0.62), and E. aquaporin 9 (0.92) expressed by PBMNC. Ne; neutrophils (n=3), Eo; eosinophils (n=2), Ba, basophils (n=3), CD4; CD4+ cells (n=3), P; PBMNC (n=1).

[0028] FIG. 2 shows the demonstration of HTm4 protein on human basophils. Cells on the glass slide were incubated with 2 µg/ml polyclonal rabbit anti-hHTm4 antibody or 2 µg/ml rabbit IgG (H+L) as a control followed by incubation with a secondary antibody, highly cross-adsorbed Alexa Fluor® 546 conjugated goat anti-rabbit IgG (H+L). After mounting using the Prolong AntiFade Kit, slides were scanned by Zeiss Laser Scanning Microscope 5 Pascal.

[0029] FIGS. 3A through 3E shows granulocyte subtype-specific transcripts for ion channels and receptors.

[0030] FIGS. 4A through 4F show a table of "normalized AD" expression levels of various genes in indicated cells and shows corresponding graphs; x axis represents "normalized AD" expression levels.

[0031] FIGS. 5A through 5D show a table of "normalized AD" levels of various genes in indicated cells and shows corresponding graphs; x axis represents "normalized AD" expression levels.

[0032] FIG. 6A through FIG. 6R show the complete list of granulocyte subtype-selective transcripts.

DETAILED DESCRIPTION OF THE INVENTION

[0033] In one aspect of the invention, one or more granulocyte-selective markers may be used for drug discovery. For example, a granulocyte-selective marker (e.g., a cell type selective transcript, its protein product, or the gene encoding the marker) may be used as a target for drug identification. Drug identification may involve a random screen of potential drug candidates (including peptides, nucleic acids, small molecules, etc.). In one embodiment, one or more granulocyte-selective markers may be used as targets for drug identification. For example, a single drug molecule that interacts (e.g., that activates, or inactivates, and/or binds to) with one or more markers may be identified. However, in some embodiments, more than one drug molecule may be identified, each one interacting with a different granulocyte-selective marker. According to aspects of the invention, drug(s) that target a specific granulocyte may be used to stimulate or inhibit activity or growth of that cell type. A cell type specific drug also may be used to kill or slow or stop the growth of a specific cell type.

[0034] Examples of markers for different granulocyte types include: Ca²⁺ channel type A1 D (GenBank accession no. BE550599), K⁺ channel Kir1.3 (GenBank accession no. U73191.1), K⁺ channel Kir2.1 (GenBank accession no. AF153820.1), PGE R type 3a2 (GenBank accession no. X83858.1), EMR-1 (GenBank accession no. NM_001974.

1), GPR105 purinergic R (GenBank accession no. NM_014879.1), GPR, Edg-4 (GenBank accession no. AF011466.1), PAR1-like GPR43 (GenBank accession no. NM_005306.1), GPR77 (GenBank accession no. NM_018485.1), GPR86 purinergic R (GenBank accession no. NM_023914.1), PAR2 (GenBank accession no. BE965369), HTm4 (GenBank accession no. L35848.1), CD244 NK cell R (GenBank accession no. NM_016382.1), Fibroblast growth factor R 2 (GenBank accession no. NM_022969.1), Low-density lipoprotein R (GenBank accession no. NM_000527.2), Butyrophilin-like R (GenBank accession no. AK025267.1), and Leukocyte Ig-like R A2 (GenBank accession no. NM_006866.1).

[0035] Some of these markers are specific for one cell type only (e.g., HTm4 (GenBank accession no. L35848.1) is preferentially expressed in basophils, and GPR105 purinergic R (GenBank accession no. NM_014879.1) is preferentially expressed in eosinophils). Others are preferentially expressed in two or three cell types (e.g., Ca²⁺ channel type A1 D (GenBank accession no. BE550599), and EMR-1 (GenBank accession no. NM_001974.1) are expressed in both basophils and eosinophils).

[0036] In one aspect, the invention provides methods for screening compounds to identify those that interact with one or more cell type selective markers disclosed herein. Cell type selective markers of the invention include receptors, ion channels (including calcium channels) and other molecules. Accordingly, candidate drug compounds may include one or more receptor binding compounds, ion channel binding compounds (including calcium channel binding compounds) and compounds that bind to one or more of the other molecules. Candidate drug compounds also may include compounds that can be transported across/through one or more ion channels. Candidate drug compounds also may include compounds that block ion transport (e.g., calcium transport).

[0037] In one embodiment, drug compounds may be agents that selectively or specifically bind to one or more cell type selective markers of the invention. For example, drug compounds may be antibodies or aptamers that bind to one or more cell type selective markers of the invention. A marker binding drug may directly inactivate the marker. Alternatively, a marker binding agent may activate the marker. In another embodiment, a marker binding agent may be used to target a second compound to cells that selectively express that marker. For example, the marker binding agent may be conjugated to one or more additional moieties to alter the physiology of the target cell (e.g., to activate, inactivate, or kill the target cell). For example, radioactive moieties, heavy metal moieties, certain enzymes, toxins, and other toxic compounds (e.g., other cytostatic or cytotoxic compounds) may be used to inactivate or kill a target cell. In contrast, activating moieties (e.g., cytokines, growth factors, etc.) may be used to activate a target cell. In certain embodiments, a binding agent (e.g., an antibody, aptamer, etc.) may be bispecific, trispecific, or multispecific (meaning that it binds to two, three, or more cell selective markers). Multispecific binding agents may be better targeting moieties if they bind to a specific combination of markers that is selectively or specifically present on the target cell type. Preferred markers for binding agents are those that are accessible to the binding agents (e.g., extracellular, membrane bound, or transmembrane proteins). However, any of the markers described herein (or combinations thereof) may be used as the invention is not limited in this respect. Antibodies to one or more leukocyte (e.g., granulocyte,

cyte, granulocyte subtype, mast cell, etc.) marker may be used in several aspects of the invention. Antibodies may be monoclonal, polyclonal, humanized, synthetic, single-chained, etc., or any useful combination thereof. Selective marker binding agents also may be conjugated to one or more detection moieties (e.g., fluorescent, radioactive, enzyme mediated, etc.) and used as detection agents to detect one or more leukocyte cell types.

[0038] In another aspect of the invention, one or more granulocyte-selective markers may be used for diagnostic and/or prognostic applications. For example, a single cell type-selective marker may be used as a marker of the presence of a specific granulocyte type-selective marker in diseased tissue. Similarly, a panel of granulocyte-selective markers (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, etc.) may be used as markers indicating the presence of a specific granulocyte-selective marker in diseased tissue (e.g., in a tumor or cancerous growth). Accordingly, any one or more of Ca²⁺ channel type A1 D (GenBank accession no. BE550599), EMR-1 (GenBank accession no. NM_001974.1), or GPR105 purinergic R (GenBank accession no. NM_014879.1) may be used to detect, for example, the presence of eosinophils in a biological sample. Similarly, one or more markers of the invention may be used to determine the ratio of different granulocyte types in a biological tissue or sample from a subject.

[0039] A biological sample includes, but is not limited to: cells, tissue, body fluid (e.g. blood, serum, etc.). The tissue may be in a subject, obtained from a subject, or may be grown in culture (e.g. from a cell line). A cell or tissue used in the invention can be a blood cell or other cell type. As used herein, cell samples, tissue samples, and/or blood samples, etc., may be obtained using methods well known to those of ordinary skill in the related medical arts. A biological sample may be, for example, a tissue biopsy sample or a biological fluid or solid.

[0040] As used herein, a subject is a mammal, preferably a human, non-human primate, cow, horse, pig, sheep, goat, dog, cat, or rodent. In all embodiments, human subjects are particularly preferred. In some embodiments, the subject is suspected of having a granulocyte disorder. In other embodiments the subject has been diagnosed with a granulocyte disorder.

[0041] The detection of one or more particular granulocyte types or granulocyte-selective markers in a biological sample, or the determination of an abnormal ratio of different cell types in a biological sample, may be useful for disease diagnostic or prognostic purposes. Allergies, cancers and infections are some examples of diseases characterized by an altered proliferation of one or more granulocyte cell type(s). Granulocyte disorders include basophil cell disorders and eosinophil cell disorders. Examples of basophil cell disorders include myeloproliferative disorders such as polycythemia vera and myelofibrosis.

[0042] Examples of basophil cell disorders include asthma, eosinophilic pneumonia, helminthic infestations and Eosinophilic Gastrointestinal Disorders. Examples of Eosinophilic Gastrointestinal Disorders include Eosinophilic Esophagitis (EE), Eosinophilic Gastritis (EG), Eosinophilic Duodenitis (ED), Eosinophilic Colitis (EC), Eosinophilic Gastroenteritis (EGE), and Eosinophilic Ileitis (EI).

[0043] Diagnosis and treatment of mast cell disorders are also encompassed by this invention. Examples of Mast Cell Disorders include Systemic Mastocytosis (with or without cutaneous manifestations such as Urticaria Pigmentosa) such

as Aggressive Mastocytosis, Indolent Mastocytosis, Mastocytosis with associated Hematologic Disorder, Mast Cell Leukemia, Cutaneous Mastocytosis such as Urticaria Pigmentosa (UP), Telengiectasia Macularis Eruptive Perstans (TMEP), Mast Cell Activation Syndrome/Disorder, and Pediatric mast cell disorders such as Solitary Mastocytoma, Urticaria Pigmentosa, and Diffuse Cutaneous Mastocytosis.

[0044] In some embodiments, the detection of an abnormal level of one or more granulocyte-selective marker(s) may be used to determine appropriate drug or therapeutic regimens (e.g., abnormal growth of a particular cell type may suggest the use of one or more drugs that inhibit that growth of, or kill, that particular cell type).

[0045] In another aspect, diagnostic methods of the invention may be used to determine whether an abnormal expression pattern of one or more granulocyte-selective marker(s) is present on a particular granulocyte type. An abnormal pattern may be indicative of a disease (e.g., cancer, allergic response, infection, etc.). An abnormal pattern of expression of a granulocyte-selective marker may be an increase or decrease in the level of expression (at the level of transcription, translation, activity, or a combination of two or more thereof) of one or more granulocyte-specific markers relative to a reference level of expression.

[0046] The reference level may be a level of the same marker(s) in a reference cell or tissue. The reference level may be a level of one or more other granulocyte-selective marker(s). The reference level may be the level of expression of one or more markers that are not granulocyte-selective. The reference level may be a predetermined control value. The reference level may be a combination of two or more of the above.

[0047] Levels of expression may be compared to controls. The control may be a predetermined value, which can take a variety of forms. It can be a single value, such as a median or mean. A control value can be established based upon comparative groups (e.g. comparative cell types), such as in cells having normal levels of expression of one or more granulocyte-selective marker. These types of control values can serve as control values for substantially similar cells that are contacted with a treatment compound. In some embodiments of the invention, a control level of expression of a granulocyte selective marker(s) is the level of expression of the granulocyte selective marker(s) in a non-granulocyte cell or tissue.

[0048] In a further aspect of the invention, one or more granulocyte-selective markers may be used for specific cell type detection, selection, and or manipulation. For example, an antibody or specific binding agent (e.g., aptamer etc.) that binds to a granulocyte-selective marker (e.g., a protein, including a membrane bound or a surface protein) may be detectably labeled (e.g., with a fluorescent label, a radioactive label, or any other detectable label or combination thereof) and used to bind to a particular cell type. The detectably labeled antibody (or other binding agent) may be used to detect a particular cell type directly in vivo (e.g., via an MRI, PET, or CAT scan or other in vivo imaging technique) or ex vivo (e.g., via microscopy such as fluorescent microscopy or other ex vivo imaging technique). The detectably labeled antibody (or other binding agent) may be used to detect the presence of markers indicative of particular cell types (e.g., in an assay for nucleic acid, protein, and/or activity levels performed on a processed sample obtained from a biological sample that includes cells or cellular debris). The detectably labeled antibody (or other binding agent) may be used to select (for or against) the presence of certain granulocyte cell

types in a cell preparation (e.g., via a cell sorting technique such as FACS). Accordingly, granulocyte or cell preparations may be enriched or depleted for one or more granulocyte subtypes (e.g., basophil, neutrophil, or eosinophil) or mast cells using methods of the invention. In one embodiment, stem cell preparations may be enriched or depleted for one or more types of granulocyte or granulocyte precursor using one or more granulocyte-selective markers described herein.

[0049] In another aspect, markers of the invention may be used as targets for molecules that alter the function and development of certain granulocyte subtypes (e.g., may change their development path and direct them from one type of granulocyte to another, particularly for stem cells and other precursor cells).

[0050] In yet another aspect of the invention, one or more granulocyte-selective markers may be useful for therapeutic applications and particularly for cell type selective or specific therapies. This can be done by targeting one or more of the granulocyte-selective markers. Accordingly, one or more compounds that bind or interact with one or more cell type-specific markers may be used therapeutically. Treatment methods of the invention may be therapeutic (e.g., they reduce or cure symptoms of a disease) or prophylactic (e.g., they prevent symptoms of the disease).

[0051] The invention also provides for methods for selecting a course of treatment of a subject having or suspected of having a granulocyte disorder. In this aspect of the invention, the selection of the course of treatment involves determining the status of the granulocyte disorder in the subject. As used herein the "status" of a granulocyte disorder means the physiological stage or clinical condition of the cell, tissue, or the subject with the granulocyte disorder. It will be understood by those of ordinary skill that the status may reflect a number of different factors relating to the granulocyte disorder in the cell, tissue, or subject. These factors include, but are not limited to: the genotype of the cell, tissue, or subject, the genetic penetrance of the disorder, the length of time the disease has been manifested in the subject, and individual cell, tissue, and/or subject parameters that define the presentation of the granulocyte disorder in the cell, tissue, or subject. The status of the granulocyte disorder in a subject, cell, or tissue may change over time and thus the determination of a subject, cell, or tissue's status at a first time point may differ from the status of the cell, tissue, or subject's status at a second, subsequent time point.

[0052] The status of granulocyte disorder in a cell, tissue, or subject may be classified using general categories such as early-stage, mid-stage, or late-stage granulocyte disorder and the physiological manifestation of the granulocyte disorder may be generally classified as mild, medium, or severe, with various gradations in between. In some embodiments, the status of the disease means the level of pathogenesis from the disease. Thus, at early stages of a granulocyte disorder, pathogenesis may be mild or non-detectable and at mid and late stages the pathogenesis may be more pronounced. As used herein, the term "pathogenesis" means the clinical and physiological process and effects of the disease.

[0053] Accordingly, aspects of the invention may be used to treat any number of diseases including cancer, allergy, inflammation, infectious diseases, cardiovascular diseases, and other diseases associated with one or more leukocyte cell types (e.g., a mast cell and/or one or more granulocyte subtypes). Methods and compositions described herein in the context of mast cells and granulocytes may be applied to

other leukocytes and leukocyte-selective markers that are described in the following examples and figures. For example, one or more CD4⁺ and/or CD8⁺ selective cell markers (e.g., with a value of 1.5 or more, 2 or more, 3 or more, 4 or more, 5 or more, in the tables included in the figures) may be used as targets to develop drugs that inactivate CD4⁺ and/or CD8⁺ cells and are thereby useful to promote allograft tolerance (e.g., tolerance of cell tissue and/or organ transplants) and/or tolerance of an implanted medical device or artificial structure). In addition, to enhancing transplantation tolerance, methods and compositions that modulate CD4⁺, CD8⁺ and/or other leukocytes, may be useful to treat cancer, infection, allergy, and other diseases described herein.

EXAMPLE

[0054] In this study, we have used high density oligonucleotide probe array (GeneChip) to measure the expression levels of approximately 20,000 different transcripts in highly purified cells. These cells were basophils, eosinophils, neutrophils, monocytes (CD14⁺), T lymphocytes (CD4⁺ and CD8⁺ cells), B lymphocytes (CD19⁺), lung-derived mast cells, cord blood-derived cultured mast cells, and nasal polyp-derived fibroblasts. The GeneChip assay allows the simultaneous measurement of large numbers of transcripts using relatively small numbers of cells. Using this technology, we could even measure triplicate transcriptome levels of basophils, the most rare granulocytes in peripheral blood.

[0055] Cell type-selective transcripts were selected based on the following criteria; (1) the average "normalized AD" expression level of each gene in a certain cell type must be 3-fold or greater than the maximal level in other cell types, and (2) must be significantly ($p < 0.01$) greater than that in other cell types. (3) The "AD" expression level provided with "absence" or "marginal" call by GeneChip Suite Software should be observed only once or not at all in the three or four independent experiments (3 experiments for basophils, 4 experiments for eosinophils and neutrophils) using different cell populations performed. (4) For the transcripts preferentially expressed for the two different cell types such as basophils and eosinophils, the average "normalized AD" expression levels in the two cell types should be within 3-fold of each other. Using these standards, we found 83 basophil-selective, 37 eosinophil-selective, 257 neutrophil-selective, 34 basophil-eosinophil-selective, 19 eosinophil-neutrophil-selective, and 17 basophil-neutrophil-selective transcripts. Due to the functional similarity with basophils, mast cell-selective transcripts were also examined, and 63 mast cell-selective and 11 mast cell-basophil-selective transcripts were also detected (Table 1, and FIGS. 6A-6R). Since mast cells, basophils and eosinophils play similar roles in allergic inflammation, the transcripts preferentially expressed for the three granulocytes by comparing their average "normalized AD" levels to other leukocytes. Thirty-four transcripts were then selected; however, most of them were overlapped with the transcripts listed in FIGS. 6A-6R. Only four transcripts (MYB, SAMS1, BACE2, and CASP3) were found not overlapped, and they were not receptors or ion channels.

[0056] Among the 491 granulocyte-selective transcripts listed in FIGS. 6A-6R, 4 ion channels, 19 GPR and 28 other receptors were further selected (FIG. 3). When plural transcripts obtained by different probe sets had identical Genbank or Unigene accession numbers (<http://www.ncbi.nlm.nih.gov/>), the transcript showing the highest expression level was selected.

Ion Channels and Receptors Preferentially Expressed by Granulocytes other than Neutrophils

[0057] Eosinophils, basophils and mast cells play an important role in the pathogenesis of allergic diseases, but do not play an essential role in killing microbes except for nematodes. On the other hand, neutrophils play a crucial role in killing microbes such as bacteria. Caution should be taken in regulating neutrophil function even in the case of neutrophil-induced inflammation. Therefore, the molecules present only in granulocytes except for neutrophils would be important pharmaceutical targets for allergic disorders.^{1,2}

[0058] Among the 51 granulocyte-selective transcripts for ion channels and receptors, we identified 17 granulocyte-selective transcripts that have not been reported for their selective expression (shown in bold letters in FIG. 3). Of these 17 transcripts, eight were preferentially expressed by granulocytes other than neutrophils. Among these eight transcripts, the two transcripts for fibroblast growth factor receptor 2 and low density lipoprotein receptor were found to be expressed by multiple tissue cell types (shown at the Web site http://www.lsbm.org/index_e.html), which displays genomic expression of 55 different human tissue cells such as brain, heart and lung cells using the same experimental system. Affymetrix, U133A as ourts. Thus, they may not be suitable as a drug target because important organs that are unrelated to allergic inflammation (such as the brain) express it. Among the six novel transcripts found to be preferentially expressed by granulocytes except for neutrophils, we focus on the following four transcripts expressed by granulocytes including basophils. They were Ca²⁺ channel (CACNA1D), a prostaglandin E receptor, (EP3A2), epidermal growth factor-like module-containing mucin-like receptor (EMR) 1 (EMR1), and HTm4 (MS4A3).

[0059] Basophils are the rarest granulocytes present in human peripheral blood and as such their complete transcriptional profiles remain unclear and no basophil-selective transcripts have previously been reported.²¹ Although eosinophils and mast cells have been considered as important therapeutic targets for allergic diseases for a long time, recent studies suggest the importance of basophils in pathogenesis of severe allergic diseases such as fatal asthma.^{2,22} Therefore, we further examined the selective expression of these four basophil-, or basophil-eosinophil-selective transcripts by using real-time RT-PCR. As shown in the FIG. 1, including a known molecule preferentially expressed by neutrophils, aquaporin 9,²³ the results obtained with GeneChip assay were confirmed by using this highly accurate and reproducible method.²⁴

[0060] Among these four molecules, we could obtain a suitable antibody against HTm4, which is a member of a family of four transmembrane-proteins which include CD 20 and high affinity Fc receptor for IgE (FcεRI) β-chain.²⁵ Genetics provided evidence for the existence of multiple loci relevant to atopic asthma on chromosome 11q13, including HTm4.²⁶ Most recently, we have published data identifying HTm4 as a hematopoietic cell cycle regulator.²⁷ Using specific antibody against HTm4, we could detect the expression of HTm4 at the protein level in basophils (FIG. 2). To confirm whether these ion channels and receptors could be potential drug targets for diseases involving basophil activation, the amount of molecules expressed by various cell types should be quantified and the effect of any identified antagonists should be tested on the cell types found to express these molecules.

[0061] As has been well documented and expected, Fc ε RI β, IL-3 receptors, IL-5 receptors, chemokine receptor CCR3,^{1,2} sialic acid binding Ig-like lectin (Siglec)-8,²⁸ Siglec-6,¹⁵ histamine H4 receptor²⁹ and chemoattractant receptor-homologous molecule expressed on Th2 cells (CRTH2)³⁰ were preferentially expressed by basophils and/or eosinophils or mast cells. These consistent observations strengthened the reliability of the present methods and research strategy. Indeed, the antibody against Siglec-8 can induce selective apoptosis of eosinophils, and is expected to be useful therapeutically.²⁸

Ion Channels and Receptors Preferentially Expressed by Granulocytes Including Neutrophils

[0062] Of the 17 transcripts that have not been reported as granulocyte-selective, nine were preferentially expressed by granulocytes including neutrophils. Pharmaceutical targets of selective granulocyte transcripts should treat inflammatory diseases without affecting the function of important organs that are unrelated to inflammation as well as the function of lymphocytes. However, four of the nine neutrophil-selective transcripts were expressed by multiple organ tissues. One of the four neutrophil-selective transcripts encoded proteinase-activated receptor (PAR)-2, a receptor for mast cell tryptase, which is linked to the pathogenesis of allergic diseases such as asthma.^{31,32} PAR-2 transcripts are also abundantly expressed by tissue types including skin and intestine which are often the target organs for allergic diseases. But the development of PAR-2 antagonists for use as anti-allergic drugs may be unsuitable because it may down regulate neutrophil function and thereby induce bacterial infection.

General Discussion

[0063] We identified 51 granulocyte-selective genes for ion channels and receptors by examining approximately 20,000 kinds of transcripts derived from 16,000 genes from 10 different types of cells using U133A GeneChip, which covers approximately half of the genes present in the human genome. The majority of these transcripts encoded molecules known or expected to be granulocyte subtype-selective such as the IL-3 receptor and Fc ε receptors.

[0064] Mast cells expressed low levels of Fc ε RI α compared to basophils, and that even neutrophils expressed a substantial level of the receptor (FIG. 3). This raises the possibility that GeneChip assay may not be suitable for detecting selective molecules. In the present study, however, only the GeneChip data obtained using cord blood-derived mast cells and lung mast cells could be employed due to the strict data selection based on the RNA quality (see Methods). As has been reported,^{14,33} peripheral blood-derived cultured mast cells or skin-derived mast cells expressed approximately 10-fold Fc ε RI α mRNA compared to cord blood-derived mast cells (data not shown). Also, as shown in FIGS. 6A-6R, only 2 of the 4 neutrophil samples expressed Fc ε RI α mRNA. This may be explained by the observation that only neutrophils obtained from some allergic donors express the molecule.³⁴

[0065] We unexpectedly found 17 granulocyte-selective transcripts including HTm4. Basophil- and/or eosinophil-selective transcripts identified in our study could be potential

therapeutic targets for allergic diseases because these granulocytes play a crucial role in allergic inflammation.^{1,2} Granulocyte-selective transcripts could also be drug targets for other inflammatory diseases such as systemic vasculitis.^{3,4} Analysis of cell type-selective transcripts from database searches is expected to minimize the efforts required for drug discovery. The public database (http://www.lsbm.org/index_e.html) shows that some granulocyte-selective transcripts (18 out of 51) detected in our study are abundantly expressed by multiple (more than 3) organ tissue cell types using the same GeneChip U133A probe array. Thus, the safety of any candidate drug must be evaluated by comparing its efficacy (on granulocytes) with its toxicity (to organs). Six out of the 17 novel granulocyte-selective molecules may be excluded from drug development due to their expression in multiple organs unrelated to the diseases. Thus, our approach has identified 11 receptors and ion channels with therapeutic potential. Especially, among the 11 receptors and ion channels, seven were basophil- and/or eosinophil-selective and were not expressed by other organs, indicating that they may be potential targets for anti-allergic drugs.

[0066] Finally, it should be stressed that basophils, the rarest leukocytes, have recently been found to play a more crucial role than we ever proposed in the pathogenesis of intractable allergic diseases such as fatal asthma.^{35,36} Thus, targeting basophil receptors and ion channels such as HTm4 and Ca²⁺ channel CACNA1D is particularly expected for the future drug discovery. The importance of molecules known to be expressed by basophils may be reevaluated regarding its selectivity. Freshly-isolated resting basophils expressed the highest level of IL-4 compared to other cell types. Because the basophil purification procedure requires more isolation steps, ex vivo manipulation may activate the cells. However, it should also be noted that basophils have been recently found as the major source of IL-4 at least in asthma models.^{37,38}

Materials and Methods

Purification of Leukocytes

[0067] All human subjects in this study provided written, informed consent, and the Ethical Review Boards at the relevant hospitals (National Center for Child Health and Development, and Jikei University School of Medicine) approved the study. The subjects used in this study were all healthy volunteers, especially having no allergic diseases.

[0068] Granulocytes and mononuclear cells were separated from venous blood of normal volunteers. Human basophils were semipurified by means of Percoll (Pharmacia, Uppsala, Sweden) density gradient centrifugation, and the cells were further purified by negative selection through use of a MACS Basophil Isolation Kit (Miltenyi BioTech, Bergisch-Gladbach, Germany), as described previously.¹⁷ Eosinophils were isolated by using Percoll (1.090 g/mL) density centrifugation. The eosinophils were further purified by negative selection with anti-CD16-bound micromagnetic beads, as described previously. Neutrophils were isolated by using Percoll (1.085 g/mL) density centrifugation and further purified by negative selection using anti-CD81 antibody and antimouse IgG-bound micromagnetic beads to eliminate contaminating eosinophils. These granulocytes purified from human peripheral blood were spun down onto slide glass by Cytospin II (Shandon Southern Instruments, Inc., Sewickley, Pa.). The

purity of these cells was evaluated based on 500 cells stained with May-Grünwald and Giemsa solutions.

[0069] For preparation of lymphocytes and monocytes, peripheral blood mononuclear cells (PBMNC) were isolated by centrifugation on lymphocyte separation medium (Organon Teknica Corp., Durham, N.C.). Monocytes (CD14⁺ cells) were prepared using magnetic beads-conjugated CD14⁺ antibody (CD14 MicroBeads; Miltenyi Biotec) from PBMNC. CD4⁺ and CD8⁺ cells were also respectively sorted using magnetic beads-conjugated CD4⁺ (CD4 MicroBeads; Miltenyi Biotec) and CD8⁺ antibodies (CD8 MicroBeads; Miltenyi Biotec) from PBMNC after depletion of CD14⁺ cells with MACS CD14 MicroBeads (Miltenyi Biotec). The purity of CD4⁺, CD8⁺ and CD14⁺ cells was evaluated by staining the magnetic beads—conjugated cells compared to feasible control cell preparations such as unpurified cells with FITC-labeled goat anti-mouse Immunoglobulin (BD Pharmingen, Tokyo, Japan). Peripheral B cells were purified by a combination of negative (MicroBeads—conjugated antibodies to CD3, CD7, CD14, CD42b, and CD56; Miltenyi Biotec) and positive (CD19 MicroBeads; Miltenyi Biotec) selection using MicroBeads (Miltenyi Biotec). To obtain platelet rich plasma, blood samples were mixed with 3.8% (w/v) sodium citrate solution (9:1) and centrifuged at 260×g for 15 min. at 20° C. To remove any contaminating erythrocytes and leukocytes, the plasma was centrifuged again at 260×g for 15 min.

[0070] Human mast cells were derived from cord blood CD34⁺ progenitor cells as described previously.¹¹⁻¹⁴ Briefly, progenitor cells purified from peripheral blood by CD34⁺ isolation kits (Miltenyi Biotec), were cultured in Iscove's modified Dulbecco medium supplemented with 1% insulin-transferrin-selenium supplements (Life Technologies), 50 μM 2-mercaptoethanol, antibiotics, and 2% fetal calf serum in the presence of 100 ng/ml stem cell factor and 50 ng/ml IL-6. After 11 to 14 weeks of culture, tryptase positive cells represented more than 99% of the cells.

Purification of Human Lung Mast Cells and Nasal Polyp-derived Fibroblasts

[0071] Normal human lung tissue dissected during surgery was obtained macroscopically after informed consent. Human lung mast cells were dispersed from chopped lung specimens by an enzymatic procedure and were purified by magnetic bead affinity selection using the mAb anti-kit, YB5. B8 (BD PharMingen, San Diego, Calif.) as described previously.¹⁹ The cells were further cultured in the presence of SCF and interleukin 6 (IL-6) for several weeks. Human nasal polyp-derived fibroblasts were obtained as previously reported.²⁰

GeneChip Expression Analysis

[0072] Human genome-wide gene expression was examined using the Human Genome U133A probe array (GeneChip, Affymetrix, Santa Clara, Calif.), which contains the oligonucleotide probe set for 22,000 full-length genes. Experiments were performed in accordance with the manufacturer's protocol (Expression Analysis Technical Manual) and previous reports.¹¹⁻¹⁴ Total RNA (3-10 μg) was extracted from 10⁷ cells. Double-stranded cDNA was synthesized using a SuperScript Choice system (Life Technologies) and a T7-(dT)24 primer (Amersham Pharmacia Biotech, Bucking-

hamshire, UK). The cDNA was subjected to in vitro transcription in the presence of biotinylated nucleoside triphosphates using a BioArray high-yield RNA transcript labeling kit (Enzo Diagnostics, Farmingdale, N.Y.). The biotinylated cRNA was hybridized with a probe array for 16 h at 45°C. In some experiments as indicated in the supplementary table, biotinylated cRNA was prepared using two-cycles of cDNA synthesis and in vitro transcription for target amplification was performed according to the manufacturer's "The Small Sample Labeling Protocol version II" (Affymetrix, Inc). For the latter protocol, we employed 100 ng total RNA. After washing, the hybridized, biotinylated cRNA was stained with streptavidin-phycoerythrin (Molecular Probes, Eugene, Oreg.) and then scanned with a HP gene array scanner. The fluorescence intensity of each probe was quantified using a computer program, GeneChip Analysis Suite 5.0 (Affymetrix). The expression level of single mRNA was determined as the average fluorescence intensity among the intensities obtained by 11 paired (perfect-matched and single nucleotide-mismatched) probes. If the intensities of mismatched probes were very high, gene expression was judged to be absent, even if a high average fluorescence was obtained with the GeneChip Analysis Suite 5.0 program. The level of gene expression was determined as the average difference (AD) using the GeneChip software. Each AD level was then normalized by dividing it with the median value of 22,283 AD levels obtained in an experiment ("normalized AD" level).

Real-Time Reverse Transcriptase (RT)-PCR

[0073] Total RNA was isolated using Isogen (Nippon gene, Tokyo, Japan) according to the manufacturer's instructions and quantified by measuring the absorbance at 260 nm. RNA was subsequently treated with DNase I (Life Technologies) reverse transcribed using Superscript II reverse transcriptase (Life Technologies). Real-time RT-PCR was performed 10 ng cDNA in 25 µl of final volume using the primers and probes supplied by "Assays-on-Demand Gene Expression system" (PE Applied Biosystem) according to the manufacturer's instructions. Measurement of gene expression was performed using the ABI PRISM 7700 Sequence Detector. The expression level of each gene was normalized to a GAPDH.

Staining of Basophils with Anti-HTm4

[0074] Basophils purified from human peripheral blood with Basophil Isolation Kit (Miltenyi Biotec) were spun down onto slide glass by Cytospin II (Shandon Southern Instruments Inc., Sewickley, Pa.). Cells were fixed with acetone for 1 minute and then blocked in goat serum in 50 mm TRIS-Cl, pH 7.4 for 1 hour. Cells were further incubated for 2 hours with 2 µg/ml of the polyclonal antibody rabbit anti-HTm4. Cells were then washed three times with PBS and incubated with a secondary antibody, highly cross-adsorbed Alexa Fluor® 546-conjugated goat anti-rabbit IgG (H+L) (Red) (Molecular Probes, Eugene, Oreg.) for one hour. After three PBS washes, air dried cells were further mounted using the Prolong Anti-Fade Kit (Molecular Probes, Eugene, Oreg.). Slides were scanned by Zeiss Laser Scanning Microscope 5 Pascal (Carl Zeiss Microimaging Inc, Thornwood, N.Y.).

Purity and Viability of the Leukocytes, and RNA Quality

[0075] We used leukocyte samples in this study only if the purity of each cell type was at least 98%, but there are >0.5%

contaminated cells in any of the samples. We could not evaluate the purity of CD19⁺ cells and platelets due to lack of feasible controls or methods. However, specific transcript markers for non-granulocytes (CD4, CD8, CD14, CD19, IgG, etc.) as well as granulocyte subtype-specific transcripts were reasonably expressed by each leukocyte type as shown in FIGS. 6A-6R. Regarding the viability, we qualified the RNA before GeneChip assay using Array Quality Metrics Comparisons Software (Affymetrix) as well as trypan blue staining (they were always >95% viable), since RNase-rich granules derived from degenerating cells rapidly destroy RNA transcripts. Briefly, to evaluate the quality of RNA, the ratio of 3'-probe set and 5'-probe set of housekeeping genes were compared as shown in FIGS. 6A-6R. According to the above software's guidance, the ratio of >2:1 at standard sample (5 µg total RNA) protocol and that of >10:1 at small sample (50 ng total RNA) protocol were recommended. As shown in FIGS. 6A-6R, the cells used in the present study had the appropriate ratios of 3'-probe set and 5'-probe set of housekeeping genes, suggesting that these cells were highly viable.

Statistical Analysis

[0076] Since logarithmic "normalized AD" levels were normally distributed within each group, unpaired parametric Student's two-tailed t-test was employed to analyze the data on a logarithmic scale.

TABLE 1

Representative cell type-selective transcripts in granulocytes			
Accession # ^a	Transcript	S.I. ^b	Normalized AD level
<u>Basophil-selective</u>			
NM_000589.1	IL-4	73.3	13.3
L35848.1	HTm4	38.2	132.1
BC005912.1	Fc ε RI α	12.7	218.9
<u>Eosinophil-selective</u>			
NM_001140.1	Arachidonate 15-lipoxygenase	74.1	18.3
NM_024703.1	FLJ22593	19.1	29.1
NM_014442.1	Siglec-8	9.8	16.9
<u>Neutrophil-selective</u>			
NM_004633.1	IL-1 R, type II	127.9	51.5
U73191.1	inward rectifier K ⁺ channel Kir1.3	107.5	98
NM_001557.1	CXCR2 (IL-8 receptor β)	39.3	105.2
<u>Mast cell-selective</u>			
AF206667.1	tryptase β	84.3	159.4
NM_001911.1	cathepsin G	51.5	72.1
BC005929.1	major basic protein	31.6	72.5
<u>Basophil-eosinophil-selective</u>			
M75914.1	IL-5R α	42.8	19.4(B), 29.3(E)
NM_004778.1	CRTH2	16.6	23.9(B), 38.1(E)
NM_001828.3	Charcot-Leyden crystal protein	15.2	229.2(B), 198.6(E)
<u>Eosinophil-neutrophil-selective</u>			
NM_005306.1	GPR 43 (PAR1-like)	21.7	11.7(E), 32.9(N)
NM_004668.1	DHHC domain containing 18	6.6	16.2(E), 44.5(N)
<u>Basophil-neutrophil-selective</u>			
NM_016006.1	CGI-58 protein	5.8	12.6(B), 21.2(N)

TABLE 1-continued

Representative cell type-selective transcripts in granulocytes			
Accession # ^a	Transcript	S.I. ^b	Normalized AD level
Basophil-mast cell-selective			
NM_001870.1	carboxypeptidase A3	59.2	111.7(M), 137.3(B)
NM_002529.2	TRK neurotrophin receptor	34.7	3.1(M), 7 (B)
NM_000139.1	Fc ϵ RI β	21.2	22.2(M), 43.8(B)

^aThe GenBank accession number (<http://www.ncbi.nlm.nih.gov>).

^bSelectivity index (S.I.) was calculated by comparing the "normalized AD" level in a cell type or of two cell types with the maximal gene expression level of the other 8 or 9 cell types. The complete list of the genes having >3 S.I. is shown in Supplementary Table 1.

[0077] FIGS. 6A-6R show the complete list of granulocyte subtype-selective transcripts. Selectivity index (S.I.) was calculated by comparing the "normalized AD" level of a cell type or of two cell types with the maximal gene expression level of the other 8 or 9 cell types including platelets (P1), CD4⁺ cells (CD4), CD8⁺ cells (CD8), CD14⁺ cells (CD14), CD19⁺ cells (CD19) and nasal polyp-derived cultured fibroblasts (Fb). Transcripts having S.I. >3-fold were shown in FIGS. 6A-6R A-H. A. Basophil (Ba)-selective transcripts. B. Eosinophil (Eo)-selective transcripts. C. Neutrophil (Ne)-selective transcripts. D. Mast cell (MC)-selective transcripts. E. Basophil and eosinophil-selective transcripts. F. Eosinophil and neutrophil-selective transcripts. G. Basophil and neutrophil-selective transcripts. H Mast cell and basophil-selective transcripts. I. Raw AD levels for the median values used to normalize the raw AD levels, and the housekeeping genes. When the result was accompanied by presence call, it was shown as a bold numeral. Italic numerals show that the raw AD levels were associated with absence call by the GeneChip analysis software. 1. Abbreviations used in the tables were (small); the results obtained by the small sample protocol (see materials and methods), R; receptor, and ICN; ion channel.

REFERENCES

[0078] Useful techniques and compositions described in the references cited herein are incorporated herein by reference. In addition, U.S. Ser. No. 60/549,865, filed on Mar. 3, 2004, the benefit of the filing date of which is claimed under 35 U.S.C. §119(e), is incorporated herein by reference in its entirety.

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Asn	Val	Gly	Phe	Asp	Ser	Gly	Ile	Asp	Arg	Ile	Phe	Leu	Val	Ser	Pro	
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atc	act	ata	gtc	cat	gaa	ata	gat	gaa	gac	agt	cct	tta	tat	gat	ttg	1229
Ile	Thr	Ile	Val	His	Glu	Ile	Asp	Glu	Asp	Ser	Pro	Leu	Tyr	Asp	Leu	
			270					275						280		
agt	aaa	cag	gac	att	gac	aac	gca	gac	ttt	gaa	atc	gtg	gtc	ata	ctg	1277
Ser	Lys	Gln	Asp	Ile	Asp	Asn	Ala	Asp	Phe	Glu	Ile	Val	Val	Ile	Leu	
		285					290					295				
gaa	ggc	atg	gtg	gaa	gcc	act	gcc	atg	acg	aca	cag	tgc	cgt	agc	tct	1325
Glu	Gly	Met	Val	Glu	Ala	Thr	Ala	Met	Thr	Thr	Gln	Cys	Arg	Ser	Ser	
		300				305					310					
tat	cta	gca	aat	gaa	atc	ctg	tgg	ggc	cac	cgc	tat	gag	cct	gtg	ctc	1373

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atagtaatga	aaatgtctca	gtatttttagg	gtcaatgaga	gccataaaaa	tataacataa	3157
tcacaagtaa	aggagataat	ggctctaaac	agctatttcc	cttttctgtg	tgcatactta	3217
tgactgaatg	tgactgaagc	attttctcct	gtggagccct	agagcagggt	actaaggaag	3277
gacacattgt	ttccagaag	cctcccctgc	ctggctgact	gccttgctag	aaacataatt	3337
tttttttct	cactgaagct	caataatgga	actctttttt	ttttttttt	taatttaaag	3397
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aactgagggtg	ttattttcaa	tgaacaagaag	aaagagatgt	taagcaatg	gttgttttag	3697
atccaaatgt	aaaggcagg	ttgggaaggt	gtttaaagag	ttggaggaat	tggttgattga	3757
gttgtaaaga	aaacttacag	aagaggcaac	aatttggttc	ttgacagtga	gaggatattg	3817
agggtctcag	ctgctgctat	tatgatgttt	tgcaaggaa	aataatcaaa	ccaaagagta	3877
ttcagtgata	tgtaaattaa	atgaagatac	agtggagaat	gggggtgacc	acaaaagagg	3937
ctccccctaa	acacacagtg	ctgccactta	aaaagacttg	agaaatttga	aagggggtgg	3997
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tttttaaagt	gtacatttta	taaagtttat	cagatatttt	catatttaaa	gccaaatgta	4177
aatagaggtc	tgtaaagaaa	aataattgcc	atagaaagta	taatttcagt	gcagtaattt	4237
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tataagggtc	gtattgctat	gttcttctgt	tatttatctc	agcatggact	gttcatttga	4357
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acacatgtca	ttagaatgca	gacggagggg	actcaccatg	aatatctggg	gttgattccc	4597
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gattcctggt	tatcctat	ttaaacaaaa	tgtagacaaa	gtgaactcta	ttttgattat	4777
tgagaaaagga	gtagttttct	atccctctaa	gagtataact	gaatcagaca	ttttaaggat	4837
gtcactatgg	cactgtgtgc	atttccaaat	tcctagaaaa	gtttgtttta	ctttgttttt	4897
attctgttaa	tgcattcttt	cttctcttta	cttccctttc	taccagtaca	ctcctatctc	4957
aactctgttt	atgtgatgag	ttctgtcccc	taaatcatat	ttcccttaca	attaataaat	5017
gtcacttcat	attttataat	aaaccactca	gtaaaagcaa	aagcttgctc	tgagaagtag	5077
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gtttccgctc	tgggctctgg	caagttgaac	aatccctagc	attgacaatc	gtgatagtta	5257
ttattttccc	atgtgtgtgc	tttttgcata	taaagctctc	ctattgtact	gcacaaacca	5317
tggattgtac	atatttttat	atattatgct	ttattttatt	atctcctaat	aaaaaaatta	5377

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aaaattgaaa aaaaaaaaaa

5397

<210> SEQ ID NO 5

<211> LENGTH: 427

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 5

Met Gly Ser Val Arg Thr Asn Arg Tyr Ser Ile Val Ser Ser Glu Glu
 1 5 10 15

Asp Gly Met Lys Leu Ala Thr Met Ala Val Ala Asn Gly Phe Gly Asn
 20 25 30

Gly Lys Ser Lys Val His Thr Arg Gln Gln Cys Arg Ser Arg Phe Val
 35 40 45

Lys Lys Asp Gly His Cys Asn Val Gln Phe Ile Asn Val Gly Glu Lys
 50 55 60

Gly Gln Arg Tyr Leu Ala Asp Ile Phe Thr Thr Cys Val Asp Ile Arg
 65 70 75 80

Trp Arg Trp Met Leu Val Ile Phe Cys Leu Ala Phe Val Leu Ser Trp
 85 90 95

Leu Phe Phe Gly Cys Val Phe Trp Leu Ile Ala Leu Leu His Gly Asp
 100 105 110

Leu Asp Ala Ser Lys Glu Gly Lys Ala Cys Val Ser Glu Val Asn Ser
 115 120 125

Phe Thr Ala Ala Phe Leu Phe Ser Ile Glu Thr Gln Thr Thr Ile Gly
 130 135 140

Tyr Gly Phe Arg Cys Val Thr Asp Glu Cys Pro Ile Ala Val Phe Met
 145 150 155 160

Val Val Phe Gln Ser Ile Val Gly Cys Ile Ile Asp Ala Phe Ile Ile
 165 170 175

Gly Ala Val Met Ala Lys Met Ala Lys Pro Lys Lys Arg Asn Glu Thr
 180 185 190

Leu Val Phe Ser His Asn Ala Val Ile Ala Met Arg Asp Gly Lys Leu
 195 200 205

Cys Leu Met Trp Arg Val Gly Asn Leu Arg Lys Ser His Leu Val Glu
 210 215 220

Ala His Val Arg Ala Gln Leu Leu Lys Ser Arg Ile Thr Ser Glu Gly
 225 230 235 240

Glu Tyr Ile Pro Leu Asp Gln Ile Asp Ile Asn Val Gly Phe Asp Ser
 245 250 255

Gly Ile Asp Arg Ile Phe Leu Val Ser Pro Ile Thr Ile Val His Glu
 260 265 270

Ile Asp Glu Asp Ser Pro Leu Tyr Asp Leu Ser Lys Gln Asp Ile Asp
 275 280 285

Asn Ala Asp Phe Glu Ile Val Val Ile Leu Glu Gly Met Val Glu Ala
 290 295 300

Thr Ala Met Thr Thr Gln Cys Arg Ser Ser Tyr Leu Ala Asn Glu Ile
 305 310 315 320

Leu Trp Gly His Arg Tyr Glu Pro Val Leu Phe Glu Glu Lys His Tyr
 325 330 335

Tyr Lys Val Asp Tyr Ser Arg Phe His Lys Thr Tyr Glu Val Pro Asn
 340 345 350

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Thr Pro Leu Cys Ser Ala Arg Asp Leu Ala Glu Lys Lys Tyr Ile Leu
 355 360 365
 Ser Asn Ala Asn Ser Phe Cys Tyr Glu Asn Glu Val Ala Leu Thr Ser
 370 375 380
 Lys Glu Glu Asp Asp Ser Glu Asn Gly Val Pro Glu Ser Thr Ser Thr
 385 390 395 400
 Asp Thr Pro Pro Asp Ile Asp Leu His Asn Gln Ala Ser Val Pro Leu
 405 410 415
 Glu Pro Arg Pro Leu Arg Arg Glu Ser Glu Ile
 420 425

<210> SEQ ID NO 6
 <211> LENGTH: 2344
 <212> TYPE: DNA
 <213> ORGANISM: Homo sapiens
 <220> FEATURE:
 <221> NAME/KEY: CDS
 <222> LOCATION: (208)..(1380)

<400> SEQUENCE: 6

gaaggcgtgg ctccctcccg ggcagtgag cctggcgccg ccgcgccgc gtcccagcag 60
 cggagtaggg cggcgctgc gcccgcacc atgggggcag cccagcccca gccgcggtaa 120
 acgcccgaact ccgcccgcgc ccgcccctgt ctgccccctc ccgctgcggc tctctggacg 180
 ccaccccctc ctcaoctega agccaac atg aag gag acc cgg ggc tac gga ggg 234
 Met Lys Glu Thr Arg Gly Tyr Gly Gly
 1 5
 gat gcc ccc ttc tgc acc cgc ctc aac cac tcc tac aca ggc atg tgg 282
 Asp Ala Pro Phe Cys Thr Arg Leu Asn His Ser Tyr Thr Gly Met Trp
 10 15 20 25
 gcg ccc gag cgt tcc gcc gag gcg cgg ggc aac ctc acg cgc cct cca 330
 Ala Pro Glu Arg Ser Ala Glu Ala Arg Gly Asn Leu Thr Arg Pro Pro
 30 35 40
 ggg tct ggc gag gat tgc gga tcg gtg tcc gtg gcc ttc ccg atc acc 378
 Gly Ser Gly Glu Asp Cys Gly Ser Val Ser Val Ala Phe Pro Ile Thr
 45 50 55
 atg ctg ctc act ggt ttc gtg ggc aac gca ctg gcc atg ctg ctc gtg 426
 Met Leu Leu Thr Gly Phe Val Gly Asn Ala Leu Ala Met Leu Leu Val
 60 65 70
 tcg cgc agc tac cgg cgc cgg gag agc aag cgc aag aag tcc ttc ctg 474
 Ser Arg Ser Tyr Arg Arg Arg Glu Ser Lys Arg Lys Lys Ser Phe Leu
 75 80 85
 ctg tgc atc ggc tgg ctg gcg ctc acc gac ctg gtc ggg cag ctt ctc 522
 Leu Cys Ile Gly Trp Leu Ala Leu Thr Asp Leu Val Gly Gln Leu Leu
 90 95 100 105
 acc acc ccg gtc gtc atc gtc gtg tac ctg tcc aag cag cgt tgg gag 570
 Thr Thr Pro Val Val Ile Val Val Tyr Leu Ser Lys Gln Arg Trp Glu
 110 115 120
 cac atc gac ccg tcg ggg cgg ctc tgc acc ttt ttc ggg ctg acc atg 618
 His Ile Asp Pro Ser Gly Arg Leu Cys Thr Phe Phe Gly Leu Thr Met
 125 130 135
 act gtt ttc ggg ctc tcc tcg ttg ttc atc gcc agc gcc atg gcc gtc 666
 Thr Val Phe Gly Leu Ser Ser Leu Phe Ile Ala Ser Ala Met Ala Val
 140 145 150
 gag cgg gcg ctg gcc atc agg gcg ccg cac tgg tat gcg agc cac atg 714
 Glu Arg Ala Leu Ala Ile Arg Ala Pro His Trp Tyr Ala Ser His Met
 155 160 165

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aag acg cgt gcc acc cgc gct gtg ctg ctc ggc gtg tgg ctg gcc gtg Lys Thr Arg Ala Thr Arg Ala Val Leu Leu Gly Val Trp Leu Ala Val 170 175 180 185	762
ctc gcc ttc gcc ctg ctg ccg gtg ctg ggc gtg ggc cag tac acc gtc Leu Ala Phe Ala Leu Leu Pro Val Leu Gly Val Gly Gln Tyr Thr Val 190 195 200	810
cag tgg ccc ggg acg tgg tgc ttc atc agc acc ggg cga ggg ggc aac Gln Trp Pro Gly Thr Trp Cys Phe Ile Ser Thr Gly Arg Gly Gly Asn 205 210 215	858
ggg act agc tct tcg cat aac tgg ggc aac ctt ttc ttc gcc tct gcc Gly Thr Ser Ser Ser His Asn Trp Gly Asn Leu Phe Phe Ala Ser Ala 220 225 230	906
ttt gcc ttc ctg ggg ctc ttg gcg ctg aca gtc acc ttt tcc tgc aac Phe Ala Phe Leu Gly Leu Leu Ala Leu Thr Val Thr Phe Ser Cys Asn 235 240 245	954
ctg gcc acc att aag gcc ctg gtg tcc cgc tgc cgg gcc aag gcc acg Leu Ala Thr Ile Lys Ala Leu Val Ser Arg Cys Arg Ala Lys Ala Thr 250 255 260 265	1002
gca tct cag tcc agt gcc cag tgg ggc cgc atc acg acc gag acg gcc Ala Ser Gln Ser Ser Ala Gln Trp Gly Arg Ile Thr Thr Glu Thr Ala 270 275 280	1050
att cag ctt atg ggg atc atg tgc gtg ctg tcg gtc tgc tgg tct ccg Ile Gln Leu Met Gly Ile Met Cys Val Leu Ser Val Cys Trp Ser Pro 285 290 295	1098
ctc ctg ata atg atg ttg aaa atg atc ttc aat cag aca tca gtt gag Leu Leu Ile Met Met Leu Lys Met Ile Phe Asn Gln Thr Ser Val Glu 300 305 310	1146
cac tgc aag aca cac acg gag aag cag aaa gaa tgc aac ttc ttc tta His Cys Lys Thr His Thr Glu Lys Gln Lys Glu Cys Asn Phe Phe Leu 315 320 325	1194
ata gct gtt cgc ctg gct tca ctg aac cag atc ttg gat cct tgg gtt Ile Ala Val Arg Leu Ala Ser Leu Asn Gln Ile Leu Asp Pro Trp Val 330 335 340 345	1242
tac ctg ctg tta aga aag atc ctt ctt cga aag ttt tgc cag atc agg Tyr Leu Leu Leu Arg Lys Ile Leu Leu Arg Lys Phe Cys Gln Ile Arg 350 355 360	1290
tac cac aca aac aac tat gea tcc agc tcc acc tcc tta ccc tgc cag Tyr His Thr Asn Asn Tyr Ala Ser Ser Ser Thr Ser Leu Pro Cys Gln 365 370 375	1338
tgt tcc tca acc ttg atg tgg agc gac cat ttg gaa aga taa Cys Ser Ser Thr Leu Met Trp Ser Asp His Leu Glu Arg 380 385 390	1380
tgaagaacg gagttggaca ttttattgca attcctgctt ccctgaattt gcatatttct	1440
tcccacctga gaaggataat tataatattt aatttggatt atttcttcat ttttatcttt	1500
ttattttaat gattgttttg tcagtaatac ccatggagat caactttatt attataatcc	1560
atgcctctga atattagagg gtttcttggg tgggattttg aatatgcatt taagaacggt	1620
gggaacaatt tcacagatga tgattggagg aaaagtgatg aaaagaaaga cctgtgttcc	1680
aggagttttc tccaacttca aacctttacg tgaatcttaa ccaaagtgga catctttaca	1740
tttcatgata gcttgctttt gcaatatgag ttgaaaaat cagtataagc ttatgatggt	1800
gaaaagtcaa catattgaga gtgataattc aattaatagg atatgaaactt aacgacatat	1860
aaaagataaa cttaacgaca tataaaagca aataagggca ggagggaatc gtgacaaaaa	1920
atatttgtgc ccaattataa ccaatgtttt agagatggtg tgtccctgtg gcttagcatg	1980

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gaactaaaag ttctaagtct caattctagt tatgtgtcat ttagtaactc aggaatctgc 2040
ttaattgtta tttctaagct tttgatgaca aaggagtgat gcagctaagg gcatccttgg 2100
agtgtcataa aaaacaattt tgaggttgaa tgattagctg ccagttagag tgataaaaaa 2160
atccaggtag gccttctgat tcacatgac caagtcagga tttcttaata tttcttttct 2220
ggcagcatat acaaaggcaa aattaataaa taacagttgt tgaataacaa actttattac 2280
gtttttataa aataaaagaa tctattttgt ctgtattaaa ataaaaagct ttgtggactt 2340
ctaa 2344

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<210> SEQ ID NO 7

<211> LENGTH: 390

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 7

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Met Lys Glu Thr Arg Gly Tyr Gly Gly Asp Ala Pro Phe Cys Thr Arg
1          5          10          15
Leu Asn His Ser Tyr Thr Gly Met Trp Ala Pro Glu Arg Ser Ala Glu
20         25         30
Ala Arg Gly Asn Leu Thr Arg Pro Gly Ser Gly Glu Asp Cys Gly
35         40         45
Ser Val Ser Val Ala Phe Pro Ile Thr Met Leu Leu Thr Gly Phe Val
50         55         60
Gly Asn Ala Leu Ala Met Leu Leu Val Ser Arg Ser Tyr Arg Arg Arg
65         70         75         80
Glu Ser Lys Arg Lys Lys Ser Phe Leu Leu Cys Ile Gly Trp Leu Ala
85         90         95
Leu Thr Asp Leu Val Gly Gln Leu Leu Thr Thr Pro Val Val Ile Val
100        105        110
Val Tyr Leu Ser Lys Gln Arg Trp Glu His Ile Asp Pro Ser Gly Arg
115        120        125
Leu Cys Thr Phe Phe Gly Leu Thr Met Thr Val Phe Gly Leu Ser Ser
130        135        140
Leu Phe Ile Ala Ser Ala Met Ala Val Glu Arg Ala Leu Ala Ile Arg
145        150        155        160
Ala Pro His Trp Tyr Ala Ser His Met Lys Thr Arg Ala Thr Arg Ala
165        170        175
Val Leu Leu Gly Val Trp Leu Ala Val Leu Ala Phe Ala Leu Leu Pro
180        185        190
Val Leu Gly Val Gly Gln Tyr Thr Val Gln Trp Pro Gly Thr Trp Cys
195        200        205
Phe Ile Ser Thr Gly Arg Gly Gly Asn Gly Thr Ser Ser Ser His Asn
210        215        220
Trp Gly Asn Leu Phe Phe Ala Ser Ala Phe Ala Phe Leu Gly Leu Leu
225        230        235        240
Ala Leu Thr Val Thr Phe Ser Cys Asn Leu Ala Thr Ile Lys Ala Leu
245        250        255
Val Ser Arg Cys Arg Ala Lys Ala Thr Ala Ser Gln Ser Ser Ala Gln
260        265        270
Trp Gly Arg Ile Thr Thr Glu Thr Ala Ile Gln Leu Met Gly Ile Met
275        280        285

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Cys Val Leu Ser Val Cys Trp Ser Pro Leu Leu Ile Met Met Leu Lys
 290 295 300

Met Ile Phe Asn Gln Thr Ser Val Glu His Cys Lys Thr His Thr Glu
 305 310 315 320

Lys Gln Lys Glu Cys Asn Phe Phe Leu Ile Ala Val Arg Leu Ala Ser
 325 330 335

Leu Asn Gln Ile Leu Asp Pro Trp Val Tyr Leu Leu Leu Arg Lys Ile
 340 345 350

Leu Leu Arg Lys Phe Cys Gln Ile Arg Tyr His Thr Asn Asn Tyr Ala
 355 360 365

Ser Ser Ser Thr Ser Leu Pro Cys Gln Cys Ser Ser Thr Leu Met Trp
 370 375 380

Ser Asp His Leu Glu Arg
 385 390

<210> SEQ ID NO 8
 <211> LENGTH: 3150
 <212> TYPE: DNA
 <213> ORGANISM: Homo sapiens
 <220> FEATURE:
 <221> NAME/KEY: CDS
 <222> LOCATION: (39)..(2699)

<400> SEQUENCE: 8

aaaagtttct tttctttgaa tgacagaact acagcata atg cgt ggc ttc aac ctg 56
 Met Arg Gly Phe Asn Leu
 1 5

ctc ctc ttc tgg gga tgt tgt gtt atg cac agc tgg gaa ggg cac ata 104
 Leu Leu Phe Trp Gly Cys Cys Val Met His Ser Trp Glu Gly His Ile
 10 15 20

aga ccc aca cgg aaa cca aac aca aag ggt aat aac tgt aga gac agt 152
 Arg Pro Thr Arg Lys Pro Asn Thr Lys Gly Asn Asn Cys Arg Asp Ser
 25 30 35

acc ttg tgc cca gct tat gcc acc tgc acc aat aca gtg gac agt tac 200
 Thr Leu Cys Pro Ala Tyr Ala Thr Cys Thr Asn Thr Val Asp Ser Tyr
 40 45 50

tat tgc gct tgc aaa caa ggc ttc ctg tcc agc aat ggg caa aat cac 248
 Tyr Cys Ala Cys Lys Gln Gly Phe Leu Ser Ser Asn Gly Gln Asn His
 55 60 65 70

ttc aag gat cca gga gtg cga tgc aaa gat att gat gaa tgt tct caa 296
 Phe Lys Asp Pro Gly Val Arg Cys Lys Asp Ile Asp Glu Cys Ser Gln
 75 80 85

agc ccc cag ccc tgt ggt cct aac tca tcc tgc aaa aac ctg tca ggg 344
 Ser Pro Gln Pro Cys Gly Pro Asn Ser Ser Cys Lys Asn Leu Ser Gly
 90 95 100

agg tac aag tgc agc tgt tta gat ggt ttc tct tct ccc act gga aat 392
 Arg Tyr Lys Cys Ser Cys Leu Asp Gly Phe Ser Ser Pro Thr Gly Asn
 105 110 115

gac tgg gtc cca gga aag ccg ggc aat ttc tcc tgt act gat atc aat 440
 Asp Trp Val Pro Gly Lys Pro Gly Asn Phe Ser Cys Thr Asp Ile Asn
 120 125 130

gag tgc ctc acc agc agc gtc tgc cct gag cat tct gac tgt gtc aac 488
 Glu Cys Leu Thr Ser Ser Val Cys Pro Glu His Ser Asp Cys Val Asn
 135 140 145 150

tcc atg gga agc tac agt tgc agc tgt caa gtt gga ttc atc tct aga 536
 Ser Met Gly Ser Tyr Ser Cys Ser Cys Gln Val Gly Phe Ile Ser Arg
 155 160 165

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aac tcc acc tgt gaa gac gtg gat gaa tgt gca gat cca aga gct tgc	584
Asn Ser Thr Cys Glu Asp Val Asp Glu Cys Ala Asp Pro Arg Ala Cys	
170 175 180	
cca gag cat gca act tgt aat aac act gtt gga aac tac tct tgt ttc	632
Pro Glu His Ala Thr Cys Asn Asn Thr Val Gly Asn Tyr Ser Cys Phe	
185 190 195	
tgc aac cca gga ttt gaa tcc agc agt ggc cac ttg agt ttc cag ggt	680
Cys Asn Pro Gly Phe Glu Ser Ser Ser Gly His Leu Ser Phe Gln Gly	
200 205 210	
ctc aaa gca tcg tgt gaa gat att gat gaa tgc act gaa atg tgc ccc	728
Leu Lys Ala Ser Cys Glu Asp Ile Asp Glu Cys Thr Glu Met Cys Pro	
215 220 225 230	
atc aat tca aca tgc acc aac act cct ggg agc tac ttt tgc acc tgc	776
Ile Asn Ser Thr Cys Thr Asn Thr Pro Gly Ser Tyr Phe Cys Thr Cys	
235 240 245	
cac cct ggc ttt gca cca agc aat gga cag ttg aat ttc aca gac caa	824
His Pro Gly Phe Ala Pro Ser Asn Gly Gln Leu Asn Phe Thr Asp Gln	
250 255 260	
gga gtg gaa tgt aga gat att gat gag tgc cgc caa gat cca tca acc	872
Gly Val Glu Cys Arg Asp Ile Asp Glu Cys Arg Gln Asp Pro Ser Thr	
265 270 275	
tgt ggt cct aat tct atc tgc acc aat gcc ctg ggc tcc tac agc tgt	920
Cys Gly Pro Asn Ser Ile Cys Thr Asn Ala Leu Gly Ser Tyr Ser Cys	
280 285 290	
ggc tgc att gca ggc ttt cat ccc aat cca gaa ggc tcc cag aaa gat	968
Gly Cys Ile Ala Gly Phe His Pro Asn Pro Glu Gly Ser Gln Lys Asp	
295 300 305 310	
ggc aac ttc agc tgc caa agg gtt ctc ttc aaa tgt aag gaa gat gtg	1016
Gly Asn Phe Ser Cys Gln Arg Val Leu Phe Lys Cys Lys Glu Asp Val	
315 320 325	
ata ccc gat aat aag cag atc cag caa tgc caa gag gga acc gca gtg	1064
Ile Pro Asp Asn Lys Gln Ile Gln Gln Cys Gln Glu Gly Thr Ala Val	
330 335 340	
aaa cct gca tat gtc tcc ttt tgt gca caa ata aat aac atc ttc agc	1112
Lys Pro Ala Tyr Val Ser Phe Cys Ala Gln Ile Asn Asn Ile Phe Ser	
345 350 355	
gtt ctg gac aaa gtg tgt gaa aat aaa acg acc gta gtt tct ctg aag	1160
Val Leu Asp Lys Val Cys Glu Asn Lys Thr Thr Val Val Ser Leu Lys	
360 365 370	
aat aca act gag agc ttt gtc cct gtg ctt aaa caa ata tcc acg tgg	1208
Asn Thr Thr Glu Ser Phe Val Pro Val Leu Lys Gln Ile Ser Thr Trp	
375 380 385 390	
act aaa ttc acc aag gaa gag acg tcc tcc ctg gcc aca gtc ttc ctg	1256
Thr Lys Phe Thr Lys Glu Glu Thr Ser Ser Leu Ala Thr Val Phe Leu	
395 400 405	
gag agt gtg gaa agc atg aca ctg gca tct ttt tgg aaa ccc tca gca	1304
Glu Ser Val Glu Ser Met Thr Leu Ala Ser Phe Trp Lys Pro Ser Ala	
410 415 420	
aat atc act ccg gct gtt cgg acg gaa tac tta gac att gag agc aaa	1352
Asn Ile Thr Pro Ala Val Arg Thr Glu Tyr Leu Asp Ile Glu Ser Lys	
425 430 435	
gtt atc aac aaa gaa tgc agt gaa gag aat gtg acg ttg gac ttg gta	1400
Val Ile Asn Lys Glu Cys Ser Glu Glu Asn Val Thr Leu Asp Leu Val	
440 445 450	
gcc aag ggg gat aag atg aag atc ggg tgt tcc aca att gag gaa tct	1448
Ala Lys Gly Asp Lys Met Lys Ile Gly Cys Ser Thr Ile Glu Glu Ser	
455 460 465 470	

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gaa tcc aca gag acc act ggt gtg gct ttt gtc tcc ttt gtg ggc atg Glu Ser Thr Glu Thr Thr Gly Val Ala Phe Val Ser Phe Val Gly Met 475 480 485	1496
gaa tcg gtt tta aat gag cgc ttc ttc aaa gac cac cag gct ccc ttg Glu Ser Val Leu Asn Glu Arg Phe Phe Lys Asp His Gln Ala Pro Leu 490 495 500	1544
acc acc tct gag atc aag ctg aag atg aat tct cga gtc gtt ggg ggc Thr Thr Ser Glu Ile Lys Leu Lys Met Asn Ser Arg Val Val Gly Gly 505 510 515	1592
ata atg act gga gag aag aaa gac ggc ttc tca gat cca atc atc tac Ile Met Thr Gly Glu Lys Lys Asp Gly Phe Ser Asp Pro Ile Ile Tyr 520 525 530	1640
act ctg gag aac att cag cca aag cag aag ttt gag agg ccc atc tgt Thr Leu Glu Asn Ile Gln Pro Lys Gln Lys Phe Glu Arg Pro Ile Cys 535 540 545 550	1688
gtt tcc tgg agc act gat gtg aag ggt gga aga tgg aca tcc ttt ggc Val Ser Trp Ser Thr Asp Val Lys Gly Gly Arg Trp Thr Ser Phe Gly 555 560 565	1736
tgt gtg atc ctg gaa gct tct gag aca tat acc atc tgc agc tgt aat Cys Val Ile Leu Glu Ala Ser Glu Thr Tyr Thr Ile Cys Ser Cys Asn 570 575 580	1784
cag atg gca aat ctt gcc gtt atc atg gcg tct ggg gag ctc acg atg Gln Met Ala Asn Leu Ala Val Ile Met Ala Ser Gly Glu Leu Thr Met 585 590 595	1832
gac ttt tcc ttg tac atc att agc cat gta ggc att atc atc tcc ttg Asp Phe Ser Leu Tyr Ile Ile Ser His Val Gly Ile Ile Ile Ser Leu 600 605 610	1880
gtg tgc ctc gtc ttg gcc atc gcc acc ttt ctg ctg tgt cgc tcc atc Val Cys Leu Val Leu Ala Ile Ala Thr Phe Leu Leu Cys Arg Ser Ile 615 620 625 630	1928
cga aat cac aac acc tac ctc cac ctg cac ctc tgc gtg tgt ctc ctc Arg Asn His Asn Thr Tyr Leu His Leu His Leu Cys Val Cys Leu Leu 635 640 645	1976
ttg gcg aag act ctc ttc ctc gcc ggt ata cac aag act gac aac aag Leu Ala Lys Thr Leu Phe Leu Ala Gly Ile His Lys Thr Asp Asn Lys 650 655 660	2024
atg ggc tgc gcc atc atc gcg ggc ttc ctg cac tac ctt ttc ctt gcc Met Gly Cys Ala Ile Ile Ala Gly Phe Leu His Tyr Leu Phe Leu Ala 665 670 675	2072
tgc ttc ttc tgg atg ctg gtg gag gct gtg ata ctg ttc ttg atg gtc Cys Phe Phe Trp Met Leu Val Glu Ala Val Ile Leu Phe Leu Met Val 680 685 690	2120
aga aac ctg aag gtg gtg aat tac ttc agc tct cgc aac atc aag atg Arg Asn Leu Lys Val Val Asn Tyr Phe Ser Ser Arg Asn Ile Lys Met 695 700 705 710	2168
ctg cac atc tgt gcc ttt ggt tat ggg ctg ccg atg ctg gtg gtg gtg Leu His Ile Cys Ala Phe Gly Tyr Gly Leu Pro Met Leu Val Val Val 715 720 725	2216
atc tct gcc agt gtg cag cca cag ggc tat gga atg cat aat cgc tgc Ile Ser Ala Ser Val Gln Pro Gln Gly Tyr Gly Met His Asn Arg Cys 730 735 740	2264
tgg ctg aat aca gag aca ggg ttc atc tgg agt ttc ttg ggg cca gtt Trp Leu Asn Thr Glu Thr Gly Phe Ile Trp Ser Phe Leu Gly Pro Val 745 750 755	2312
tgc aca gtt ata gtg atc aac tcc ctt ctc ctg acc tgg acc ttg tgg Cys Thr Val Ile Val Ile Asn Ser Leu Leu Leu Thr Trp Thr Leu Trp 760 765 770	2360

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atc ctg agg cag agg ctt tcc agt gtt aat gcc gaa gtc tca acg cta	2408
Ile Leu Arg Gln Arg Leu Ser Ser Val Asn Ala Glu Val Ser Thr Leu	
775 780 785 790	
aaa gac acc agg tta ctg acc ttc aag gcc ttt gcc cag ctc ttc atc	2456
Lys Asp Thr Arg Leu Leu Thr Phe Lys Ala Phe Ala Gln Leu Phe Ile	
795 800 805	
ctg ggc tgc tcc tgg gtg ctg ggc att ttt cag att gga cct gtg gca	2504
Leu Gly Cys Ser Trp Val Leu Gly Ile Phe Gln Ile Gly Pro Val Ala	
810 815 820	
ggt gtc atg gct tac ctg ttc acc atc atc aac agc ctg cag ggg gcc	2552
Gly Val Met Ala Tyr Leu Phe Thr Ile Ile Asn Ser Leu Gln Gly Ala	
825 830 835	
ttc atc ttc ctc atc cac tgt ctg ctc aac gcc cag gta cga gaa gaa	2600
Phe Ile Phe Leu Ile His Cys Leu Leu Asn Gly Gln Val Arg Glu Glu	
840 845 850	
tac aag agg tgg atc act ggg aag acg aag ccc agc tcc cag tcc cag	2648
Tyr Lys Arg Trp Ile Thr Gly Lys Thr Lys Pro Ser Ser Gln Ser Gln	
855 860 865 870	
acc tca agg atc ttg ctg tcc tcc atg cca tcc gct tcc aag acg ggt	2696
Thr Ser Arg Ile Leu Leu Ser Ser Met Pro Ser Ala Ser Lys Thr Gly	
875 880 885	
taa agtctcttct tgctttcaaa tatgctatgg agccacagtt gaggacagta	2749
gtttcctgca ggagcctacc ctgaaatctc ttctcagctt aacatggaaa tgaggatccc	2809
accagcccca gaacctctg ggggaagaatg ttggggggeg tcttctgtg gttgtatgca	2869
ctgatgagaa atcaggcggt tctgctccaa acgaccattt tatcttctgtg ctctgcaact	2929
tcttcaattc cagagtttct gagaacagac ccaaattcaa tggcatgacc aagaacacct	2989
ggctaccatt ttgttttctc ctgcocttgt tgggtgcatgg ttctaagcat gccctccag	3049
agcctatcat acgctgata cagagaacct ctcaataaat gatttgtcgc ctgtctgact	3109
gatttacctc aggaaaaaaaa aaaaaaaaaa aaaaaaaaaa a	3150

<210> SEQ ID NO 9

<211> LENGTH: 886

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 9

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Ser Trp Glu Gly His Ile Arg Pro Thr Arg Lys Pro Asn Thr Lys Gly	
20 25 30	
Asn Asn Cys Arg Asp Ser Thr Leu Cys Pro Ala Tyr Ala Thr Cys Thr	
35 40 45	
Asn Thr Val Asp Ser Tyr Tyr Cys Ala Cys Lys Gln Gly Phe Leu Ser	
50 55 60	
Ser Asn Gly Gln Asn His Phe Lys Asp Pro Gly Val Arg Cys Lys Asp	
65 70 75 80	
Ile Asp Glu Cys Ser Gln Ser Pro Gln Pro Cys Gly Pro Asn Ser Ser	
85 90 95	
Cys Lys Asn Leu Ser Gly Arg Tyr Lys Cys Ser Cys Leu Asp Gly Phe	
100 105 110	
Ser Ser Pro Thr Gly Asn Asp Trp Val Pro Gly Lys Pro Gly Asn Phe	
115 120 125	

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Ser Cys Thr Asp Ile Asn Glu Cys Leu Thr Ser Ser Val Cys Pro Glu
 130 135 140

His Ser Asp Cys Val Asn Ser Met Gly Ser Tyr Ser Cys Ser Cys Gln
 145 150 155 160

Val Gly Phe Ile Ser Arg Asn Ser Thr Cys Glu Asp Val Asp Glu Cys
 165 170 175

Ala Asp Pro Arg Ala Cys Pro Glu His Ala Thr Cys Asn Asn Thr Val
 180 185 190

Gly Asn Tyr Ser Cys Phe Cys Asn Pro Gly Phe Glu Ser Ser Ser Gly
 195 200 205

His Leu Ser Phe Gln Gly Leu Lys Ala Ser Cys Glu Asp Ile Asp Glu
 210 215 220

Cys Thr Glu Met Cys Pro Ile Asn Ser Thr Cys Thr Asn Thr Pro Gly
 225 230 235 240

Ser Tyr Phe Cys Thr Cys His Pro Gly Phe Ala Pro Ser Asn Gly Gln
 245 250 255

Leu Asn Phe Thr Asp Gln Gly Val Glu Cys Arg Asp Ile Asp Glu Cys
 260 265 270

Arg Gln Asp Pro Ser Thr Cys Gly Pro Asn Ser Ile Cys Thr Asn Ala
 275 280 285

Leu Gly Ser Tyr Ser Cys Gly Cys Ile Ala Gly Phe His Pro Asn Pro
 290 295 300

Glu Gly Ser Gln Lys Asp Gly Asn Phe Ser Cys Gln Arg Val Leu Phe
 305 310 315 320

Lys Cys Lys Glu Asp Val Ile Pro Asp Asn Lys Gln Ile Gln Gln Cys
 325 330 335

Gln Glu Gly Thr Ala Val Lys Pro Ala Tyr Val Ser Phe Cys Ala Gln
 340 345 350

Ile Asn Asn Ile Phe Ser Val Leu Asp Lys Val Cys Glu Asn Lys Thr
 355 360 365

Thr Val Val Ser Leu Lys Asn Thr Thr Glu Ser Phe Val Pro Val Leu
 370 375 380

Lys Gln Ile Ser Thr Trp Thr Lys Phe Thr Lys Glu Glu Thr Ser Ser
 385 390 395 400

Leu Ala Thr Val Phe Leu Glu Ser Val Glu Ser Met Thr Leu Ala Ser
 405 410 415

Phe Trp Lys Pro Ser Ala Asn Ile Thr Pro Ala Val Arg Thr Glu Tyr
 420 425 430

Leu Asp Ile Glu Ser Lys Val Ile Asn Lys Glu Cys Ser Glu Glu Asn
 435 440 445

Val Thr Leu Asp Leu Val Ala Lys Gly Asp Lys Met Lys Ile Gly Cys
 450 455 460

Ser Thr Ile Glu Glu Ser Glu Ser Thr Glu Thr Thr Gly Val Ala Phe
 465 470 475 480

Val Ser Phe Val Gly Met Glu Ser Val Leu Asn Glu Arg Phe Phe Lys
 485 490 495

Asp His Gln Ala Pro Leu Thr Thr Ser Glu Ile Lys Leu Lys Met Asn
 500 505 510

Ser Arg Val Val Gly Gly Ile Met Thr Gly Glu Lys Lys Asp Gly Phe
 515 520 525

Ser Asp Pro Ile Ile Tyr Thr Leu Glu Asn Ile Gln Pro Lys Gln Lys

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530				535				540							
Phe	Glu	Arg	Pro	Ile	Cys	Val	Ser	Trp	Ser	Thr	Asp	Val	Lys	Gly	Gly
545				550				555							560
Arg	Trp	Thr	Ser	Phe	Gly	Cys	Val	Ile	Leu	Glu	Ala	Ser	Glu	Thr	Tyr
				565				570							575
Thr	Ile	Cys	Ser	Cys	Asn	Gln	Met	Ala	Asn	Leu	Ala	Val	Ile	Met	Ala
			580					585							590
Ser	Gly	Glu	Leu	Thr	Met	Asp	Phe	Ser	Leu	Tyr	Ile	Ile	Ser	His	Val
	595						600								605
Gly	Ile	Ile	Ile	Ser	Leu	Val	Cys	Leu	Val	Leu	Ala	Ile	Ala	Thr	Phe
	610					615					620				
Leu	Leu	Cys	Arg	Ser	Ile	Arg	Asn	His	Asn	Thr	Tyr	Leu	His	Leu	His
	625					630					635				640
Leu	Cys	Val	Cys	Leu	Leu	Leu	Ala	Lys	Thr	Leu	Phe	Leu	Ala	Gly	Ile
				645						650					655
His	Lys	Thr	Asp	Asn	Lys	Met	Gly	Cys	Ala	Ile	Ile	Ala	Gly	Phe	Leu
			660												670
His	Tyr	Leu	Phe	Leu	Ala	Cys	Phe	Phe	Trp	Met	Leu	Val	Glu	Ala	Val
			675												685
Ile	Leu	Phe	Leu	Met	Val	Arg	Asn	Leu	Lys	Val	Val	Asn	Tyr	Phe	Ser
	690					695									700
Ser	Arg	Asn	Ile	Lys	Met	Leu	His	Ile	Cys	Ala	Phe	Gly	Tyr	Gly	Leu
	705					710					715				720
Pro	Met	Leu	Val	Val	Val	Ile	Ser	Ala	Ser	Val	Gln	Pro	Gln	Gly	Tyr
				725							730				735
Gly	Met	His	Asn	Arg	Cys	Trp	Leu	Asn	Thr	Glu	Thr	Gly	Phe	Ile	Trp
				740											750
Ser	Phe	Leu	Gly	Pro	Val	Cys	Thr	Val	Ile	Val	Ile	Asn	Ser	Leu	Leu
			755												765
Leu	Thr	Trp	Thr	Leu	Trp	Ile	Leu	Arg	Gln	Arg	Leu	Ser	Ser	Val	Asn
			770												780
Ala	Glu	Val	Ser	Thr	Leu	Lys	Asp	Thr	Arg	Leu	Leu	Thr	Phe	Lys	Ala
						790					795				800
Phe	Ala	Gln	Leu	Phe	Ile	Leu	Gly	Cys	Ser	Trp	Val	Leu	Gly	Ile	Phe
				805											815
Gln	Ile	Gly	Pro	Val	Ala	Gly	Val	Met	Ala	Tyr	Leu	Phe	Thr	Ile	Ile
				820											830
Asn	Ser	Leu	Gln	Gly	Ala	Phe	Ile	Phe	Leu	Ile	His	Cys	Leu	Leu	Asn
				835											845
Gly	Gln	Val	Arg	Glu	Glu	Tyr	Lys	Arg	Trp	Ile	Thr	Gly	Lys	Thr	Lys
				850											860
Pro	Ser	Ser	Gln	Ser	Gln	Thr	Ser	Arg	Ile	Leu	Leu	Ser	Ser	Met	Pro
				865							875				880
Ser	Ala	Ser	Lys	Thr	Gly										
				885											

<210> SEQ ID NO 10
 <211> LENGTH: 2428
 <212> TYPE: DNA
 <213> ORGANISM: Homo sapiens
 <220> FEATURE:
 <221> NAME/KEY: CDS
 <222> LOCATION: (213)..(1229)

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<400> SEQUENCE: 10

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aaacgctcac tgggcaaac accttcactg aaaagagacc tcatattatg caaaaaaaat	180
cttaaaaggc ctctgccttc agaagttaca ag atg atc aat tca acc tcc aca	233
Met Ile Asn Ser Thr Ser Thr	
1 5	
cag cct cca gat gaa tcc tgc tct cag aac ctc ctg atc act cag cag	281
Gln Pro Pro Asp Glu Ser Cys Ser Gln Asn Leu Leu Ile Thr Gln Gln	
10 15 20	
atc att cct gtg ctg tac tgt atg gtc ttc att gca gga atc cta ctc	329
Ile Ile Pro Val Leu Tyr Cys Met Val Phe Ile Ala Gly Ile Leu Leu	
25 30 35	
aat gga gtg tca gga tgg ata ttc ttt tac gtg ccc agc tct gag agt	377
Asn Gly Val Ser Gly Trp Ile Phe Phe Tyr Val Pro Ser Ser Glu Ser	
40 45 50 55	
ttc atc atc tat ctc aag aac att gtt att gct gac ttt gtg atg agc	425
Phe Ile Ile Tyr Leu Lys Asn Ile Val Ile Ala Asp Phe Val Met Ser	
60 65 70	
ctg act ttt cct ttc aag atc ctt ggt gac tca ggc ctt ggt ccc tgg	473
Leu Thr Phe Pro Phe Lys Ile Leu Gly Asp Ser Gly Leu Gly Pro Trp	
75 80 85	
cag ctg aac gtg ttt gtg tgc agg gtc tct gcc gtg ctc ttc tac gtc	521
Gln Leu Asn Val Phe Val Cys Arg Val Ser Ala Val Leu Phe Tyr Val	
90 95 100	
aac atg tac gtc agc att gtg ttc ttt ggg ctc atc agc ttt gac aga	569
Asn Met Tyr Val Ser Ile Val Phe Phe Gly Leu Ile Ser Phe Asp Arg	
105 110 115	
tat tat aaa att gta aag cct ctt tgg act tct ttc atc cag tca gtg	617
Tyr Tyr Lys Ile Val Lys Pro Leu Trp Thr Ser Phe Ile Gln Ser Val	
120 125 130 135	
agt tac agc aaa ctt ctg tca gtg ata gta tgg atg ctc atg ctc ctc	665
Ser Tyr Ser Lys Leu Leu Ser Val Ile Val Trp Met Leu Met Leu Leu	
140 145 150	
ctt gct gtt cca aat att att ctc acc aac cag agt gtt agg gag gtt	713
Leu Ala Val Pro Asn Ile Ile Leu Thr Asn Gln Ser Val Arg Glu Val	
155 160 165	
aca caa ata aaa tgt ata gaa ctg aaa agt gaa ctg gga cgg aag tgg	761
Thr Gln Ile Lys Cys Ile Glu Leu Lys Ser Glu Leu Gly Arg Lys Trp	
170 175 180	
cac aaa gca tca aac tac atc ttc gtg gcc atc ttc tgg att gtg ttt	809
His Lys Ala Ser Asn Tyr Ile Phe Val Ala Ile Phe Trp Ile Val Phe	
185 190 195	
ctt ttg tta atc gtt ttc tat act gct atc aca aag aaa atc ttt aag	857
Leu Leu Leu Ile Val Phe Tyr Thr Ala Ile Thr Lys Lys Ile Phe Lys	
200 205 210 215	
tcc cac ctt aag tca agt cgg aat tcc act tcg gtc aaa aag aaa tct	905
Ser His Leu Lys Ser Ser Arg Asn Ser Thr Ser Val Lys Lys Lys Ser	
220 225 230	
agc cgc aac ata ttc agc atc gtg ttt gtg ttt ttt gtc tgt ttt gta	953
Ser Arg Asn Ile Phe Ser Ile Val Phe Val Phe Phe Val Cys Phe Val	
235 240 245	
cct tac cat att gcc aga atc ccc tac aca aag agt cag acc gaa gct	1001
Pro Tyr His Ile Ala Arg Ile Pro Tyr Thr Lys Ser Gln Thr Glu Ala	
250 255 260	

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cat tac agc tgc cag tca aaa gaa atc ttg cgg tat atg aaa gaa ttc 1049
His Tyr Ser Cys Gln Ser Lys Glu Ile Leu Arg Tyr Met Lys Glu Phe
   265                               270                               275

act ctg cta cta tct gct gca aat gta tgc ttg gac cct att att tat 1097
Thr Leu Leu Leu Ser Ala Ala Asn Val Cys Leu Asp Pro Ile Ile Tyr
 280                               285                               290                               295

ttc ttt cta tgc cag cgg ttt agg gaa atc tta tgt aag aaa ttg cac 1145
Phe Phe Leu Cys Gln Pro Phe Arg Glu Ile Leu Cys Lys Lys Leu His
                               300                               305                               310

att cca tta aaa gct cag aat gac cta gac att tcc aga atc aaa aga 1193
Ile Pro Leu Lys Ala Gln Asn Asp Leu Asp Ile Ser Arg Ile Lys Arg
                               315                               320                               325

gga aat aca aca ctt gaa agc aca gat act ttg tga gttcctaccc 1239
Gly Asn Thr Thr Leu Glu Ser Thr Asp Thr Leu
                               330                               335

tcttccaaag aaagaccacg tgtgcatggt gtcactttca attacataac agaaatcaat 1299

aagatatgtg ccctcatcat aaatatcatc tctagcactg ccatccaatt tagttcaata 1359

aaattcaaat ataagtttcc atgctttttt gtaacatcaa agaaaacata cccatcagta 1419

atttctctaa tactgacctt tctattctct attaataaaa aattaatata tacaattatt 1479

caattctatt atattaaaat aagttaaagt ttataaccac tagtctggtc agttaatgta 1539

gaaatttaaa tagtaataaa aacacaacat aatcaaagac aactcactca ggcattctct 1599

ttctctaaat accagaatct agtatgtaat tgttttcaac actgtcctta aagactaaact 1659

tgaagcagg cacagtttga tgaagggcta gagagctggt tgcaataaaa agtcaggttt 1719

tttctctgat ttgaagaagc aggaaaagct gacaccaga caatcactta agaaaccct 1779

tattgatgta tttcatggca ctgcaaagga agaggaatat taattgtata cttagcaaga 1839

aaattttttt tttctgatag cactttgagg atattagata catgctaaat atgttttcta 1899

caaagactta cgtcatttaa tgagcctggg gttctgggtg tagaatattt ttaagtaggc 1959

tttactgaga gaaactaaat attggcatac gttatcagca acttcccctg ttcaatagta 2019

tgggaaaaat aagatgactg ggaaaaagac acaccacac cgtagaacat atattaatct 2079

actggcgaat gggaaaggag accattttct tagaaagcaa ataaactga tttttttaa 2139

tctaaaattt acattaatga gtgcaaaata acacataaaa tgaaaattca cacatcacat 2199

tttctggaa aacagacgga ttttacttct ggagacatgg catacgggta ctgacttatg 2259

agctacaaaa actaaattct ttctctgcta ttaactggct agaagacatt catctatttt 2319

tcaaatgttc tttcaaaaca tttttataag taatgtttgt atctatttca tgctttactg 2379

tctatatact aataaagaaa tgttttaata ccgaaaaaaaa aaaaaaaaaa 2428
    
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<210> SEQ ID NO 11
<211> LENGTH: 338
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 11
    
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Met Ile Asn Ser Thr Ser Thr Gln Pro Pro Asp Glu Ser Cys Ser Gln
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Asn Leu Leu Ile Thr Gln Gln Ile Ile Pro Val Leu Tyr Cys Met Val
   20             25             30

Phe Ile Ala Gly Ile Leu Leu Asn Gly Val Ser Gly Trp Ile Phe Phe
    
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Asn	Glu	Thr	Ile	Gly	Phe	Phe	Tyr	Asn	Asn	Ser	Gly	Lys	Glu	Leu	Ser	
10					15					20					25	
tcc	cac	tgg	cgg	ccc	aag	gat	gtg	gtc	gtg	gtg	gca	ctg	ggg	ctg	acc	207
Ser	His	Trp	Arg	Pro	Lys	Asp	Val	Val	Val	Val	Ala	Leu	Gly	Leu	Thr	
				30					35					40		
gtc	agc	gtg	ctg	gtg	ctg	ctg	acc	aat	ctg	ctg	gtc	ata	gca	gcc	atc	255
Val	Ser	Val	Leu	Val	Leu	Leu	Thr	Asn	Leu	Leu	Val	Ile	Ala	Ala	Ile	
			45					50					55			
gcc	tcc	aac	cgc	cgc	ttc	cac	cag	ccc	atc	tac	tac	ctg	ctc	ggc	aat	303
Ala	Ser	Asn	Arg	Arg	Phe	His	Gln	Pro	Ile	Tyr	Tyr	Leu	Leu	Gly	Asn	
		60					65					70				
ctg	gcc	gcg	gct	gac	ctc	ttc	gcg	ggc	gtg	gcc	tac	ctc	ttc	ctc	atg	351
Leu	Ala	Ala	Ala	Asp	Leu	Phe	Ala	Gly	Val	Ala	Tyr	Leu	Phe	Leu	Met	
			75			80						85				
ttc	cac	act	ggt	ccc	cgc	aca	gcc	cga	ctt	tca	ctt	gag	ggc	tgg	ttc	399
Phe	His	Thr	Gly	Pro	Arg	Thr	Ala	Arg	Leu	Ser	Leu	Glu	Gly	Trp	Phe	
90					95					100					105	
ctg	cgg	cag	ggc	ttg	ctg	gac	aca	agc	ctc	act	gcg	tcg	gtg	gcc	aca	447
Leu	Arg	Gln	Gly	Leu	Leu	Asp	Thr	Ser	Leu	Thr	Ala	Ser	Val	Ala	Thr	
				110					115					120		
ctg	ctg	gcc	atc	gcc	gtg	gag	cgg	cac	cgc	agt	gtg	atg	gcc	gtg	cag	495
Leu	Leu	Ala	Ile	Ala	Val	Glu	Arg	His	Arg	Ser	Val	Met	Ala	Val	Gln	
			125					130					135			
ctg	cac	agc	cgc	ctg	ccc	cgt	ggc	cgc	gtg	gtc	atg	ctc	att	gtg	ggc	543
Leu	His	Ser	Arg	Leu	Pro	Arg	Gly	Arg	Val	Val	Met	Leu	Ile	Val	Gly	
		140					145					150				
gtg	tgg	gtg	gct	gcc	ctg	ggc	ctg	ggg	ctg	ctg	cct	gcc	cac	tcc	tgg	591
Val	Trp	Val	Ala	Ala	Leu	Gly	Leu	Gly	Leu	Leu	Pro	Ala	His	Ser	Trp	
	155				160						165					
cac	tgc	ctc	tgt	gcc	ctg	gac	cgc	tgc	tca	cgc	atg	gca	ccc	ctg	ctc	639
His	Cys	Leu	Cys	Ala	Leu	Asp	Arg	Cys	Ser	Arg	Met	Ala	Pro	Leu	Leu	
170					175					180					185	
agc	cgc	tcc	tat	ttg	gcc	gtc	tgg	gct	ctg	tcg	agc	ctg	ctt	gtc	ttc	687
Ser	Arg	Ser	Tyr	Leu	Ala	Val	Trp	Ala	Leu	Ser	Ser	Leu	Leu	Val	Phe	
			190						195					200		
ctg	ctc	atg	gtg	gct	gtg	tac	acc	cgc	att	ttc	ttc	tac	gtg	cgg	cgg	735
Leu	Leu	Met	Val	Ala	Val	Tyr	Thr	Arg	Ile	Phe	Phe	Tyr	Val	Arg	Arg	
			205					210					215			
cga	gtg	cag	cgc	atg	gca	gag	cat	gtc	agc	tgc	cac	ccc	cgc	tac	cga	783
Arg	Val	Gln	Arg	Met	Ala	Glu	His	Val	Ser	Cys	His	Pro	Arg	Tyr	Arg	
		220				225						230				
gag	acc	acg	ctc	agc	ctg	gtc	aag	act	ggt	gtc	atc	atc	ctg	ggg	gcg	831
Glu	Thr	Thr	Leu	Ser	Leu	Val	Lys	Thr	Val	Val	Ile	Ile	Leu	Gly	Ala	
		235				240					245					
ttc	gtg	gtc	tgc	tgg	aca	cca	ggc	cag	gtg	gta	ctg	ctc	ctg	gat	ggt	879
Phe	Val	Val	Cys	Trp	Thr	Pro	Gly	Gln	Val	Val	Leu	Leu	Leu	Asp	Gly	
250					255					260					265	
tta	ggc	tgt	gag	tcc	tgc	aat	gtc	ctg	gct	gta	gaa	aag	tac	ttc	cta	927
Leu	Gly	Cys	Glu	Ser	Cys	Asn	Val	Leu	Ala	Val	Glu	Lys	Tyr	Phe	Leu	
			270					275						280		
ctg	ttg	gcc	gag	gcc	aac	tca	ctg	gtc	aat	gct	gct	gtg	tac	tct	tgc	975
Leu	Leu	Ala	Glu	Ala	Asn	Ser	Leu	Val	Asn	Ala	Ala	Val	Tyr	Ser	Cys	
			285					290					295			
cga	gat	gct	gag	atg	cgc	cgc	acc	ttc	cgc	cgc	ctt	ctc	tgc	tgc	gcg	1023
Arg	Asp	Ala	Glu	Met	Arg	Arg	Thr	Phe	Arg	Arg	Leu	Leu	Cys	Cys	Ala	
		300					305					310				
tgc	ctc	cgc	cag	tcc	acc	cgc	gag	tct	gtc	cac	tat	aca	tcc	tct	gcc	1071

-continued

Cys	Leu	Arg	Gln	Ser	Thr	Arg	Glu	Ser	Val	His	Tyr	Thr	Ser	Ser	Ala		
315						320					325						
cag	gga	ggt	gcc	agc	act	cgc	atc	atg	ctt	ccc	gag	aac	ggc	cac	cca		1119
Gln	Gly	Gly	Ala	Ser	Thr	Arg	Ile	Met	Leu	Pro	Glu	Asn	Gly	His	Pro		
330					335					340					345		
ctg	atg	act	cca	ccc	ttt	agc	tac	ctt	gaa	ctt	cag	cgg	tac	gcg	gca		1167
Leu	Met	Thr	Pro	Pro	Phe	Ser	Tyr	Leu	Glu	Leu	Gln	Arg	Tyr	Ala	Ala		
				350					355						360		
agc	aac	aaa	tcc	aca	gcc	cct	gat	gac	ttg	tgg	gtg	ctc	ctg	gct	caa		1215
Ser	Asn	Lys	Ser	Thr	Ala	Pro	Asp	Asp	Leu	Trp	Val	Leu	Leu	Ala	Gln		
			365					370						375			
ccc	aac	caa	cag	gac	tga	ctgactggca	ggacaaggtc	tggcatggca									1263
Pro	Asn	Gln	Gln	Asp													
			380														
cagcaccact	gccaggcctc	cccaggcaca	ccactctgcc	cagggaatgg	gggctttggg												1323
tcactcctcca	ctgcctgggg	gagtcagatg	gggtgcagga	atctggctct	tcagccatct												1383
caggtttagg	gggtttgtaa	cagacattat	tctgttttca	ctgcgtatcc	ttgtaagcc												1443
ctgtggactg	gttcctgctg	tgtgatgctg	agggttttaa	ggtagggaga	gataagggct												1503
ctctcggggc	atgetacccg	gtatgactgg	gtaatgagga	cagactgtgg	acaccccatc												1563
tacctgagtc	tgattcttta	gcagcagaga	ctgaggggtg	cagagtgtga	gctgggaaag												1623
gtttgtggct	ccttgacagc	tccagggact	ggcctgtccc	caatagaatt	gaagcagtcc												1683
acggggaggg	gatgatacaa	ggagtaaacc	tttctttaca	ctcaaaaaa	a												1734

<210> SEQ ID NO 13
 <211> LENGTH: 382
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 13

Met	Val	Ile	Met	Gly	Gln	Cys	Tyr	Tyr	Asn	Glu	Thr	Ile	Gly	Phe	Phe		
1				5					10					15			
Tyr	Asn	Asn	Ser	Gly	Lys	Glu	Leu	Ser	Ser	His	Trp	Arg	Pro	Lys	Asp		
			20					25					30				
Val	Val	Val	Val	Ala	Leu	Gly	Leu	Thr	Val	Ser	Val	Leu	Val	Leu	Leu		
			35				40					45					
Thr	Asn	Leu	Leu	Val	Ile	Ala	Ala	Ile	Ala	Ser	Asn	Arg	Arg	Phe	His		
			50			55					60						
Gln	Pro	Ile	Tyr	Tyr	Leu	Leu	Gly	Asn	Leu	Ala	Ala	Ala	Asp	Leu	Phe		
65					70				75					80			
Ala	Gly	Val	Ala	Tyr	Leu	Phe	Leu	Met	Phe	His	Thr	Gly	Pro	Arg	Thr		
				85					90					95			
Ala	Arg	Leu	Ser	Leu	Glu	Gly	Trp	Phe	Leu	Arg	Gln	Gly	Leu	Leu	Asp		
			100					105					110				
Thr	Ser	Leu	Thr	Ala	Ser	Val	Ala	Thr	Leu	Leu	Ala	Ile	Ala	Val	Glu		
			115				120					125					
Arg	His	Arg	Ser	Val	Met	Ala	Val	Gln	Leu	His	Ser	Arg	Leu	Pro	Arg		
			130			135					140						
Gly	Arg	Val	Val	Met	Leu	Ile	Val	Gly	Val	Trp	Val	Ala	Ala	Leu	Gly		
145				150						155				160			
Leu	Gly	Leu	Leu	Pro	Ala	His	Ser	Trp	His	Cys	Leu	Cys	Ala	Leu	Asp		
				165				170						175			

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Arg Cys Ser Arg Met Ala Pro Leu Leu Ser Arg Ser Tyr Leu Ala Val
 180 185 190

Trp Ala Leu Ser Ser Leu Leu Val Phe Leu Leu Met Val Ala Val Tyr
 195 200 205

Thr Arg Ile Phe Phe Tyr Val Arg Arg Arg Val Gln Arg Met Ala Glu
 210 215 220

His Val Ser Cys His Pro Arg Tyr Arg Glu Thr Thr Leu Ser Leu Val
 225 230 235 240

Lys Thr Val Val Ile Ile Leu Gly Ala Phe Val Val Cys Trp Thr Pro
 245 250 255

Gly Gln Val Val Leu Leu Leu Asp Gly Leu Gly Cys Glu Ser Cys Asn
 260 265 270

Val Leu Ala Val Glu Lys Tyr Phe Leu Leu Leu Ala Glu Ala Asn Ser
 275 280 285

Leu Val Asn Ala Ala Val Tyr Ser Cys Arg Asp Ala Glu Met Arg Arg
 290 295 300

Thr Phe Arg Arg Leu Leu Cys Cys Ala Cys Leu Arg Gln Ser Thr Arg
 305 310 315 320

Glu Ser Val His Tyr Thr Ser Ser Ala Gln Gly Gly Ala Ser Thr Arg
 325 330 335

Ile Met Leu Pro Glu Asn Gly His Pro Leu Met Thr Pro Pro Phe Ser
 340 345 350

Tyr Leu Glu Leu Gln Arg Tyr Ala Ala Ser Asn Lys Ser Thr Ala Pro
 355 360 365

Asp Asp Leu Trp Val Leu Leu Ala Gln Pro Asn Gln Gln Asp
 370 375 380

<210> SEQ ID NO 14
 <211> LENGTH: 993
 <212> TYPE: DNA
 <213> ORGANISM: Homo sapiens
 <220> FEATURE:
 <221> NAME/KEY: CDS
 <222> LOCATION: (1)..(993)

<400> SEQUENCE: 14

atg ctg ccg gac tgg aag agc tcc ttg atc ctc atg gct tac atc atc	48
Met Leu Pro Asp Trp Lys Ser Ser Leu Ile Leu Met Ala Tyr Ile Ile	
1 5 10 15	
atc ttc ctc act ggc ctc cct gcc aac ctc ctg gcc ctg cgg gcc ttt	96
Ile Phe Leu Thr Gly Leu Pro Ala Asn Leu Leu Ala Leu Arg Ala Phe	
20 25 30	
gtg ggg cgg atc cgc cag ccc cag cct gca cct gtg cac atc ctc ctg	144
Val Gly Arg Ile Arg Gln Pro Gln Pro Ala Pro Val His Ile Leu Leu	
35 40 45	
ctg agc ctg acg ctg gcc gac ctc ctc ctg ctg ctg ctg ctg ccc ttc	192
Leu Ser Leu Thr Leu Ala Asp Leu Leu Leu Leu Leu Leu Leu Pro Phe	
50 55 60	
aag atc atc gag gct gcg tcg aac ttc cgc tgg tac ctg ccc aag gtc	240
Lys Ile Ile Glu Ala Ala Ser Asn Phe Arg Trp Tyr Leu Pro Lys Val	
65 70 75 80	
gtc tgc gcc ctc acg agt ttt ggc ttc tac agc agc atc tac tgc agc	288
Val Cys Ala Leu Thr Ser Phe Gly Phe Tyr Ser Ser Ile Tyr Cys Ser	
85 90 95	
acg tgg ctc ctg gcg gcc atc agc atc gag cgc tac ctg gga gtg gct	336
Thr Trp Leu Leu Ala Gly Ile Ser Ile Glu Arg Tyr Leu Gly Val Ala	

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100	105	110	
ttc ccc gtg cag tac aag ctg tcc cgc cgg cct ctg tat gga gtg att Phe Pro Val Gln Tyr Lys Leu Ser Arg Arg Pro Leu Tyr Gly Val Ile 115 120 125			384
gca gct ctg gtg gcc tgg gtt atg tcc ttt ggt cac tgc acc atc gtg Ala Ala Leu Val Ala Trp Val Met Ser Phe Gly His Cys Thr Ile Val 130 135 140			432
atc atc gtt caa tac ttg aac acg act gag cag gtc aga agt ggc aat Ile Ile Val Gln Tyr Leu Asn Thr Thr Glu Gln Val Arg Ser Gly Asn 145 150 155 160			480
gaa att acc tgc tac gag aac ttc acc gat aac cag ttg gac gtg gtg Glu Ile Thr Cys Tyr Glu Asn Phe Thr Asp Asn Gln Leu Asp Val Val 165 170 175			528
ctg ccc gtg cgg ctg gag ctg tgc ctg gtg ctc ttc ttc atc ccc atg Leu Pro Val Arg Leu Glu Leu Cys Leu Val Leu Phe Phe Ile Pro Met 180 185 190			576
gca gtc acc atc ttc tgc tac tgg cgt ttt gtg tgg atc atg ctc tcc Ala Val Thr Ile Phe Cys Tyr Trp Arg Phe Val Trp Ile Met Leu Ser 195 200 205			624
cag ccc ctt gtg ggg gcc cag agg cgg cgc cga gcc gtg ggg ctg gct Gln Pro Leu Val Gly Ala Gln Arg Arg Arg Arg Ala Val Gly Leu Ala 210 215 220			672
gtg gtg acg ctg ctc aat ttc ctg gtg tgc ttc gga cct tac aac gtg Val Val Thr Leu Leu Asn Phe Leu Val Cys Phe Gly Pro Tyr Asn Val 225 230 235 240			720
tcc cac ctg gtg ggg tat cac cag aga aaa agc ccc tgg tgg cgg tca Ser His Leu Val Gly Tyr His Gln Arg Lys Ser Pro Trp Trp Arg Ser 245 250 255			768
ata gcc gtg gtg ttc agt tca ctc aac gcc agt ctg gac ccc ctg ctc Ile Ala Val Val Phe Ser Ser Leu Asn Ala Ser Leu Asp Pro Leu Leu 260 265 270			816
ttc tat ttc tct tct tca gtg gtg cgc agg gca ttt ggg aga ggg ctg Phe Tyr Phe Ser Ser Ser Val Val Arg Arg Ala Phe Gly Arg Gly Leu 275 280 285			864
cag gtg ctg cgg aat cag ggc tcc tcc ctg ttg gga cgc aga ggc aaa Gln Val Leu Arg Asn Gln Gly Ser Ser Leu Leu Gly Arg Arg Gly Lys 290 295 300			912
gac aca gca gag ggg aca aat gag gac agg ggt gtg ggt caa gga gaa Asp Thr Ala Glu Gly Thr Asn Glu Asp Arg Gly Val Gly Gln Gly Glu 305 310 315 320			960
ggg atg cca agt tcg gac ttc act aca gag tag Gly Met Pro Ser Ser Asp Phe Thr Thr Glu 325 330			993
 <210> SEQ ID NO 15 <211> LENGTH: 330 <212> TYPE: PRT <213> ORGANISM: Homo sapiens <400> SEQUENCE: 15			
Met Leu Pro Asp Trp Lys Ser Ser Leu Ile Leu Met Ala Tyr Ile Ile 1 5 10 15			
Ile Phe Leu Thr Gly Leu Pro Ala Asn Leu Leu Ala Leu Arg Ala Phe 20 25 30			
Val Gly Arg Ile Arg Gln Pro Gln Pro Ala Pro Val His Ile Leu Leu 35 40 45			
Leu Ser Leu Thr Leu Ala Asp Leu Leu Leu Leu Leu Leu Leu Pro Phe			

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50	55	60
Lys 65	Ile Ile Glu Ala Ala Ser Asn Phe Arg Trp Tyr Leu Pro Lys Val 80	
	70	75
Val 85	Cys Ala Leu Thr Ser Phe Gly Phe Tyr Ser Ser Ile Tyr Cys Ser 95	
	85	90
Thr 100	Trp Leu Leu Ala Gly Ile Ser Ile Glu Arg Tyr Leu Gly Val Ala 110	
	100	105
Phe 115	Pro Val Gln Tyr Lys Leu Ser Arg Arg Pro Leu Tyr Gly Val Ile 125	
	115	120
Ala 130	Ala Leu Val Ala Trp Val Met Ser Phe Gly His Cys Thr Ile Val 140	
	130	135
Ile 145	Ile Val Gln Tyr Leu Asn Thr Thr Glu Gln Val Arg Ser Gly Asn 160	
	145	150
Glu 165	Ile Thr Cys Tyr Glu Asn Phe Thr Asp Asn Gln Leu Asp Val Val 175	
	165	170
Leu 180	Pro Val Arg Leu Glu Leu Cys Leu Val Leu Phe Phe Ile Pro Met 190	
	180	185
Ala 195	Val Thr Ile Phe Cys Tyr Trp Arg Phe Val Trp Ile Met Leu Ser 205	
	195	200
Gln 210	Pro Leu Val Gly Ala Gln Arg Arg Arg Arg Ala Val Gly Leu Ala 220	
	210	215
Val 225	Val Thr Leu Leu Asn Phe Leu Val Cys Phe Gly Pro Tyr Asn Val 240	
	225	230
Ser 245	His Leu Val Gly Tyr His Gln Arg Lys Ser Pro Trp Trp Arg Ser 255	
	245	250
Ile 260	Ala Val Val Phe Ser Ser Leu Asn Ala Ser Leu Asp Pro Leu Leu 270	
	260	265
Phe 275	Tyr Phe Ser Ser Ser Val Val Arg Arg Ala Phe Gly Arg Gly Leu 285	
	275	280
Gln 290	Val Leu Arg Asn Gln Gly Ser Ser Leu Leu Gly Arg Arg Gly Lys 300	
	290	295
Asp 305	Thr Ala Glu Gly Thr Asn Glu Asp Arg Gly Val Gly Gln Gly Glu 320	
	305	310
Gly 325	Met Pro Ser Ser Asp Phe Thr Thr Glu 330	
	325	330

<210> SEQ ID NO 16
 <211> LENGTH: 1287
 <212> TYPE: DNA
 <213> ORGANISM: Homo sapiens
 <220> FEATURE:
 <221> NAME/KEY: CDS
 <222> LOCATION: (72)..(1085)

<400> SEQUENCE: 16
 cctgtgtgcc acgtgtgga caaatcttaa ctctcaagg actccaaaa ccagagacac 60
 caggagcctg a atg ggg aac gat tct gtc agc tac gag tat ggg gat tac 110
 Met Gly Asn Asp Ser Val Ser Tyr Glu Tyr Gly Asp Tyr
 1 5 10
 agc gac ctc tgc gac cgc cct gtg gac tgc ctg gat ggc gcc tgc ctg 158
 Ser Asp Leu Ser Asp Arg Pro Val Asp Cys Leu Asp Gly Ala Cys Leu
 15 20 25
 gcc atc gac cgc ctg cgc gtg gcc ccg ctc cca ctg tat gcc gcc atc 206
 Ala Ile Asp Pro Leu Arg Val Ala Pro Leu Pro Leu Tyr Ala Ala Ile

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30	35	40	45	
ttc ctg gtg ggg gtg cgg ggc aat gcc atg gtg gcc tgg gtg gct ggg Phe Leu Val Gly Val Pro Gly Asn Ala Met Val Ala Trp Val Ala Gly	50	55	60	254
aag gtg gcc cgc cgg agg gtg ggt gcc acc tgg ttg ctc cac ctg gcc Lys Val Ala Arg Arg Arg Val Gly Ala Thr Trp Leu Leu His Leu Ala	65	70	75	302
gtg gcg gat ttg ctg tgc tgt ttg tct ctg ccc atc ctg gca gtg ccc Val Ala Asp Leu Leu Cys Cys Leu Ser Leu Pro Ile Leu Ala Val Pro	80	85	90	350
att gcc cgt gga ggc cac tgg cgg tat ggt gca gtg ggc tgt cgg gcg Ile Ala Arg Gly Gly His Trp Pro Tyr Gly Ala Val Gly Cys Arg Ala	95	100	105	398
ctg ccc tcc atc atc ctg ctg acc atg tat gcc agc gtc ctg ctc ctg Leu Pro Ser Ile Ile Leu Leu Thr Met Tyr Ala Ser Val Leu Leu Leu	110	115	120	446
gca gct ctc agt gcc gac ctc tgc ttc ctg gct ctc ggg cct gcc tgg Ala Ala Leu Ser Ala Asp Leu Cys Phe Leu Ala Leu Gly Pro Ala Trp	130	135	140	494
tgg tct acg gtt cag cgg gcg tgc ggg gtg cag gtg gcc tgt ggg gca Trp Ser Thr Val Gln Arg Ala Cys Gly Val Gln Val Ala Cys Gly Ala	145	150	155	542
gcc tgg aca ctg gcc ttg ctg ctc acc gtg ccc tcc gcc atc tac cgc Ala Trp Thr Leu Ala Leu Leu Thr Val Pro Ser Ala Ile Tyr Arg	160	165	170	590
cgg ctg cac cag gag cac ttc cca gcc cgg ctg cag tgt gtg gtg gac Arg Leu His Gln Glu His Phe Pro Ala Arg Leu Gln Cys Val Val Asp	175	180	185	638
tac ggc ggc tcc tcc agc acc gag aat gcg gtg act gcc atc cgg ttt Tyr Gly Gly Ser Ser Ser Thr Glu Asn Ala Val Thr Ala Ile Arg Phe	190	195	200	686
ctt ttt ggc ttc ctg ggg ccc ctg gtg gcc gtg gcc agc tgc cac agt Leu Phe Gly Phe Leu Gly Pro Leu Val Ala Val Ala Ser Cys His Ser	210	215	220	734
gcc ctc ctg tgc tgg gca gcc cga cgc tgc cgg ccg ctg gcc aca gcc Ala Leu Leu Cys Trp Ala Ala Arg Arg Cys Arg Pro Leu Gly Thr Ala	225	230	235	782
att gtg gtg ggg ttt ttt gtc tgc tgg gca ccc tac cac ctg ctg ggg Ile Val Val Gly Phe Phe Val Cys Trp Ala Pro Tyr His Leu Leu Gly	240	245	250	830
ctg gtg ctc act gtg gcg gcc cgg aac tcc gca ctc ctg gcc agg gcc Leu Val Leu Thr Val Ala Ala Pro Asn Ser Ala Leu Leu Ala Arg Ala	255	260	265	878
ctg cgg gct gaa ccc ctc atc gtg ggc ctt gcc ctc gct cac agc tgc Leu Arg Ala Glu Pro Leu Ile Val Gly Leu Ala Leu Ala His Ser Cys	270	275	280	926
ctc aat ccc atg ctc ttc ctg tat ttt ggg agg gct caa ctc cgc cgg Leu Asn Pro Met Leu Phe Leu Tyr Phe Gly Arg Ala Gln Leu Arg Arg	290	295	300	974
tca ctg cca gct gcc tgt cac tgg gcc ctg agg gag tcc cag gcc cag Ser Leu Pro Ala Ala Cys His Trp Ala Leu Arg Glu Ser Gln Gly Gln	305	310	315	1022
gac gaa agt gtg gac agc aag aaa tcc acc agc cat gac ctg gtc tcg Asp Glu Ser Val Asp Ser Lys Ser Thr Ser His Asp Leu Val Ser	320	325	330	1070
gag atg gag gtg tag gctggagaga cattgtgggt gtgtatcttc ttatctcatt Glu Met Glu Val				1125

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335
tcacaagact ggcttcaggc atagctggat ccaggagctc aatgatgtct tcattttatt 1185
ccttccttca ttcaacagat atccatcatg cacttgctat gtgcaaggcc tttttaggca 1245
ctagagatat agcagtgacc aaaacagaca caaatcctgc cc 1287

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<210> SEQ ID NO 17
<211> LENGTH: 337
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

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<400> SEQUENCE: 17

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Met Gly Asn Asp Ser Val Ser Tyr Glu Tyr Gly Asp Tyr Ser Asp Leu
1      5      10      15
Ser Asp Arg Pro Val Asp Cys Leu Asp Gly Ala Cys Leu Ala Ile Asp
20      25      30
Pro Leu Arg Val Ala Pro Leu Pro Leu Tyr Ala Ala Ile Phe Leu Val
35      40      45
Gly Val Pro Gly Asn Ala Met Val Ala Trp Val Ala Gly Lys Val Ala
50      55      60
Arg Arg Arg Val Gly Ala Thr Trp Leu Leu His Leu Ala Val Ala Asp
65      70      75      80
Leu Leu Cys Cys Leu Ser Leu Pro Ile Leu Ala Val Pro Ile Ala Arg
85      90      95
Gly Gly His Trp Pro Tyr Gly Ala Val Gly Cys Arg Ala Leu Pro Ser
100     105     110
Ile Ile Leu Leu Thr Met Tyr Ala Ser Val Leu Leu Leu Ala Ala Leu
115     120     125
Ser Ala Asp Leu Cys Phe Leu Ala Leu Gly Pro Ala Trp Trp Ser Thr
130     135     140
Val Gln Arg Ala Cys Gly Val Gln Val Ala Cys Gly Ala Ala Trp Thr
145     150     155     160
Leu Ala Leu Leu Leu Thr Val Pro Ser Ala Ile Tyr Arg Arg Leu His
165     170     175
Gln Glu His Phe Pro Ala Arg Leu Gln Cys Val Val Asp Tyr Gly Gly
180     185     190
Ser Ser Ser Thr Glu Asn Ala Val Thr Ala Ile Arg Phe Leu Phe Gly
195     200     205
Phe Leu Gly Pro Leu Val Ala Val Ala Ser Cys His Ser Ala Leu Leu
210     215     220
Cys Trp Ala Ala Arg Arg Cys Arg Pro Leu Gly Thr Ala Ile Val Val
225     230     235     240
Gly Phe Phe Val Cys Trp Ala Pro Tyr His Leu Leu Gly Leu Val Leu
245     250     255
Thr Val Ala Ala Pro Asn Ser Ala Leu Leu Ala Arg Ala Leu Arg Ala
260     265     270
Glu Pro Leu Ile Val Gly Leu Ala Leu Ala His Ser Cys Leu Asn Pro
275     280     285
Met Leu Phe Leu Tyr Phe Gly Arg Ala Gln Leu Arg Arg Ser Leu Pro
290     295     300
Ala Ala Cys His Trp Ala Leu Arg Glu Ser Gln Gly Gln Asp Glu Ser
305     310     315     320

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Val	Asp	Ser	Lys	Lys	Ser	Thr	Ser	His	Asp	Leu	Val	Ser	Glu	Met	Glu	
				325					330					335		

Val

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<210> SEQ ID NO 18
<211> LENGTH: 2858
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens
<220> FEATURE:
<221> NAME/KEY: CDS
<222> LOCATION: (174)..(1175)

<400> SEQUENCE: 18

aacagtat ttccttttcaa cacatctatt gaaagtgttg gataaatgca ggatgttaat      60
atgctataaa cataaagtct gtttttaaaa aatagcattt gaaaatcatg aagggtcttt      120
tgttttcttt tgtttgtata tatgtttatt ggtaacaggt gacactggaa gca atg      176
Met
1
aac acc aca gtg atg caa ggc ttc aac aga tct gag cgg tgc ccc aga      224
Asn Thr Thr Val Met Gln Gly Phe Asn Arg Ser Glu Arg Cys Pro Arg
5 10 15
gac act cgg ata gta cag ctg gta ttc cca gcc ctc tac aca gtg gtt      272
Asp Thr Arg Ile Val Gln Leu Val Phe Pro Ala Leu Tyr Thr Val Val
20 25 30
ttc ttg acc ggc atc ctg ctg aat act ttg gct ctg tgg gtg ttt gtt      320
Phe Leu Thr Gly Ile Leu Leu Asn Thr Leu Ala Leu Trp Val Phe Val
35 40 45
cac atc ccc agc tcc tcc acc ttc atc atc tac ctc aaa aac act ttg      368
His Ile Pro Ser Ser Thr Phe Ile Ile Tyr Leu Lys Asn Thr Leu
50 55 60 65
gtg gcc gac ttg ata atg aca ctc atg ctt cct ttc aaa atc ctc tct      416
Val Ala Asp Leu Ile Met Thr Leu Met Leu Pro Phe Lys Ile Leu Ser
70 75 80
gac tca cac ctg gca ccc tgg cag ctc aga gct ttt gtg tgt cgt ttt      464
Asp Ser His Leu Ala Pro Trp Gln Leu Arg Ala Phe Val Cys Arg Phe
85 90 95
tct tcg gtg ata ttt tat gag acc atg tat gtg ggc atc gtg ctg tta      512
Ser Ser Val Ile Phe Tyr Glu Thr Met Tyr Val Gly Ile Val Leu Leu
100 105 110
ggg ctc ata gcc ttt gac aga ttc ctc aag atc atc aga cct ttg aga      560
Gly Leu Ile Ala Phe Asp Arg Phe Leu Lys Ile Ile Arg Pro Leu Arg
115 120 125
aat att ttt cta aaa aaa cct gtt ttt gca aaa acg gtc tca atc ttc      608
Asn Ile Phe Leu Lys Lys Pro Val Phe Ala Lys Thr Val Ser Ile Phe
130 135 140 145
atc tgg ttc ttt ttg ttc ttc atc tcc ctg cca aat acg atc ttg agc      656
Ile Trp Phe Phe Leu Phe Phe Ile Ser Leu Pro Asn Thr Ile Leu Ser
150 155 160
aac aag gaa gca aca cca tcg tct gtg aaa aag tgt gct tcc tta aag      704
Asn Lys Glu Ala Thr Pro Ser Ser Val Lys Lys Cys Ala Ser Leu Lys
165 170 175
ggg cct ctg ggg ctg aaa tgg cat caa atg gta aat aac ata tgc cag      752
Gly Pro Leu Gly Leu Lys Trp His Gln Met Val Asn Asn Ile Cys Gln
180 185 190
ttt att ttc tgg act gtt ttt atc cta atg ctt gtg ttt tat gtg gtt      800
Phe Ile Phe Trp Thr Val Phe Ile Leu Met Leu Val Phe Tyr Val Val
195 200 205

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ttgaacttta tactcttgta taaatttcta actttcagaa aatgccatac tctgttttgg 2565
caccacacat gtatatttcc ccttggtaca cttggaagac tttatccat ctgtgaaacc 2625
ctatgttgtc atcacttggc ccatgaaata ttacctggcc aatateccac catcacctca 2685
aacccaatca cccctcctc tgtatgctgt cacacctata ttattaaact taccacattg 2745
cattgtaatt acttctcgac ctttgatct actcttttag taactgatgt atatatctga 2805
aaggagagat tgtttcattg tgcaatcaat aaatgtttga taaaataaag ccc 2858

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<210> SEQ ID NO 19
<211> LENGTH: 333
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

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<400> SEQUENCE: 19

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Met Asn Thr Thr Val Met Gln Gly Phe Asn Arg Ser Glu Arg Cys Pro
1 5 10 15
Arg Asp Thr Arg Ile Val Gln Leu Val Phe Pro Ala Leu Tyr Thr Val
20 25 30
Val Phe Leu Thr Gly Ile Leu Leu Asn Thr Leu Ala Leu Trp Val Phe
35 40 45
Val His Ile Pro Ser Ser Ser Thr Phe Ile Ile Tyr Leu Lys Asn Thr
50 55 60
Leu Val Ala Asp Leu Ile Met Thr Leu Met Leu Pro Phe Lys Ile Leu
65 70 75 80
Ser Asp Ser His Leu Ala Pro Trp Gln Leu Arg Ala Phe Val Cys Arg
85 90 95
Phe Ser Ser Val Ile Phe Tyr Glu Thr Met Tyr Val Gly Ile Val Leu
100 105 110
Leu Gly Leu Ile Ala Phe Asp Arg Phe Leu Lys Ile Ile Arg Pro Leu
115 120 125
Arg Asn Ile Phe Leu Lys Lys Pro Val Phe Ala Lys Thr Val Ser Ile
130 135 140
Phe Ile Trp Phe Phe Leu Phe Phe Ile Ser Leu Pro Asn Thr Ile Leu
145 150 155 160
Ser Asn Lys Glu Ala Thr Pro Ser Ser Val Lys Lys Cys Ala Ser Leu
165 170 175
Lys Gly Pro Leu Gly Leu Lys Trp His Gln Met Val Asn Asn Ile Cys
180 185 190
Gln Phe Ile Phe Trp Thr Val Phe Ile Leu Met Leu Val Phe Tyr Val
195 200 205
Val Ile Ala Lys Lys Val Tyr Asp Ser Tyr Arg Lys Ser Lys Ser Lys
210 215 220
Asp Arg Lys Asn Asn Lys Lys Leu Glu Gly Lys Val Phe Val Val Val
225 230 235 240
Ala Val Phe Phe Val Cys Phe Ala Pro Phe His Phe Ala Arg Val Pro
245 250 255
Tyr Thr His Ser Gln Thr Asn Asn Lys Thr Asp Cys Arg Leu Gln Asn
260 265 270
Gln Leu Phe Ile Ala Lys Glu Thr Thr Leu Phe Leu Ala Ala Thr Asn
275 280 285
Ile Cys Met Asp Pro Leu Ile Tyr Ile Phe Leu Cys Lys Lys Phe Thr
290 295 300

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Glu Lys Leu Pro Cys Met Gln Gly Arg Lys Thr Thr Ala Ser Ser Gln
305 310 315 320

Glu Asn His Ser Ser Gln Thr Asp Asn Ile Thr Leu Gly
325 330

<210> SEQ ID NO 20
<211> LENGTH: 878
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 20

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ttttttttt tttaagtgg taaaaaaaaa ttggttattt ataatcaat tacacaataa    60
aataattatt tttaaaagtc acaaatacaa tcgtggtata aagtcatttg ggcacaaagt    120
atctcttaaa tatgtggcaa actatttgtc caaagagatg tggtcocaaac ccgtcgaagg    180
ctttataatt tggtattaga taacaagggtg aacaaaactg acaataaata ctccaacgaa    240
ttatttttta aaactaaggg gggcaaaggc tattctaagg ggcaaaacaa tctattactc    300
agacctacct gaaaatttca cgtgaagtcg atcaaaagt atacaaaatt ggtatttaca    360
tgtttaaaat ccggtattggc atttttcttt aataataata cataaaaaaa ctcagagggt    420
taataaagaa ataattcaaa gtctaataa gtcaacaaac agatttcatt ataagctgga    480
acataaaaga gacaccatgg ttggctgtct cttttcaaaa attatcacgg ccacttggtc    540
aaacgggaag cagcattcag aacaatggtt ctcaaactc ggggtggcat aaacaccatg    600
caggttggtt accacacaga ttctctggcc tgttcccagt ctgaagctct cataaaggat    660
ctgaggaatc tgcttcgtga caagattcag actatttatt tattatcac ccaagctgga    720
gtgcaggggt gcaacccggt caggaaacct cgctcggag taaaaggaa accaaatcgg    780
ggcccaggcc ctgagaatgg gttcaaacgg gccaccacc ggtaacggta tcagaaaaaa    840
acggtccaga aggccagggg tcaaccgaac caagaagc    878

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<210> SEQ ID NO 21
<211> LENGTH: 1646
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens
<220> FEATURE:
<221> NAME/KEY: CDS
<222> LOCATION: (99)..(743)

<400> SEQUENCE: 21

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tagtgatcct ttctgagtgt ctccacttg cgacaagggt gacttgggag gaaagccgtc    60
tgccaaagcc tgaagcctcc aagccataaa caacccca atg gcc tcc cac gaa gtt    116
Met Ala Ser His Glu Val
1 5
gat aat gca gag ctg ggg tca gcc tct gcc cat ggt acc cca ggc agt    164
Asp Asn Ala Glu Leu Gly Ser Ala Ser Ala His Gly Thr Pro Gly Ser
10 15 20
gag acg gga cca gaa gag ctg aat act tct gtc tac cac ccc ata aat    212
Glu Thr Gly Pro Glu Glu Leu Asn Thr Ser Val Tyr His Pro Ile Asn
25 30 35
gga tca cca gat tat cag aaa gca aaa tta caa gtt ctt ggg gcc atc    260
Gly Ser Pro Asp Tyr Gln Lys Ala Lys Leu Gln Val Leu Gly Ala Ile
40 45 50
cag atc ctg aat gca gca atg att ctg gct ttg ggt gtc ttt ctg ggt    308
Gln Ile Leu Asn Ala Ala Met Ile Leu Ala Leu Gly Val Phe Leu Gly

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55	60	65	70	
tcc ttg caa tac cca tac cac ttc caa aag cac ttc ttt ttc ttc acc				356
Ser Leu Gln Tyr Pro Tyr His Phe Gln Lys His Phe Phe Phe Phe Thr	75	80	85	
ttc tac aca ggc tac ccg att tgg ggt gct gtg ttt ttc tgt agt tca				404
Phe Tyr Thr Gly Tyr Pro Ile Trp Gly Ala Val Phe Phe Cys Ser Ser	90	95	100	
gga acc ttg tct gtt gta gca ggg ata aaa ccc aca aga aca tgg ata				452
Gly Thr Leu Ser Val Val Ala Gly Ile Lys Pro Thr Arg Thr Trp Ile	105	110	115	
cag aac agt ttt gga atg aac att gcc agt gct aca att gca cta gtg				500
Gln Asn Ser Phe Gly Met Asn Ile Ala Ser Ala Thr Ile Ala Leu Val	120	125	130	
ggg act gct ttt ctc tca cta aat ata gca gtt aat atc cag tca tta				548
Gly Thr Ala Phe Leu Ser Leu Asn Ile Ala Val Asn Ile Gln Ser Leu	135	140	145	150
agg agt tgt cac tct tca tca gag tca ccg gac cta tgc aat tac atg				596
Arg Ser Cys His Ser Ser Ser Glu Ser Pro Asp Leu Cys Asn Tyr Met	155	160	165	
ggc tcc ata tca aat ggc atg gtg tct cta ctg ctg att ctc acc ttg				644
Gly Ser Ile Ser Asn Gly Met Val Ser Leu Leu Leu Ile Leu Thr Leu	170	175	180	
ctg gaa tta tgc gta act atc tct acc ata gcc atg tgg tgc aat gca				692
Leu Glu Leu Cys Val Thr Ile Ser Thr Ile Ala Met Trp Cys Asn Ala	185	190	195	
aac tgc tgt aat tca aga gag gaa att tcc tca cct ccc aat tct gtg				740
Asn Cys Cys Asn Ser Arg Glu Glu Ile Ser Ser Pro Pro Asn Ser Val	200	205	210	
taa tcaagaatac ctccctatga aaataattct gagagcatga atatttgacc				793
ttaaactctcc agtgactcag agcttcaccc acaaactcag gagaacataa goctgctcgt				853
aaagctcaat ccttctatca tggcaccaat cacaagaacc ttggacgttt gactgactct				913
atcctttctc tcctaactat aaatcctatt tgtgtgtcgt gggtatggaa ggacagatat				973
atttctttag gcattcttgg atatctgtaa cttctatgat cattaactcca aagttgtttc				1033
cagaaattgg ttctatttct tcttatccac ctactccatt gctttatgag gtttaaggaa				1093
ggaaggcggg ataatcccta ttcaatatat tttttctaaa atccaacttc tgaccgcca				1153
gtaggaagaa aaatgagaca ttttttccat tacagagaaa tgcttcttga ctttaacatc				1213
agcattataa aaagtgtcaa ataaaaaatt accatcatta tcattaaaat aaattttcac				1273
tgtatttgag atgggagggt taaggctcag ggattttatt tcagtgaact gctggaactc				1333
acacatgcc tgatatgtaa atgatgatt atgttgccga gtctgagagc aagcccaaat				1393
gtgttcttca aaggacaatg ggaactgta aagtagagaa ctaaagaata aggcctttag				1453
aatctgacac atctgggttc aaattctgaa actgtcactt attacctgta tgaacatggg				1513
caaattatct aatctctctg atctattttt cctcatctgt aaaatagggtg taataataac				1573
aactactttg tcggttctc tgagggttaa atgaaaataa aaagaaaatg tgaacagca				1633
ccacaggtac ttg				1646

<210> SEQ ID NO 22
 <211> LENGTH: 214
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens

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<400> SEQUENCE: 22

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Met Ala Ser His Glu Val Asp Asn Ala Glu Leu Gly Ser Ala Ser Ala
1           5           10           15
His Gly Thr Pro Gly Ser Glu Thr Gly Pro Glu Glu Leu Asn Thr Ser
20           25           30
Val Tyr His Pro Ile Asn Gly Ser Pro Asp Tyr Gln Lys Ala Lys Leu
35           40           45
Gln Val Leu Gly Ala Ile Gln Ile Leu Asn Ala Ala Met Ile Leu Ala
50           55           60
Leu Gly Val Phe Leu Gly Ser Leu Gln Tyr Pro Tyr His Phe Gln Lys
65           70           75           80
His Phe Phe Phe Phe Thr Phe Tyr Thr Gly Tyr Pro Ile Trp Gly Ala
85           90           95
Val Phe Phe Cys Ser Ser Gly Thr Leu Ser Val Val Ala Gly Ile Lys
100          105          110
Pro Thr Arg Thr Trp Ile Gln Asn Ser Phe Gly Met Asn Ile Ala Ser
115          120          125
Ala Thr Ile Ala Leu Val Gly Thr Ala Phe Leu Ser Leu Asn Ile Ala
130          135          140
Val Asn Ile Gln Ser Leu Arg Ser Cys His Ser Ser Ser Glu Ser Pro
145          150          155          160
Asp Leu Cys Asn Tyr Met Gly Ser Ile Ser Asn Gly Met Val Ser Leu
165          170          175
Leu Leu Ile Leu Thr Leu Leu Glu Leu Cys Val Thr Ile Ser Thr Ile
180          185          190
Ala Met Trp Cys Asn Ala Asn Cys Cys Asn Ser Arg Glu Glu Ile Ser
195          200          205
Ser Pro Pro Asn Ser Val
210
    
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<210> SEQ ID NO 23
<211> LENGTH: 2481
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens
<220> FEATURE:
<221> NAME/KEY: CDS
<222> LOCATION: (179)..(1276)
    
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<400> SEQUENCE: 23

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ggccttgatca gctcacagca ggcgtaaca gcctctaatt gaggaaactg tggetggaca      60
ggttgcaagg cagttctgct cccatcgtc ctcttgctga ctggggactg ctgagcccgt      120
gcacggcaga gactctggtg ggggtggagg gctggcctgg cccctctgct ctgtggaa      178
atg ctg ggg caa gtg gtc acc ctc ata ctc ctc ctg ctc ctc aag gtg      226
Met Leu Gly Gln Val Val Thr Leu Ile Leu Leu Leu Leu Lys Val
1           5           10           15
tat cag ggc aaa gga tgc cag gga tca gct gac cat gtg gtt agc atc      274
Tyr Gln Gly Lys Gly Cys Gln Gly Ser Ala Asp His Val Val Ser Ile
20           25           30
tcg gga gtg cct ctt cag tta caa cca aac agc ata cag acg aag gtt      322
Ser Gly Val Pro Leu Gln Leu Gln Pro Asn Ser Ile Gln Thr Lys Val
35           40           45
gac agc att gca tgg aag aag ttg ctg ccc tca caa aat gga ttt cat      370
Asp Ser Ile Ala Trp Lys Lys Leu Leu Pro Ser Gln Asn Gly Phe His
50           55           60
    
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cac ata ttg aag tgg gag aat ggc tct ttg cct tcc aat act tcc aat	418
His Ile Leu Lys Trp Glu Asn Gly Ser Leu Pro Ser Asn Thr Ser Asn	
65 70 75 80	
gat aga ttc agt ttt ata gtc aag aac ttg agt ctt ctc atc aag gca	466
Asp Arg Phe Ser Phe Ile Val Lys Asn Leu Ser Leu Leu Ile Lys Ala	
85 90 95	
gct cag cag cag gac agt ggc ctc tac tgc ctg gag gtc acc agt ata	514
Ala Gln Gln Gln Asp Ser Gly Leu Tyr Cys Leu Glu Val Thr Ser Ile	
100 105 110	
tct gga aaa gtt cag aca gcc acg ttc cag gtt ttt gta ttt gat aaa	562
Ser Gly Lys Val Gln Thr Ala Thr Phe Gln Val Phe Val Phe Asp Lys	
115 120 125	
gtt gag aaa ccc cgc cta cag ggg cag ggg aag atc ctg gac aga ggg	610
Val Glu Lys Pro Arg Leu Gln Gly Gln Gly Lys Ile Leu Asp Arg Gly	
130 135 140	
aga tgc caa gtg gct ctg tct tgc ttg gtc tcc agg gat ggc aat gtg	658
Arg Cys Gln Val Ala Leu Ser Cys Leu Val Ser Arg Asp Gly Asn Val	
145 150 155 160	
tcc tat gct tgg tac aga ggg agc aag ctg atc cag aca gca ggg aac	706
Ser Tyr Ala Trp Tyr Arg Gly Ser Lys Leu Ile Gln Thr Ala Gly Asn	
165 170 175	
ctc acc tac ctg gac gag gag gtt gac att aat ggc act cac aca tat	754
Leu Thr Tyr Leu Asp Glu Glu Val Asp Ile Asn Gly Thr His Thr Tyr	
180 185 190	
acc tgc aat gtc agc aat cct gtt agc tgg gaa agc cac acc ctg aat	802
Thr Cys Asn Val Ser Asn Pro Val Ser Trp Glu Ser His Thr Leu Asn	
195 200 205	
ctc act cag gac tgt cag aat gcc cat cag gaa ttc aga ttt tgg ccg	850
Leu Thr Gln Asp Cys Gln Asn Ala His Gln Glu Phe Arg Phe Trp Pro	
210 215 220	
ttt ttg gtg atc atc gtg att cta agc gca ctg ttc ctt ggc acc ctt	898
Phe Leu Val Ile Ile Val Ile Leu Ser Ala Leu Phe Leu Gly Thr Leu	
225 230 235 240	
gcc tgc ttc tgt gtg tgg agg aga aag agg aag gag aag cag tca gag	946
Ala Cys Phe Cys Val Trp Arg Arg Lys Arg Lys Glu Lys Gln Ser Glu	
245 250 255	
acc agt ccc aag gaa ttt ttg aca att tac gaa gat gtc aag gat ctg	994
Thr Ser Pro Lys Glu Phe Leu Thr Ile Tyr Glu Asp Val Lys Asp Leu	
260 265 270	
aaa acc agg aga aat cac gag cag gag cag act ttt cct gga ggg ggg	1042
Lys Thr Arg Arg Asn His Glu Gln Glu Gln Thr Phe Pro Gly Gly Gly	
275 280 285	
agc acc atc tac tct atg atc cag tcc cag tct tct gct ccc acg tca	1090
Ser Thr Ile Tyr Ser Met Ile Gln Ser Gln Ser Ser Ala Pro Thr Ser	
290 295 300	
caa gaa cct gca tat aca tta tat tca tta att cag cct tcc agg aag	1138
Gln Glu Pro Ala Tyr Thr Leu Tyr Ser Leu Ile Gln Pro Ser Arg Lys	
305 310 315 320	
tct gga tcc agg aag agg aac cac agc cct tcc ttc aat agc act atc	1186
Ser Gly Ser Arg Lys Arg Asn His Ser Pro Ser Phe Asn Ser Thr Ile	
325 330 335	
tat gaa gtg att gga aag agt caa cct aaa gcc cag aac cct gct cga	1234
Tyr Glu Val Ile Gly Lys Ser Gln Pro Lys Ala Gln Asn Pro Ala Arg	
340 345 350	
ttg agc cgc aaa gag ctg gag aac ttt gat gtt tat tcc tag	1276
Leu Ser Arg Lys Glu Leu Glu Asn Phe Asp Val Tyr Ser	
355 360 365	

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ttgctgcagc aattctcacc tttcttgcaac atcagcatct gctttgggaa ttggcacagt 1336
ggatgacggc acaggagtct ctatagaaca gttcctagtc tggagaggat atggaaattt 1396
gttcttgttc tatattttgt tttgaaaatg atgtctaaca accatgataa gagcaaggct 1456
gttaaataat atcttccaat ttacagatca gacatgaatg ggtggagggg ttaggttgtt 1516
cacaaaaggc cacattccaa gtatttgtaa tctagaaagt gttatgtaag tgatgttatt 1576
agcatcgaga ttcctccacc ctgattttca agctgtcact tgttcccttt tctcccctct 1636
ctgggttgac tgcatttcta gactctcgcc ggcccaggcc catcttccaa agcaagagga 1696
aggaatgata atggtgactc aggggaagaa gaaacagccc tcctctgaaa gcctggactg 1756
tccggctgtg aactggctgg caggttctgc acgtgggtgg gggccagggc ctgggcttta 1816
ctcaattgca gagaaaaaac tttctcctg catctcatac ctttacctct gccagttgg 1876
ccaccagggg gactgggctg aaggagagat agatggtgca aagcaagccc atctctaagt 1936
agaaaaatca cccagagcac atgctgacct gataactggg gtgttgagac cagctttgtc 1996
catggtatga tgtttgattt atgaagacgc attgtagtaa atccatttgg cttcttcata 2056
gaagtggctt cccagaggaa gaggcctctc agaaacctg ttctatttaa gttctgagtc 2116
ctgatgagtg tccccagga tgcacattga agggagggct caggcagctg agggctgaga 2176
atgaggcagt tggaatctag acactatgct gggttccctg agtcgtcagg ccagacattt 2236
caacaaggct gtggggagca gggctgtgac tctggctgag cccaggaaag cgacaagggt 2296
gaactgggag aggacttact cagagacccc aacaggtgat actgcacaaa gcctggttct 2356
tcaattttcc taccctgtat ctaacatagg agtttcatat aaaacggtga tatcatgcag 2416
atgcagtctg aattccttgc ctgaattaa tttatgtatc ctctcaaaa aaaaaaaaaa 2476
aaaaa 2481

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<210> SEQ ID NO 24
<211> LENGTH: 365
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

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<400> SEQUENCE: 24

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Met Leu Gly Gln Val Val Thr Leu Ile Leu Leu Leu Leu Lys Val
1             5             10             15
Tyr Gln Gly Lys Gly Cys Gln Gly Ser Ala Asp His Val Val Ser Ile
20             25             30
Ser Gly Val Pro Leu Gln Leu Gln Pro Asn Ser Ile Gln Thr Lys Val
35             40             45
Asp Ser Ile Ala Trp Lys Lys Leu Leu Pro Ser Gln Asn Gly Phe His
50             55             60
His Ile Leu Lys Trp Glu Asn Gly Ser Leu Pro Ser Asn Thr Ser Asn
65             70             75             80
Asp Arg Phe Ser Phe Ile Val Lys Asn Leu Ser Leu Leu Ile Lys Ala
85             90             95
Ala Gln Gln Gln Asp Ser Gly Leu Tyr Cys Leu Glu Val Thr Ser Ile
100            105            110
Ser Gly Lys Val Gln Thr Ala Thr Phe Gln Val Phe Val Phe Asp Lys
115            120            125
Val Glu Lys Pro Arg Leu Gln Gly Gln Gly Lys Ile Leu Asp Arg Gly

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agc tgg ggt cgt ttc atc tgc ctg gtc gtg gtc acc atg gca acc ttg Ser Trp Gly Arg Phe Ile Cys Leu Val Val Val Thr Met Ala Thr Leu 5 10 15	646
tcc ctg gcc cgg ccc tcc ttc agt tta gtt gag gat acc aca tta gag Ser Leu Ala Arg Pro Ser Phe Ser Leu Val Glu Asp Thr Thr Leu Glu 20 25 30	694
cca gaa gag cca cca acc aaa tac caa atc tct caa cca gaa gtg tac Pro Glu Glu Pro Pro Thr Lys Tyr Gln Ile Ser Gln Pro Glu Val Tyr 35 40 45 50	742
gtg gct gcg cca ggg gag tcg cta gag gtg cgc tgc ctg ttg aaa gat Val Ala Ala Pro Gly Glu Ser Leu Glu Val Arg Cys Leu Leu Lys Asp 55 60 65	790
gcc gcc gtg atc agt tgg act aag gat ggg gtg cac ttg ggg ccc aac Ala Ala Val Ile Ser Trp Thr Lys Asp Gly Val His Leu Gly Pro Asn 70 75 80	838
aat agg aca gtg ctt att ggg gag tac ttg cag ata aag gcc gcc acg Asn Arg Thr Val Leu Ile Gly Glu Tyr Leu Gln Ile Lys Gly Ala Thr 85 90 95	886
cct aga gac tcc ggc ctc tat gct tgt act gcc agt agg act gta gac Pro Arg Asp Ser Gly Leu Tyr Ala Cys Thr Ala Ser Arg Thr Val Asp 100 105 110	934
agt gaa act tgg tac ttc atg gtg aat gtc aca gat gcc atc tca tcc Ser Glu Thr Trp Tyr Phe Met Val Asn Val Thr Asp Ala Ile Ser Ser 115 120 125 130	982
gga gat gat gag gat gac acc gat ggt gcg gaa gat ttt gtc agt gag Gly Asp Asp Glu Asp Asp Thr Asp Gly Ala Glu Asp Phe Val Ser Glu 135 140 145	1030
aac agt aac aac aag aga gca cca tac tgg acc aac aca gaa aag atg Asn Ser Asn Asn Lys Arg Ala Pro Tyr Trp Thr Asn Thr Glu Lys Met 150 155 160	1078
gaa aag cgg ctc cat gct gtg cct gcg gcc aac act gtc aag ttt cgc Glu Lys Arg Leu His Ala Val Pro Ala Ala Asn Thr Val Lys Phe Arg 165 170 175	1126
tgc cca gcc ggg ggg aac cca atg cca acc atg cgg tgg ctg aaa aac Cys Pro Ala Gly Gly Asn Pro Met Pro Thr Met Arg Trp Leu Lys Asn 180 185 190	1174
ggg aag gag ttt aag cag gag cat cgc att gga gcc tac aag gta cga Gly Lys Glu Phe Lys Gln Glu His Arg Ile Gly Gly Tyr Lys Val Arg 195 200 205 210	1222
aac cag cac tgg agc ctc att atg gaa agt gtg gtc cca tct gac aag Asn Gln His Trp Ser Leu Ile Met Glu Ser Val Val Pro Ser Asp Lys 215 220 225	1270
gga aat tat acc tgt gtg gtg gag aat gaa tac ggg tcc atc aat cac Gly Asn Tyr Thr Cys Val Val Glu Asn Glu Tyr Gly Ser Ile Asn His 230 235 240	1318
acg tac cac ctg gat gtt gtg gag cga tcg cct cac cgg ccc atc ctc Thr Tyr His Leu Asp Val Val Glu Arg Ser Pro His Arg Pro Ile Leu 245 250 255	1366
caa gcc gga ctg ccg gca aat gcc tcc aca gtg gtc gga gga gac gta Gln Ala Gly Leu Pro Ala Asn Ala Ser Thr Val Val Gly Gly Asp Val 260 265 270	1414
gag ttt gtc tgc aag gtt tac agt gat gcc cag ccc cac atc cag tgg Glu Phe Val Cys Lys Val Tyr Ser Asp Ala Gln Pro His Ile Gln Trp 275 280 285 290	1462
atc aag cac gtg gaa aag aac gcc agt aaa tac ggg ccc gac ggg ctg Ile Lys His Val Glu Lys Asn Gly Ser Lys Tyr Gly Pro Asp Gly Leu 295 300 305	1510

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ccc tac ctc aag gtt ctc aag cac tcg ggg ata aat agt tcc aat gca	1558
Pro Tyr Leu Lys Val Leu Lys His Ser Gly Ile Asn Ser Ser Asn Ala	
310 315 320	
gaa gtg ctg gct ctg ttc aat gtg acc gag gcg gat gct ggg gaa tat	1606
Glu Val Leu Ala Leu Phe Asn Val Thr Glu Ala Asp Ala Gly Glu Tyr	
325 330 335	
ata tgt aag gtc tcc aat tat ata ggg cag gcc aac cag tct gcc tgg	1654
Ile Cys Lys Val Ser Asn Tyr Ile Gly Gln Ala Asn Gln Ser Ala Trp	
340 345 350	
ctc act gtc ctg cca aaa cag caa gcg cct gga aga gaa aag gag att	1702
Leu Thr Val Leu Pro Lys Gln Gln Ala Pro Gly Arg Glu Lys Glu Ile	
355 360 365 370	
aca gct tcc cca gac tac ctg gag ata gcc att tac tgc ata ggg gtc	1750
Thr Ala Ser Pro Asp Tyr Leu Glu Ile Ala Ile Tyr Cys Ile Gly Val	
375 380 385	
ttc tta atc gcc tgt atg gtg gta aca gtc atc ctg tgc cga atg aag	1798
Phe Leu Ile Ala Cys Met Val Val Thr Val Ile Leu Cys Arg Met Lys	
390 395 400	
aac acg acc aag aag cca gac ttc agc agc cag ccg gct gtg cac aag	1846
Asn Thr Thr Lys Lys Pro Asp Phe Ser Ser Gln Pro Ala Val His Lys	
405 410 415	
ctg acc aaa cgt atc ccc ctg cgg aga cag gta aca gtt tcg gct gag	1894
Leu Thr Lys Arg Ile Pro Leu Arg Arg Gln Val Thr Val Ser Ala Glu	
420 425 430	
tcc agc tcc tcc atg aac tcc aac acc ccg ctg gtg agg ata aca aca	1942
Ser Ser Ser Ser Met Asn Ser Asn Thr Pro Leu Val Arg Ile Thr Thr	
435 440 445 450	
cgc ctc tct tca acg gca gac acc ccc atg ctg gca ggg gtc tcc gag	1990
Arg Leu Ser Ser Thr Ala Asp Thr Pro Met Leu Ala Gly Val Ser Glu	
455 460 465	
tat gaa ctt cca gag gac cca aaa tgg gag ttt cca aga gat aag ctg	2038
Tyr Glu Leu Pro Glu Asp Pro Lys Trp Glu Phe Pro Arg Asp Lys Leu	
470 475 480	
aca ctg ggc aag ccc ctg gga gaa ggt tgc ttt ggg caa gtg gtc atg	2086
Thr Leu Gly Lys Pro Leu Gly Glu Gly Cys Phe Gly Gln Val Val Met	
485 490 495	
gcg gaa gca gtg gga att gac aaa gac aag ccc aag gag gcg gtc acc	2134
Ala Glu Ala Val Gly Ile Asp Lys Asp Lys Pro Lys Glu Ala Val Thr	
500 505 510	
gtg gcc gtg aag atg ttg aaa gat gat gcc aca gag aaa gac ctt tct	2182
Val Ala Val Lys Met Leu Lys Asp Asp Ala Thr Glu Lys Asp Leu Ser	
515 520 525 530	
gat ctg gtg tca gag atg gag atg atg aag atg att ggg aaa cac aag	2230
Asp Leu Val Ser Glu Met Glu Met Met Lys Met Ile Gly Lys His Lys	
535 540 545	
aat atc ata aat ctt ctt gga gcc tgc aca cag gat ggg cct ctc tat	2278
Asn Ile Ile Asn Leu Leu Gly Ala Cys Thr Gln Asp Gly Pro Leu Tyr	
550 555 560	
gtc ata gtt gag tat gcc tct aaa ggc aac ctc cga gaa tac ctc cga	2326
Val Ile Val Glu Tyr Ala Ser Lys Gly Asn Leu Arg Glu Tyr Leu Arg	
565 570 575	
gcc cgg agg cca ccc ggg atg gag tac tcc tat gac att aac cgt gtt	2374
Ala Arg Arg Pro Pro Gly Met Glu Tyr Ser Tyr Asp Ile Asn Arg Val	
580 585 590	
cct gag gag cag atg acc ttc aag gac ttg gtg tca tgc acc tac cag	2422
Pro Glu Glu Gln Met Thr Phe Lys Asp Leu Val Ser Cys Thr Tyr Gln	
595 600 605 610	

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ctg gcc aga ggc atg gag tac ttg gct tcc caa aaa tgt att cat cga Leu Ala Arg Gly Met Glu Tyr Leu Ala Ser Gln Lys Cys Ile His Arg 615 620 625	2470
gat tta gca gcc aga aat gtt ttg gta aca gaa aac aat gtg atg aaa Asp Leu Ala Ala Arg Asn Val Leu Val Thr Glu Asn Asn Val Met Lys 630 635 640	2518
ata gca gac ttt gga ctc gcc aga gat atc aac aat ata gac tat tac Ile Ala Asp Phe Gly Leu Ala Arg Asp Ile Asn Asn Ile Asp Tyr Tyr 645 650 655	2566
aaa aag acc acc aat ggg cgg ctt cca gtc aag tgg atg gct cca gaa Lys Lys Thr Thr Asn Gly Arg Leu Pro Val Lys Trp Met Ala Pro Glu 660 665 670	2614
gcc ctg ttt gat aga gta tac act cat cag agt gat gtc tgg tcc ttc Ala Leu Phe Asp Arg Val Tyr Thr His Gln Ser Asp Val Trp Ser Phe 675 680 685 690	2662
ggg gtg tta atg tgg gag atc ttc act tta ggg ggc tcg ccc tac cca Gly Val Leu Met Trp Glu Ile Phe Thr Leu Gly Gly Ser Pro Tyr Pro 695 700 705	2710
ggg att ccc gtg gag gaa ctt ttt aag ctg ctg aag gaa gga cac aga Gly Ile Pro Val Glu Glu Leu Phe Lys Leu Leu Lys Glu Gly His Arg 710 715 720	2758
atg gat aag cca gcc aac tgc acc aac gaa ctg tac atg atg atg agg Met Asp Lys Pro Ala Asn Cys Thr Asn Glu Leu Tyr Met Met Met Arg 725 730 735	2806
gac tgt tgg cat gca gtg ccc tcc cag aga cca acg ttc aag cag ttg Asp Cys Trp His Ala Val Pro Ser Gln Arg Pro Thr Phe Lys Gln Leu 740 745 750	2854
gta gaa gac ttg gat cga att ctc act ctc aca acc aat gag gaa tac Val Glu Asp Leu Asp Arg Ile Leu Thr Leu Thr Thr Asn Glu Glu Tyr 755 760 765 770	2902
ttg gac ctc agc caa cct ctc gaa cag tat tca cct agt tac cct gac Leu Asp Leu Ser Gln Pro Leu Glu Gln Tyr Ser Pro Ser Tyr Pro Asp 775 780 785	2950
aca aga agt tct tct tca gga gat gat tct gtt ttt tct cca gac Thr Arg Ser Ser Cys Ser Ser Gly Asp Asp Ser Val Phe Ser Pro Asp 790 795 800	2998
ccc atg cct tac gaa cca tgc ctt cct cag tat cca cac ata aac ggc Pro Met Pro Tyr Glu Pro Cys Leu Pro Gln Tyr Pro His Ile Asn Gly 805 810 815	3046
agt gtt aaa aca tga atgactgtgt ctgcctgtcc ccaaacagga cagcactggg Ser Val Lys Thr 820	3101
aacctagcta cactgagcag ggagaccatg cctcccagag cttgttgtct ccacttgat	3161
atatggatca gaggagtaaa taattggaaa agtaatcagc atatgtgtaa agatttatac	3221
agttgaaaac ttgtaacttt ccccaggagg agaagaaggt ttctggagca gtggactgcc	3281
acaagccacc atgtaacccc tctcacctgc cgtgcgtact ggctgtggac cagtaggact	3341
caaggtggac gtgcgttctg ccttctctgt taattttgta ataattggag aagatttatg	3401
tcagcacaca cttacagagc acaaatgcag tatatagggt ctggatgtat gtaaatatat	3461
tcaaattatg tataaatata tattatata ttacaaggag ttattttttg tattgatatt	3521
aatggatgt cccaatgcac ctagaaaatt ggtctctctt tttttaatag ctatttgcta	3581
aatgctgttc ttacacataa tttcttaatt ttcaccgagc agaggtggaa aaatactttt	3641
gctttcaggg aaaatggat aacgttaatt tattaataaa ttggaatat acaaaacaat	3701

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taatcattta tagttttttt tgtaatttaa gtggcatttc tatgcaggca gcacagcaga 3761
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caatataatga ctaatttggg gaaaatgaag ttttgattta tttgtgttta aatgctgctg 3881
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ccaagataaa tgggtaccagc gtcctcttaa aagatgcctt aatccattcc ttgaggacag 4061
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aatagccgtg caagatgaat gcagattaca ctgatcttat gtgttacaaa attggagaaa 4481
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<210> SEQ ID NO 26

<211> LENGTH: 822

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 26

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20     25     30
Leu Glu Pro Glu Glu Pro Pro Thr Lys Tyr Gln Ile Ser Gln Pro Glu
35     40     45
Val Tyr Val Ala Ala Pro Gly Glu Ser Leu Glu Val Arg Cys Leu Leu
50     55     60
Lys Asp Ala Ala Val Ile Ser Trp Thr Lys Asp Gly Val His Leu Gly
65     70     75     80
Pro Asn Asn Arg Thr Val Leu Ile Gly Glu Tyr Leu Gln Ile Lys Gly
85     90     95
Ala Thr Pro Arg Asp Ser Gly Leu Tyr Ala Cys Thr Ala Ser Arg Thr
100    105    110
Val Asp Ser Glu Thr Trp Tyr Phe Met Val Asn Val Thr Asp Ala Ile
115    120    125
Ser Ser Gly Asp Asp Glu Asp Asp Thr Asp Gly Ala Glu Asp Phe Val
130    135    140
Ser Glu Asn Ser Asn Asn Lys Arg Ala Pro Tyr Trp Thr Asn Thr Glu
145    150    155    160
Lys Met Glu Lys Arg Leu His Ala Val Pro Ala Ala Asn Thr Val Lys
165    170    175
Phe Arg Cys Pro Ala Gly Gly Asn Pro Met Pro Thr Met Arg Trp Leu
180    185    190
Lys Asn Gly Lys Glu Phe Lys Gln Glu His Arg Ile Gly Gly Tyr Lys

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Asp	Lys	Gly	Asn	Tyr	Thr	Cys	Val	Val	Glu	Asn	Glu	Tyr	Gly	Ser	Ile
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Asn	His	Thr	Tyr	His	Leu	Asp	Val	Val	Glu	Arg	Ser	Pro	His	Arg	Pro
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Ile	Leu	Gln	Ala	Gly	Leu	Pro	Ala	Asn	Ala	Ser	Thr	Val	Val	Gly	Gly
			260					265					270		
Asp	Val	Glu	Phe	Val	Cys	Lys	Val	Tyr	Ser	Asp	Ala	Gln	Pro	His	Ile
		275					280					285			
Gln	Trp	Ile	Lys	His	Val	Glu	Lys	Asn	Gly	Ser	Lys	Tyr	Gly	Pro	Asp
	290					295					300				
Gly	Leu	Pro	Tyr	Leu	Lys	Val	Leu	Lys	His	Ser	Gly	Ile	Asn	Ser	Ser
305					310					315					320
Asn	Ala	Glu	Val	Leu	Ala	Leu	Phe	Asn	Val	Thr	Glu	Ala	Asp	Ala	Gly
				325					330					335	
Glu	Tyr	Ile	Cys	Lys	Val	Ser	Asn	Tyr	Ile	Gly	Gln	Ala	Asn	Gln	Ser
			340					345					350		
Ala	Trp	Leu	Thr	Val	Leu	Pro	Lys	Gln	Gln	Ala	Pro	Gly	Arg	Glu	Lys
		355					360					365			
Glu	Ile	Thr	Ala	Ser	Pro	Asp	Tyr	Leu	Glu	Ile	Ala	Ile	Tyr	Cys	Ile
	370					375					380				
Gly	Val	Phe	Leu	Ile	Ala	Cys	Met	Val	Val	Thr	Val	Ile	Leu	Cys	Arg
385					390					395					400
Met	Lys	Asn	Thr	Thr	Lys	Lys	Pro	Asp	Phe	Ser	Ser	Gln	Pro	Ala	Val
				405					410					415	
His	Lys	Leu	Thr	Lys	Arg	Ile	Pro	Leu	Arg	Arg	Gln	Val	Thr	Val	Ser
			420					425				430			
Ala	Glu	Ser	Ser	Ser	Ser	Met	Asn	Ser	Asn	Thr	Pro	Leu	Val	Arg	Ile
		435					440					445			
Thr	Thr	Arg	Leu	Ser	Ser	Thr	Ala	Asp	Thr	Pro	Met	Leu	Ala	Gly	Val
	450					455					460				
Ser	Glu	Tyr	Glu	Leu	Pro	Glu	Asp	Pro	Lys	Trp	Glu	Phe	Pro	Arg	Asp
465					470					475					480
Lys	Leu	Thr	Leu	Gly	Lys	Pro	Leu	Gly	Glu	Gly	Cys	Phe	Gly	Gln	Val
			485					490						495	
Val	Met	Ala	Glu	Ala	Val	Gly	Ile	Asp	Lys	Asp	Lys	Pro	Lys	Glu	Ala
			500					505					510		
Val	Thr	Val	Ala	Val	Lys	Met	Leu	Lys	Asp	Asp	Ala	Thr	Glu	Lys	Asp
		515					520					525			
Leu	Ser	Asp	Leu	Val	Ser	Glu	Met	Glu	Met	Met	Lys	Met	Ile	Gly	Lys
	530					535					540				
His	Lys	Asn	Ile	Ile	Asn	Leu	Leu	Gly	Ala	Cys	Thr	Gln	Asp	Gly	Pro
545					550					555					560
Leu	Tyr	Val	Ile	Val	Glu	Tyr	Ala	Ser	Lys	Gly	Asn	Leu	Arg	Glu	Tyr
			565						570					575	
Leu	Arg	Ala	Arg	Arg	Pro	Pro	Gly	Met	Glu	Tyr	Ser	Tyr	Asp	Ile	Asn
		580						585					590		
Arg	Val	Pro	Glu	Glu	Gln	Met	Thr	Phe	Lys	Asp	Leu	Val	Ser	Cys	Thr
		595					600					605			

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Tyr Gln Leu Ala Arg Gly Met Glu Tyr Leu Ala Ser Gln Lys Cys Ile
 610 615 620
 His Arg Asp Leu Ala Ala Arg Asn Val Leu Val Thr Glu Asn Asn Val
 625 630 635 640
 Met Lys Ile Ala Asp Phe Gly Leu Ala Arg Asp Ile Asn Asn Ile Asp
 645 650 655
 Tyr Tyr Lys Lys Thr Thr Asn Gly Arg Leu Pro Val Lys Trp Met Ala
 660 665 670
 Pro Glu Ala Leu Phe Asp Arg Val Tyr Thr His Gln Ser Asp Val Trp
 675 680 685
 Ser Phe Gly Val Leu Met Trp Glu Ile Phe Thr Leu Gly Gly Ser Pro
 690 695 700
 Tyr Pro Gly Ile Pro Val Glu Glu Leu Phe Lys Leu Leu Lys Glu Gly
 705 710 715 720
 His Arg Met Asp Lys Pro Ala Asn Cys Thr Asn Glu Leu Tyr Met Met
 725 730 735
 Met Arg Asp Cys Trp His Ala Val Pro Ser Gln Arg Pro Thr Phe Lys
 740 745 750
 Gln Leu Val Glu Asp Leu Asp Arg Ile Leu Thr Leu Thr Thr Asn Glu
 755 760 765
 Glu Tyr Leu Asp Leu Ser Gln Pro Leu Glu Gln Tyr Ser Pro Ser Tyr
 770 775 780
 Pro Asp Thr Arg Ser Ser Cys Ser Ser Gly Asp Asp Ser Val Phe Ser
 785 790 795 800
 Pro Asp Pro Met Pro Tyr Glu Pro Cys Leu Pro Gln Tyr Pro His Ile
 805 810 815
 Asn Gly Ser Val Lys Thr
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<210> SEQ ID NO 27
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 <213> ORGANISM: Homo sapiens
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 <221> NAME/KEY: CDS
 <222> LOCATION: (94)..(2676)

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 Met Gly Pro Trp Gly Trp Lys
 1 5
 ttg cgc tgg acc gtc gcc ttg ctc ctc gcc gcg gcg ggg act gca gtg 162
 Leu Arg Trp Thr Val Ala Leu Leu Leu Ala Ala Ala Gly Thr Ala Val
 10 15 20
 ggc gac aga tgt gaa aga aac gag ttc cag tgc caa gac ggg aaa tgc 210
 Gly Asp Arg Cys Glu Arg Asn Glu Phe Gln Cys Gln Asp Gly Lys Cys
 25 30 35
 atc tcc tac aag tgg gtc tgc gat ggc agc gct gag tgc cag gat ggc 258
 Ile Ser Tyr Lys Trp Val Cys Asp Gly Ser Ala Glu Cys Gln Asp Gly
 40 45 50 55
 tct gat gag tcc cag gag acg tgc ttg tct gtc acc tgc aaa tcc ggg 306
 Ser Asp Glu Ser Gln Glu Thr Cys Leu Ser Val Thr Cys Lys Ser Gly
 60 65 70

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Asp Phe Ser Cys Gly Gly Arg Val Asn Arg Cys Ile Pro Gln Phe Trp	
75	80
agg tgc gat ggc caa gtg gac tgc gac aac ggc tca gac gag caa ggc	402
Arg Cys Asp Gly Gln Val Asp Cys Asp Asn Gly Ser Asp Glu Gln Gly	
90	95
tgt ccc ccc aag acg tgc tcc cag gac gag ttt cgc tgc cac gat ggg	450
Cys Pro Pro Lys Thr Cys Ser Gln Asp Glu Phe Arg Cys His Asp Gly	
105	110
aag tgc atc tct cgg cag ttc gtc tgt gac tca gac cgg gac tgc ttg	498
Lys Cys Ile Ser Arg Gln Phe Val Cys Asp Ser Asp Arg Asp Cys Leu	
120	125
gac ggc tca gac gag gcc tcc tgc cgg gtg ctc acc tgt ggt ccc gcc	546
Asp Gly Ser Asp Glu Ala Ser Cys Pro Val Leu Thr Cys Gly Pro Ala	
140	145
agc ttc cag tgc aac agc tcc acc tgc atc ccc cag ctg tgg gcc tgc	594
Ser Phe Gln Cys Asn Ser Ser Thr Cys Ile Pro Gln Leu Trp Ala Cys	
155	160
gac aac gac ccc gac tgc gaa gat ggc tgc gat gag tgg ccg cag cgc	642
Asp Asn Asp Pro Asp Cys Glu Asp Gly Ser Asp Glu Trp Pro Gln Arg	
170	175
tgt agg ggt ctt tac gtg ttc caa ggg gac agt agc ccc tgc tgc gcc	690
Cys Arg Gly Leu Tyr Val Phe Gln Gly Asp Ser Ser Pro Cys Ser Ala	
185	190
ttc gag ttc cac tgc cta agt ggc gag tgc atc cac tcc agc tgg cgc	738
Phe Glu Phe His Cys Leu Ser Gly Glu Cys Ile His Ser Ser Trp Arg	
200	205
tgt gat ggt ggc ccc gac tgc aag gac aaa tct gac gag gaa aac tgc	786
Cys Asp Gly Gly Pro Asp Cys Lys Asp Lys Ser Asp Glu Glu Asn Cys	
220	225
gct gtg gcc acc tgt cgc cct gac gaa ttc cag tgc tct gat gga aac	834
Ala Val Ala Thr Cys Arg Pro Asp Glu Phe Gln Cys Ser Asp Gly Asn	
235	240
tgc atc cat ggc agc cgg cag tgt gac cgg gaa tat gac tgc aag gac	882
Cys Ile His Gly Ser Arg Gln Cys Asp Arg Glu Tyr Asp Cys Lys Asp	
250	255
atg agc gat gaa gtt ggc tgc gtt aat gtg aca ctc tgc gag gga ccc	930
Met Ser Asp Glu Val Gly Cys Val Asn Val Thr Leu Cys Glu Gly Pro	
265	270
aac aag ttc aag tgt cac agc ggc gaa tgc atc acc ctg gac aaa gtc	978
Asn Lys Phe Lys Cys His Ser Gly Glu Cys Ile Thr Leu Asp Lys Val	
280	285
tgc aac atg gct aga gac tgc cgg gac tgg tca gat gaa ccc atc aaa	1026
Cys Asn Met Ala Arg Asp Cys Arg Asp Trp Ser Asp Glu Pro Ile Lys	
300	305
gag tgc ggg acc aac gaa tgc ttg gac aac aac ggc ggc tgt tcc cac	1074
Glu Cys Gly Thr Asn Glu Cys Leu Asp Asn Asn Gly Gly Cys Ser His	
315	320
gtc tgc aat gac ctt aag atc ggc tac gag tgc ctg tgc ccc gac ggc	1122
Val Cys Asn Asp Leu Lys Ile Gly Tyr Glu Cys Leu Cys Pro Asp Gly	
330	335
ttc cag ctg gtg gcc cag cga aga tgc gaa gat atc gat gag tgt cag	1170
Phe Gln Leu Val Ala Gln Arg Arg Cys Glu Asp Ile Asp Glu Cys Gln	
345	350
gat ccc gac acc tgc agc cag ctc tgc gtg aac ctg gag ggt ggc tac	1218
Asp Pro Asp Thr Cys Ser Gln Leu Cys Val Asn Leu Glu Gly Gly Tyr	
360	365
	370
	375

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tgc aag gct gtg ggc tcc atc gcc tac ctc ttc ttc acc aac cgg cac	1314
Cys Lys Ala Val Gly Ser Ile Ala Tyr Leu Phe Phe Thr Asn Arg His	
395 400 405	
gag gtc agg aag atg acg ctg gac cgg agc gag tac acc agc ctc atc	1362
Glu Val Arg Lys Met Thr Leu Asp Arg Ser Glu Tyr Thr Ser Leu Ile	
410 415 420	
ccc aac ctg agg aac gtg gtc gct ctg gac acg gag gtg gcc agc aat	1410
Pro Asn Leu Arg Asn Val Val Ala Leu Asp Thr Glu Val Ala Ser Asn	
425 430 435	
aga atc tac tgg tct gac ctg tcc cag aga atg atc tgc agc acc cag	1458
Arg Ile Tyr Trp Ser Asp Leu Ser Gln Arg Met Ile Cys Ser Thr Gln	
440 445 450 455	
ctt gac aga gcc cac ggc gtc tct tcc tat gac acc gtc atc agc agg	1506
Leu Asp Arg Ala His Gly Val Ser Ser Tyr Asp Thr Val Ile Ser Arg	
460 465 470	
gac atc cag gcc ccc gac ggg ctg gct gtg gac tgg atc cac agc aac	1554
Asp Ile Gln Ala Pro Asp Gly Leu Ala Val Asp Trp Ile His Ser Asn	
475 480 485	
atc tac tgg acc gac tct gtc ctg ggc act gtc tct gtt gcg gat acc	1602
Ile Tyr Trp Thr Asp Ser Val Leu Gly Thr Val Ser Val Ala Asp Thr	
490 495 500	
aag ggc gtg aag agg aaa acg tta ttc agg gag aac ggc tcc aag cca	1650
Lys Gly Val Lys Arg Lys Thr Leu Phe Arg Glu Asn Gly Ser Lys Pro	
505 510 515	
agg gcc atc gtg gtg gat cct gtt cat ggc ttc atg tac tgg act gac	1698
Arg Ala Ile Val Val Asp Pro Val His Gly Phe Met Tyr Trp Thr Asp	
520 525 530 535	
tgg gga act ccc gcc aag atc aag aaa ggg ggc ctg aat ggt gtg gac	1746
Trp Gly Thr Pro Ala Lys Ile Lys Lys Gly Gly Leu Asn Gly Val Asp	
540 545 550	
atc tac tcg ctg gtg act gaa aac att cag tgg ccc aat ggc atc acc	1794
Ile Tyr Ser Leu Val Thr Glu Asn Ile Gln Trp Pro Asn Gly Ile Thr	
555 560 565	
cta gat ctc ctc agt ggc cgc ctc tac tgg gtt gac tcc aaa ctt cac	1842
Leu Asp Leu Leu Ser Gly Arg Leu Tyr Trp Val Asp Ser Lys Leu His	
570 575 580	
tcc atc tca agc atc gat gtc aat ggg ggc aac cgg aag acc atc ttg	1890
Ser Ile Ser Ser Ile Asp Val Asn Gly Gly Asn Arg Lys Thr Ile Leu	
585 590 595	
gag gat gaa aag agg ctg gcc cac ccc ttc tcc ttg gcc gtc ttt gag	1938
Glu Asp Glu Lys Arg Leu Ala His Pro Phe Ser Leu Ala Val Phe Glu	
600 605 610 615	
gac aaa gta ttt tgg aca gat atc atc aac gaa gcc att ttc agt gcc	1986
Asp Lys Val Phe Trp Thr Asp Ile Ile Asn Glu Ala Ile Phe Ser Ala	
620 625 630	
aac cgc ctc aca ggt tcc gat gtc aac ttg ttg gct gaa aac cta ctg	2034
Asn Arg Leu Thr Gly Ser Asp Val Asn Leu Leu Ala Glu Asn Leu Leu	
635 640 645	
tcc cca gag gat atg gtc ctc ttc cac aac ctc acc cag cca aga gga	2082
Ser Pro Glu Asp Met Val Leu Phe His Asn Leu Thr Gln Pro Arg Gly	
650 655 660	
gtg aac tgg tgt gag agg acc acc ctg agc aat ggc ggc tgc cag tat	2130
Val Asn Trp Cys Glu Arg Thr Thr Leu Ser Asn Gly Gly Cys Gln Tyr	
665 670 675	

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ctg tgc ctc cct gcc ccg cag atc aac ccc cac tcg ccc aag ttt acc	2178
Leu Cys Leu Pro Ala Pro Gln Ile Asn Pro His Ser Pro Lys Phe Thr	
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tgc gcc tgc ccg gac ggc atg ctg ctg gcc agg gac atg agg agc tgc	2226
Cys Ala Cys Pro Asp Gly Met Leu Leu Ala Arg Asp Met Arg Ser Cys	
700 705 710	
ctc aca gag gct gag gct gca gtg gcc acc cag gag aca tcc acc gtc	2274
Leu Thr Glu Ala Glu Ala Ala Val Ala Thr Gln Glu Thr Ser Thr Val	
715 720 725	
agg cta aag gtc agc tcc aca gcc gta agg aca cag cac aca acc acc	2322
Arg Leu Lys Val Ser Ser Thr Ala Val Arg Thr Gln His Thr Thr Thr	
730 735 740	
cgg cct gtt ccc gac acc tcc cgg ctg cct ggg gcc acc cct ggg ctc	2370
Arg Pro Val Pro Asp Thr Ser Arg Leu Pro Gly Ala Thr Pro Gly Leu	
745 750 755	
acc acg gtg gag ata gtg aca atg tct cac caa gct ctg ggc gac gtt	2418
Thr Thr Val Glu Ile Val Thr Met Ser His Gln Ala Leu Gly Asp Val	
760 765 770 775	
gct ggc aga gga aat gag aag aag ccc agt agc gtg agg gct ctg tcc	2466
Ala Gly Arg Gly Asn Glu Lys Lys Pro Ser Ser Val Arg Ala Leu Ser	
780 785 790	
att gtc ctc ccc atc gtg ctc ctc gtc ttc ctt tgc ctg ggg gtc ttc	2514
Ile Val Leu Pro Ile Val Leu Leu Val Phe Leu Cys Leu Gly Val Phe	
795 800 805	
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Leu Leu Trp Lys Asn Trp Arg Leu Lys Asn Ile Asn Ser Ile Asn Phe	
810 815 820	
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Asp Asn Pro Val Tyr Gln Lys Thr Thr Glu Asp Glu Val His Ile Cys	
825 830 835	
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His Asn Gln Asp Gly Tyr Ser Tyr Pro Ser Arg Gln Met Val Ser Leu	
840 845 850 855	
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caggacacca gcctggtgcc catcctcccg acccctacc acttccattc ccgtggtctc	3486
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catgatcgag ccactgcact ccagcctggg caacagatga agaccctatt tcagaaatac 4566
aactataaaa aaaataaata aatcctccag tctggatcgt ttgacgggac ttcaggttct 4626
ttctgaaatc gccgtgttac tgttgactg atgtccggag agacagtgc agcctccgtc 4686
agactccgc gtgaagatgt cacaagggat tggcaattgt cccagggac aaaacactgt 4746
gtcccccca gtgcagggaa ccgtgataag cctttctggt ttcggagcac gtaaatgctg 4806
ccctgtacag atagtgggga tttttgtta tgtttgact ttgtatattg gttgaaactg 4866
ttatcactta tatatatata tacacacata tatataaaat ctatttattt ttgcaaacc 4926
tggttctgtg attgttctg tgactattct cggggccctg tgtaggggtt tattgcctct 4986
gaaatgcctc tctttatgt acaaagatta tttgcacgaa ctggactgtg tgcaacgctt 5046
tttgggagaa tgatgtcccc gttgtatgta tgagtggctt ctgggagatg ggtgtcactt 5106
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<210> SEQ ID NO 28
<211> LENGTH: 860
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

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<400> SEQUENCE: 28

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Met Gly Pro Trp Gly Trp Lys Leu Arg Trp Thr Val Ala Leu Leu Leu
1          5          10         15
Ala Ala Ala Gly Thr Ala Val Gly Asp Arg Cys Glu Arg Asn Glu Phe
20         25         30
Gln Cys Gln Asp Gly Lys Cys Ile Ser Tyr Lys Trp Val Cys Asp Gly
35         40         45
Ser Ala Glu Cys Gln Asp Gly Ser Asp Glu Ser Gln Glu Thr Cys Leu
50         55         60

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-continued

Ser	Val	Thr	Cys	Lys	Ser	Gly	Asp	Phe	Ser	Cys	Gly	Gly	Arg	Val	Asn
65					70					75					80
Arg	Cys	Ile	Pro	Gln	Phe	Trp	Arg	Cys	Asp	Gly	Gln	Val	Asp	Cys	Asp
				85				90						95	
Asn	Gly	Ser	Asp	Glu	Gln	Gly	Cys	Pro	Pro	Lys	Thr	Cys	Ser	Gln	Asp
			100					105						110	
Glu	Phe	Arg	Cys	His	Asp	Gly	Lys	Cys	Ile	Ser	Arg	Gln	Phe	Val	Cys
		115					120					125			
Asp	Ser	Asp	Arg	Asp	Cys	Leu	Asp	Gly	Ser	Asp	Glu	Ala	Ser	Cys	Pro
		130				135					140				
Val	Leu	Thr	Cys	Gly	Pro	Ala	Ser	Phe	Gln	Cys	Asn	Ser	Ser	Thr	Cys
145					150					155					160
Ile	Pro	Gln	Leu	Trp	Ala	Cys	Asp	Asn	Asp	Pro	Asp	Cys	Glu	Asp	Gly
			165					170						175	
Ser	Asp	Glu	Trp	Pro	Gln	Arg	Cys	Arg	Gly	Leu	Tyr	Val	Phe	Gln	Gly
			180					185						190	
Asp	Ser	Ser	Pro	Cys	Ser	Ala	Phe	Glu	Phe	His	Cys	Leu	Ser	Gly	Glu
		195					200					205			
Cys	Ile	His	Ser	Ser	Trp	Arg	Cys	Asp	Gly	Gly	Pro	Asp	Cys	Lys	Asp
	210					215					220				
Lys	Ser	Asp	Glu	Glu	Asn	Cys	Ala	Val	Ala	Thr	Cys	Arg	Pro	Asp	Glu
225					230					235					240
Phe	Gln	Cys	Ser	Asp	Gly	Asn	Cys	Ile	His	Gly	Ser	Arg	Gln	Cys	Asp
			245					250						255	
Arg	Glu	Tyr	Asp	Cys	Lys	Asp	Met	Ser	Asp	Glu	Val	Gly	Cys	Val	Asn
			260					265						270	
Val	Thr	Leu	Cys	Glu	Gly	Pro	Asn	Lys	Phe	Lys	Cys	His	Ser	Gly	Glu
		275					280					285			
Cys	Ile	Thr	Leu	Asp	Lys	Val	Cys	Asn	Met	Ala	Arg	Asp	Cys	Arg	Asp
	290					295					300				
Trp	Ser	Asp	Glu	Pro	Ile	Lys	Glu	Cys	Gly	Thr	Asn	Glu	Cys	Leu	Asp
305					310					315					320
Asn	Asn	Gly	Gly	Cys	Ser	His	Val	Cys	Asn	Asp	Leu	Lys	Ile	Gly	Tyr
				325					330					335	
Glu	Cys	Leu	Cys	Pro	Asp	Gly	Phe	Gln	Leu	Val	Ala	Gln	Arg	Arg	Cys
			340					345						350	
Glu	Asp	Ile	Asp	Glu	Cys	Gln	Asp	Pro	Asp	Thr	Cys	Ser	Gln	Leu	Cys
		355					360						365		
Val	Asn	Leu	Glu	Gly	Gly	Tyr	Lys	Cys	Gln	Cys	Glu	Glu	Gly	Phe	Gln
	370					375						380			
Leu	Asp	Pro	His	Thr	Lys	Ala	Cys	Lys	Ala	Val	Gly	Ser	Ile	Ala	Tyr
385					390					395					400
Leu	Phe	Phe	Thr	Asn	Arg	His	Glu	Val	Arg	Lys	Met	Thr	Leu	Asp	Arg
				405					410					415	
Ser	Glu	Tyr	Thr	Ser	Leu	Ile	Pro	Asn	Leu	Arg	Asn	Val	Val	Ala	Leu
			420					425						430	
Asp	Thr	Glu	Val	Ala	Ser	Asn	Arg	Ile	Tyr	Trp	Ser	Asp	Leu	Ser	Gln
		435					440					445			
Arg	Met	Ile	Cys	Ser	Thr	Gln	Leu	Asp	Arg	Ala	His	Gly	Val	Ser	Ser
	450					455						460			
Tyr	Asp	Thr	Val	Ile	Ser	Arg	Asp	Ile	Gln	Ala	Pro	Asp	Gly	Leu	Ala

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<211> LENGTH: 2070

<212> TYPE: DNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 29

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cacggctcct gcgcctgaga cagctggcct gacctccaaa tcatccatcc acccctgctg   120
tcacatgttt tcatagtgtg agatcaaccc acaggaatat ccatggcttt tgtgctcatt   180
ttggttctca gtttctacga gctgggtgca ggacagtggc aagtcactgg accgggcaag   240
tttgtccagg ccttggtggg ggaggacgcc gtgttctect gctccctctt tcttgagacc   300
agtgcagagg ctatggaagt gcggttcttc aggaatcagt tccatgctgt ggtccacctc   360
tacagagatg ggaagactg ggaatctaag cagatgccac agtatcgagg gagaactgag   420
tttgtgaagg actccattgc aggggggcgt gtctctctaa ggctaaaaaa catcactccc   480
tcggacatcg gctctgatgg gtgctggttc agttcccaga tttacgatga ggaggccacc   540
tgggagctgc ggttggcagc actgggctca ctctctctca tttccatcgt gggatatgtt   600
gacggaggta tccagttact ctgcctgtcc tcaggctggt tccccagcc cacagccaag   660
tggaaaggtc cacaaggaca ggatttgtct tcagactcca gagcaaatgc agatgggtac   720
agcctgtatg atgtggagat tcaccattata gtccaggaaa atgctgggag catattgtgt   780
tccatccacc ttgctgagca gagtcatgag gtggaatcca aggtattgat aggagagacg   840
ttttccagc cctcaccttg gcgcctggct tctattttac tcgggttact ctgtggtgcc   900
ctgtgtggtg ttgtcatggg gatgataatt gttttcttca aatccaaagg gaaaatccag   960
gcggaactgg actggagaag aaagcacgga caggcagaat tgagagacgc ccggaaacac  1020
gcagtggagg tgactctgga tccagagacg gctcaccoga agctctgcgt ttctgatctg  1080
aaaactgtaa cccatagaaa agctcccag gaggtgcctc actctgagaa gagatttaca  1140
aggaagagtg tgggtgcttc tcagggtttc caagcagga aacattactg ggaggtggac  1200
gtgggacaaa atgtagggtg gtatgtggga gtgtgtcggg atgacgtaga cagggggaag  1260
aacaatgtga ctttgtctcc caacaatggg tattgggtcc tcagactgac aacagaacat  1320
ttgtatttca cattcaatcc ccattttacc agcctcccc ccagcacc ccctacacga  1380
gtaggggtct tcttgacta tgaggggtgg accatctcct tcttcaatac aatgaccag  1440
tcccttattt ataccctgct gacatgtcag tttgaaggct tggtagagacc ctatatccag  1500
catgcatgt atgacgagga aaaggggact cccatattca tatgtccagt gtctgggga  1560
tgagacagag aagaccctgc ttaaagggcc ccacaccaca gaccagaca cagccaaggg  1620
agagtgtccc cgacaggtgg cccagcttc ctctccggag cctgcgcaca gagagtccag  1680
cccccactc tcttttaggg agctgaggtt cttctgcct gagcctgca gcagcggcag  1740
tcacagcttc cagatgaggg gggattggcc tgaccctgtg ggagtcagaa gccatggctg  1800
ccctgaagtg gggacggaat agactcacat taggtttagt ttgtgaaaac tccatccagc  1860
taagcgatct tgaacaagtc acaacctccc aggctcctca tttgctagtc acggacagtg  1920
attcctgct cacagtgaa gattaaagag acaacgaatg tgaatcatgc ttgcaggttt  1980
gagggcacag tgtttgctaa tgatgtgttt ttatattata cttttccca ccataaactc  2040
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<210> SEQ ID NO 30
<211> LENGTH: 1696
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens
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<221> NAME/KEY: CDS
<222> LOCATION: (88)..(1488)

<400> SEQUENCE: 30

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cagagcaggg cagtgggagg agacgcc atg acc ccc atc ctc acg gtc ctg atc      114
                Met Thr Pro Ile Leu Thr Val Leu Ile
                1                    5

tgt ctc ggg ctg agt ctg ggc ccc agg acc cac gtg cag gca ggg cac      162
Cys Leu Gly Leu Ser Leu Gly Pro Arg Thr His Val Gln Ala Gly His
10                15                20                25

ctc ccc aag ccc acc ctc tgg gct gag cca ggc tct gtg atc atc cag      210
Leu Pro Lys Pro Thr Leu Trp Ala Glu Pro Gly Ser Val Ile Ile Gln
30                35                40

gga agt cct gtg acc ctc agg tgt cag ggg agc ctt cag gct gag gag      258
Gly Ser Pro Val Thr Leu Arg Cys Gln Gly Ser Leu Gln Ala Glu Glu
45                50                55

tac cat cta tat agg gaa aac aaa tca gca tcc tgg gtt aga cgg ata      306
Tyr His Leu Tyr Arg Glu Asn Lys Ser Ala Ser Trp Val Arg Arg Ile
60                65                70

caa gag cct ggg aag aat ggc cag ttc ccc atc cca tcc atc acc tgg      354
Gln Glu Pro Gly Lys Asn Gly Gln Phe Pro Ile Pro Ser Ile Thr Trp
75                80                85

gaa cac gca ggg cgg tat cac tgt cag tac tac agc cac aat cac tca      402
Glu His Ala Gly Arg Tyr His Cys Gln Tyr Tyr Ser His Asn His Ser
90                95                100                105

tca gag tac agt gac ccc ctg gag ctg gtg gtg aca gga gcc tac agc      450
Ser Glu Tyr Ser Asp Pro Leu Glu Leu Val Val Thr Gly Ala Tyr Ser
110                115                120

aaa ccc acc ctc tca gct ctg ccc agc cct gtg gtg acc tta gga ggg      498
Lys Pro Thr Leu Ser Ala Leu Pro Ser Pro Val Val Thr Leu Gly Gly
125                130                135

aac gtg acc ctc cag tgt gtc tca cag gtg gca ttt gac ggc ttc att      546
Asn Val Thr Leu Gln Cys Val Ser Gln Val Ala Phe Asp Gly Phe Ile
140                145                150

ctg tgt aag gaa gga gaa gat gaa cac cca caa cgc ctg aac tcc cat      594
Leu Cys Lys Glu Gly Glu Asp Glu His Pro Gln Arg Leu Asn Ser His
155                160                165

tcc cat gcc cgt ggg tgg tcc tgg gcc atc ttc tcc gtg ggc ccc gtg      642
Ser His Ala Arg Gly Trp Ser Trp Ala Ile Phe Ser Val Gly Pro Val
170                175                180                185

agc ccg agt cgc agg tgg tcg tac agg tgc tat gct tat gac tcg aac      690
Ser Pro Ser Arg Trp Ser Tyr Arg Cys Tyr Ala Tyr Asp Ser Asn
190                195                200

tct ccc tat gtg tgg tct cta ccc agt gat ctc ctg gag ctc ctg gtc      738
Ser Pro Tyr Val Trp Ser Leu Pro Ser Asp Leu Leu Glu Leu Leu Val
205                210                215

cca ggt gtt tct aag aag cca tca ctc tca gtg cag cca ggt cct atg      786
Pro Gly Val Ser Lys Lys Pro Ser Leu Ser Val Gln Pro Gly Pro Met
220                225                230

gtg gcc cct ggg gag agc ctg acc ctc cag tgt gtc tct gat gtc ggc      834
Val Ala Pro Gly Glu Ser Leu Thr Leu Gln Cys Val Ser Asp Val Gly
235                240                245

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tac gac aga ttt gtt ctg tat aag gag gga gaa cgt gac ttc ctc cag      882
Tyr Asp Arg Phe Val Leu Tyr Lys Glu Gly Glu Arg Asp Phe Leu Gln
250                255                260                265

cgc cct ggt tgg cag ccc cag gct ggg ctc tcc cag gcc aac ttc acc      930
Arg Pro Gly Trp Gln Pro Gln Ala Gly Leu Ser Gln Ala Asn Phe Thr
                270                275                280

ctg ggc cct gtg agc ccc tcc cac ggg ggc cag tac aga tgc tac agt      978
Leu Gly Pro Val Ser Pro Ser His Gly Gly Gln Tyr Arg Cys Tyr Ser
                285                290                295

gca cac aac ctc tcc tcc gag tgg tgc gcc ccc agt gac ccc ctg gac     1026
Ala His Asn Leu Ser Ser Glu Trp Ser Ala Pro Ser Asp Pro Leu Asp
                300                305                310

atc ctg atc aca gga cag ttc tat gac aga ccc tct ctc tgc gtg cag     1074
Ile Leu Ile Thr Gly Gln Phe Tyr Asp Arg Pro Ser Leu Ser Val Gln
                315                320                325

cgg gtc ccc aca gta gcc cca gga aag aac gtg acc ctg ctg tgt cag     1122
Pro Val Pro Thr Val Ala Pro Gly Lys Asn Val Thr Leu Leu Cys Gln
330                335                340                345

tca cgg ggg cag ttc cac act ttc ctt ctg acc aag gag ggg gca ggc     1170
Ser Arg Gly Gln Phe His Thr Phe Leu Leu Thr Lys Glu Gly Ala Gly
                350                355                360

cat ccc cca ctg cat ctg aga tca gag cac caa gct cag cag aac cag     1218
His Pro Pro Leu His Leu Arg Ser Glu His Gln Ala Gln Gln Asn Gln
                365                370                375

gct gaa ttc cgc atg ggt cct gtg acc tca gcc cac gtg ggg acc tac     1266
Ala Glu Phe Arg Met Gly Pro Val Thr Ser Ala His Val Gly Thr Tyr
                380                385                390

aga tgc tac agc tca ctc agc tcc aac ccc tac ctg ctg tct ctc ccc     1314
Arg Cys Tyr Ser Ser Leu Ser Ser Asn Pro Tyr Leu Leu Ser Leu Pro
                395                400                405

agt gac ccc ctg gag ctc gtg gtc tca gca tcc cta ggc caa cac ccc     1362
Ser Asp Pro Leu Glu Leu Val Val Ser Ala Ser Leu Gly Gln His Pro
410                415                420                425

cag gat tac aca gtg gag aat ctc atc cgc atg ggt gtg gct ggc ttg     1410
Gln Asp Tyr Thr Val Glu Asn Leu Ile Arg Met Gly Val Ala Gly Leu
                430                435                440

gtc ctg gtg gtc ctc ggg att ctg cta ttt gag gct cag cac agc cag     1458
Val Leu Val Val Leu Gly Ile Leu Leu Phe Glu Ala Gln His Ser Gln
                445                450                455

aga agc cta caa gat gca gcc ggg agg tga acagcagaga ggacaatgca     1508
Arg Ser Leu Gln Asp Ala Ala Gly Arg
                460                465

tacttcagcg tggaggagcc tcagggacag atctgatgat cccaggaggc tctggaggac 1568

aatctaggac ctacattatc tggactgtat gctggtcatt tctagagaca gcaatcaata 1628

tttgagtgta aggaaactgt ctgggggtgat tcctagaaga tcattaaact gtggtacatt 1688

tttttgtc                                                                1696

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<211> LENGTH: 466
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

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Pro Arg Thr His Val Gln Ala Gly His Leu Pro Lys Pro Thr Leu Trp
 20 25 30
 Ala Glu Pro Gly Ser Val Ile Ile Gln Gly Ser Pro Val Thr Leu Arg
 35 40 45
 Cys Gln Gly Ser Leu Gln Ala Glu Glu Tyr His Leu Tyr Arg Glu Asn
 50 55 60
 Lys Ser Ala Ser Trp Val Arg Arg Ile Gln Glu Pro Gly Lys Asn Gly
 65 70 75 80
 Gln Phe Pro Ile Pro Ser Ile Thr Trp Glu His Ala Gly Arg Tyr His
 85 90 95
 Cys Gln Tyr Tyr Ser His Asn His Ser Ser Glu Tyr Ser Asp Pro Leu
 100 105 110
 Glu Leu Val Val Thr Gly Ala Tyr Ser Lys Pro Thr Leu Ser Ala Leu
 115 120 125
 Pro Ser Pro Val Val Thr Leu Gly Gly Asn Val Thr Leu Gln Cys Val
 130 135 140
 Ser Gln Val Ala Phe Asp Gly Phe Ile Leu Cys Lys Glu Gly Glu Asp
 145 150 155 160
 Glu His Pro Gln Arg Leu Asn Ser His Ser His Ala Arg Gly Trp Ser
 165 170 175
 Trp Ala Ile Phe Ser Val Gly Pro Val Ser Pro Ser Arg Arg Trp Ser
 180 185 190
 Tyr Arg Cys Tyr Ala Tyr Asp Ser Asn Ser Pro Tyr Val Trp Ser Leu
 195 200 205
 Pro Ser Asp Leu Leu Glu Leu Leu Val Pro Gly Val Ser Lys Lys Pro
 210 215 220
 Ser Leu Ser Val Gln Pro Gly Pro Met Val Ala Pro Gly Glu Ser Leu
 225 230 235 240
 Thr Leu Gln Cys Val Ser Asp Val Gly Tyr Asp Arg Phe Val Leu Tyr
 245 250 255
 Lys Glu Gly Glu Arg Asp Phe Leu Gln Arg Pro Gly Trp Gln Pro Gln
 260 265 270
 Ala Gly Leu Ser Gln Ala Asn Phe Thr Leu Gly Pro Val Ser Pro Ser
 275 280 285
 His Gly Gly Gln Tyr Arg Cys Tyr Ser Ala His Asn Leu Ser Ser Glu
 290 295 300
 Trp Ser Ala Pro Ser Asp Pro Leu Asp Ile Leu Ile Thr Gly Gln Phe
 305 310 315 320
 Tyr Asp Arg Pro Ser Leu Ser Val Gln Pro Val Pro Thr Val Ala Pro
 325 330 335
 Gly Lys Asn Val Thr Leu Leu Cys Gln Ser Arg Gly Gln Phe His Thr
 340 345 350
 Phe Leu Leu Thr Lys Glu Gly Ala Gly His Pro Pro Leu His Leu Arg
 355 360 365
 Ser Glu His Gln Ala Gln Gln Asn Gln Ala Glu Phe Arg Met Gly Pro
 370 375 380
 Val Thr Ser Ala His Val Gly Thr Tyr Arg Cys Tyr Ser Ser Leu Ser
 385 390 395 400
 Ser Asn Pro Tyr Leu Leu Ser Leu Pro Ser Asp Pro Leu Glu Leu Val
 405 410 415
 Val Ser Ala Ser Leu Gly Gln His Pro Gln Asp Tyr Thr Val Glu Asn

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420	425	430
Leu Ile Arg Met Gly Val Ala	Gly Leu Val Leu Val Val	Leu Gly Ile
435	440	445
Leu Leu Phe Glu Ala Gln His Ser Gln Arg Ser	Leu Gln Asp Ala Ala	
450	455	460
Gly Arg		
465		

We claim:

1. A method for diagnosing a granulocyte disorder comprising:
 - detecting in a biological sample from a subject a level of expression of one or more granulocyte-selective markers,
 - comparing the level of expression of each of the one or more granulocyte-selective markers with a reference level of expression, wherein a statistically significant difference between the level of expression of at least one granulocyte-selective marker and an expected level of expression for the at least one granulocyte-selective marker is indicative of a granulocyte disorder in the subject.
2. The method of claim 1, wherein the reference level of expression for a granulocyte-selective marker is a normal level of expression of the granulocyte-selective marker in a normal granulocyte.
3. The method of claim 1, wherein the biological sample is a blood sample.
4. The method of claim 1, wherein the biological sample is a tissue sample.
5. The method of claim 1, wherein the level of expression of each of the one or more granulocyte-selective markers is determined by determining an amount of an mRNA in the biological sample corresponding to each of the one or more granulocyte-selective markers.
6. The method of claim 5, wherein the method of determining the amount of mRNA comprises reverse transcription polymerase chain reaction (RT-PCR) amplification.
7. The method of claim 1, wherein the level of expression of each of the one or more granulocyte-selective markers is determined by determining an amount of a protein in the biological sample corresponding to each of the one or more granulocyte-selective markers.
8. The method of claim 7, wherein the method of determining the amount of a protein that corresponds to a granulocyte-selective marker comprises contacting the biological sample with an antibody that binds to the protein.
9. The method of claim 1, wherein a higher level of expression of at least one of the one or more granulocyte-selective markers in the biological sample compared to the expected level of expression for the at least one granulocyte-selective marker is indicative of the granulocyte disorder.
10. The method of claim 1, wherein a lower level of expression of at least one of the one or more granulocyte-selective markers in the biological sample compared to the expected level of expression for the at least one granulocyte-selective marker is indicative of the granulocyte disorder.

11. The method of claim 1, wherein the granulocyte disorder comprises an abnormally high number of one or more types of granulocyte in the biological sample.
12. The method of claim 1, wherein the granulocyte disorder comprises an abnormally low number of one or more types of granulocyte in the biological sample.
13. The method of claim 1, wherein the granulocyte disorder comprises an abnormal pattern of expression of one or more granulocyte selective markers in one or more types of granulocyte in the biological sample.
14. A method for diagnosing a non-neutrophil granulocyte disorder or mast cell disorder comprising:
 - detecting in a biological sample from a subject a level of expression of one or more non-neutrophil granulocyte or mast cell selective markers,
 - comparing the level of expression of each of the one or more non-neutrophil granulocyte or mast cell selective markers with a reference level of expression, wherein a statistically significant difference between the level of expression of at least one non-neutrophil granulocyte or mast cell selective marker and an expected level of expression for the at least one non-neutrophil granulocyte or mast cell selective marker is indicative of a non-neutrophil granulocyte disorder or mast cell disorder in the subject.
15. The method of claim 14, wherein the non-neutrophil granulocyte disorder is a basophil disorder.
16. The method of claim 15, wherein the basophil disorder is a basophil-associated tumor or cancer.
17. The method of claim 14, wherein the non-neutrophil granulocyte disorder is an eosinophil disorder.
18. The method of claim 17, wherein the eosinophil disorder is an eosinophil-associated tumor or cancer.
19. The method of claim 14, wherein the mast cell disorder is a mast cell-associated tumor or cancer.
- 20-48. (canceled)
49. An assay for identifying a compound that alters at least one physiological property of a granulocyte comprising:
 - contacting a granulocyte with a candidate compound that interacts with a granulocyte-selective marker,
 - determining at least one physiological property of the granulocyte after contact with the candidate compound,
 - comparing the at least one physiological property to one at least one reference property to determine whether the candidate compound alters at least one physiological property of the granulocyte.
- 50-71. (canceled)

* * * * *

专利名称(译)	粒细胞亚型选择性受体和离子通道及其用途		
公开(公告)号	US20080187908A1	公开(公告)日	2008-08-07
申请号	US10/591628	申请日	2005-03-03
[标]申请(专利权)人(译)	安泽CHAKERñ		
申请(专利权)人(译)	安泽CHAKERñ		
当前申请(专利权)人(译)	安泽CHAKERñ		
[标]发明人	ADRA CHAKER N		
发明人	ADRA, CHAKER N.		
IPC分类号	C12Q1/68 G01N33/53		
CPC分类号	C12Q1/6809 C12Q1/6883 C12Q2600/158 C12Q2565/501		
优先权	60/549865 2004-03-03 US		
外部链接	Espacenet USPTO		

摘要(译)

本发明部分涉及优先在粒细胞中表达的粒细胞型选择标记及其在药物筛选试验中的用途。另外，粒细胞型选择标记可用于诊断和治疗粒细胞病症和评估粒细胞病症治疗的功效。

