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(54) DIAGNOSTIC AND MEDICAMENT FOR ANALYSING THE CELL SURFACE PROTEOME OF TUMOUR AND INFLAMMATORY CELLS AND FOR TREATING TUMOROUS AND INFLAMMATORY DISEASES, PREFERABLY USING A SPECIFIC CHEMOKINE RECEPTOR ANALYSIS AND THE CHEMOKINE RECEPTOR-LIGAND INTERACTION

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(57) **ABSTRACT**

The present invention relates to the provision of a medicament and of a diagnostic agent obtained by proteome analysis, preferably containing at least two different chemokine receptor ligands or chemokine receptor antibodies, and further to the use of at least two different chemokine receptor ligands, chemokine receptor antibodies and/or two different chemokine receptors. As inhibitors, the medicament preferably contains ligands or antibodies of at least two chemokine receptors or the related algorithms of the surface chemokine receptor proteome, and the use of at least one chemokine receptor ligand and/or chemokine receptor, peptides and antibodies and their use for the diagnostics and therapy of tumor diseases and inflammatory diseases. By way of analogy, clusters of analyzed tumor cell surface proteomes, such as ectoproteases, adhesion molecules or various receptor types, can also be used.

The invention relates to a method for the purpose of diagnosis and therapy and the medical and industrial use of chemokines and their corresponding receptors, their antagonists including antibodies was found to inhibit cancer growth including metastatic spread, and to suppress inflammatory and auto-immune diseases. The method is based on the finding that chemokines act on specific tumor and inflammation cells via autocrine, paracrine and endocrine routes through the disease-specific constellation of the chemokine receptor proteome. Primary and secondary tumors as well as specific inflammation cells are controlled with respect to their migration and proliferation behavior. By diagnostically detecting the chemokines whose expression and regulation is locally increased and the presence of the chemokine receptor compositions, the possibility arises of critically suppressing or completely preventing cancer growth, metastatic spread of tumors as well as inflammatory and auto-immune diseases.

DIAGNOSTIC AND MEDICAMENT FOR ANALYSING THE CELL SURFACE PROTEOME OF TUMOUR AND INFLAMMATORY CELLS AND FOR TREATING TUMOROUS AND INFLAMMATORY DISEASES, PREFERABLY USING A SPECIFIC CHEMOKINE RECEPTOR ANALYSIS AND THE CHEMOKINE RECEPTOR-LIGAND INTERACTION

[0001] The present invention relates to the provision of a medicament and of a diagnostic agent obtained by proteome analysis, preferably containing at least two different chemokine receptor ligands or chemokine receptor antibodies, and further to the use of at least two different chemokine receptor ligands, chemokine receptor antibodies and/or two different chemokine receptors. The medicament comprises the use of inhibitors, ligands or antibodies of at least two chemokine receptors or the related algorithms of the surface chemokine receptor proteome, and the use of at least one chemokine receptor ligand and/or chemokine receptor, peptides and antibodies and their use for the diagnostics and therapy of tumor diseases and inflammatory diseases. By way of analogy, clusters of analyzed tumor cell surface proteomes, such as ectoproteases, adhesion molecules or various receptor types, can also be used.

[0002] In recent time, it has been found more and more often that substances of the regulation of cellular growth and cell migration are of great diagnostic and therapeutic interest, and that a large number of unknown factors are likely to exist which control cancer growth, while primary and secondary tumors and the invaded organs are interacting. Surprisingly, these factors are of clinically useful importance. They include, in particular, the CC and CXC type chemokines, preferably, for example, HCC-1 to HCC-3 and SDF-1 (Schulz-Knappe P. et al., J. Exp. Med. 183: 295, 1996; Pardigol A. et al., Proc. Natl. Acad. Sci. USA 95: 6308, 1998; Nagasawa T. et al., Proc. Natl. Acad. Sci. USA 91: 2305, 1994). Thus, in recent works, it could be demonstrated that cell lines of tumor cells, inter alia, possess the receptors for the known chemokines MCP-1 and RANTES (Wang J. M. et al., Int. J. Cancer 75: 900, 1998). Thus, these tumor cell lines can respond to specific chemokines through stimulation of the receptors. When the corresponding chemokine peptide is formed in appropriate cells, tissues and organs, an autocrine, paracrine or endocrine reaction may occur, influencing cell migration and cell proliferation. Thus, kidney metastases are said to be formed preferentially from those tumors which possess receptors for MCP-1 and RANTES because a strong expression of these chemokines is observed in the kidney (Wang J. M. et al., Int. J. Cancer 75: 900, 1998). In further recent works, it was also established that certain chemokines inhibit tumor growth (Wang J. M. et al., J. Interferon Cytokine Res. 16: 53, 1996), so that tumor growth may also be influenced negatively by a chemokine administration. The role of chemokines in the migration of tumor cells was observed in breast carcinoma cell lines (Youngs et al., Int. J. Cancer 71: 257, 1997). The control of angiogenesis is also influenced positively or negatively by various cytokines. Thus, the chemokine receptor CXCR4, through which the chemokine SDF-1 displays its activity, is essential to the vascularization of the gastrointestinal tract (Tachibana K. et al., Nature 393: 591, 1998). Thus, these factors may also be of critical importance within the scope of the paracrine control of the vascularization of tumors and thus to tumor maintenance.

[0003] The results known to date with respect to the chemokine system and tumors are always based on the observation of individual chemokine receptors. However, because over 15 chemokine receptors have become known in the meantime with over 40 related chemokines, the human chemokine system is extremely complex and moreover redundant. Thus, the previously applied diagnostic and therapeutic method approaches are not optimal for performing specific diagnostics and a specific therapy based on the chemokine system. With the method applied according to the invention, surprisingly, a solution to these problems can be found, thus for the first time allowing reliable diagnostics and therapy of tumor and inflammatory diseases based on the chemokine system or other tumor surface proteome clusters.

[0004] One object of the invention is to improve the diagnostics of tumors and of the presence of inflammatory processes. Another object is to provide an improved treatment of tumors and inflammatory diseases.

[0005] This object is achieved by a diagnostic agent and a medicament according to the invention.

[0006] The diagnostic agent according to the invention contains at least two different ligands of receptors which are involved in a pathological process.

[0007] Preferably, the diagnostic agent according to the invention contains at least two different chemokine receptor ligands, such as protein peptide structures, which interact with chemokine receptors (or other tumor cell surface proteins), namely chemokine receptor ligands, chemokine receptor antagonists and/or chemokine receptor antibodies. Preferably, the chemokine receptor ligands are chemokines, chemokine derivatives, agonists or antagonists of chemokine receptors, antibodies or antibody fragments which at least partially block the binding site of the chemokine receptor and surprisingly result in an inhibition of tumor growth.

[0008] More preferably, the chemokines are selected from the group consisting of the natural chemokines C, CC, CXC, CX_3C, their analogues, binding proteins and antibodies which bind to the specific receptors in accordance with the chemokines mentioned.

[0009] According to the invention, the chemokine receptors are detected and analyzed as a whole or partial proteome including the corresponding chemokine receptor ligands in primary and secondary tumors and circulating single cells, preferably by (1) immunochemical methods (immunohistochemistry using serial sections or multiple successive or simultaneous single sections, FACS analysis), and (2) additionally or alternatively the expression on the transcriptional level by molecular-biological methods (PCR or Northern analysis, in-situ hybridization). Clusters of analyzed tumor cell surface proteomes, such as ectoproteases, adhesion molecules or various receptor types, can also be employed according to the invention.

[0010] Closely related to the diagnostic agent according to the invention is the method according to the invention for recognizing receptors involved in pathological processes, wherein expression profiles are examined on the proteome level using cell-biological or cytochemical methods, especially by immunochemical methods, immunohistochemistry using serial sections or multiple successive or simultaneous

single sections, FACS analysis and/or the expression of receptors on the transcriptional level by molecular-biological methods, especially PCR, Northern analysis and/or in-situ hybridization methods.

[0011] Thus, the present invention also relates to the use of at least two different chemokine receptor ligands and/or two different chemokine receptors for the diagnostic characterization of tumors, which is different for each tumor type and each individual tumor. In particular, the method according to the invention can be applied to tumors from the group consisting of colorectal tumors and prostatic tumors. However, tumors of other organ systems may also be approached diagnostically and thus therapeutically as well with the method according to the invention. In addition, said at least two different chemokine receptors and/or two different chemokine receptor ligands may also be employed for the diagnosis of inflammatory processes, such as organ rejection responses, and for the diagnosis of auto-immune diseases. Thus, especially tumors, inflammatory diseases and auto-immune diseases of the blood system, the lymph system, the cardiovascular system, the nervous system, the respiratory tract, the digestive tract, the endocrine system, the skin including integumentary appendages, the locomotor system and the urogenital tract including the kidney can be diagnosed.

[0012] In contrast to commonly known diagnostic methods, the diagnostic agent according to the invention enables an extension of the cytological characterization of tumor tissues, which may also be used to develop a specific therapy after the diagnosis. Of the chemokine receptors found (and by analogy of other tumor cell proteome clusters), the antagonists/agonists of the related chemokines and the specific chemokine receptor antibodies are employed for influencing the cellular growth. When doing so, an accelerated occurrence of tumor cell death (apoptosis) is surprisingly observed.

[0013] The present invention also relates to a medicament containing at least one inhibitor of at least two chemokine receptors.

[0014] The medicament according to the invention preferably contains antagonists of chemokine receptors, antibodies or antibody fragments which at least partially block the binding site of the chemokine receptor. However, a chemokine receptor/ligand interaction, preferably a protein/protein (peptide) interaction with non-specific molecules obtained from natural extracts, from synthetic or recombinantly prepared binding proteins and from other peptide-protein libraries, is also sufficient to bring about the surprising effect of the apoptosis of tumor cells.

[0015] The inhibitors of at least two chemokine receptors which may be used in the medicament according to the invention may be used for the preparation of a medicament for treating tumors, inflammatory diseases, auto-immune diseases of the bone marrow and other organs, graft rejection reactions. Thus, in particular, tumors, inflammatory diseases and auto-immune diseases of the blood system, the lymph system, the cardiovascular system, the nervous system, the respiratory tract, the digestive tract, the endocrine system, the skin including integumentary appendages, the locomotor system and the urogenital tract including the kidney can be treated.

[0016] Preferably, inhibitors or protein ligands are used which are selected from the group consisting of antagonists of chemokine receptors, antibodies or antibody fragments which at least partially block the binding site of the chemokine receptor.

[0017] The tumors which can be treated are especially selected from the group consisting of colorectal tumors, prostatic tumors and other tumor diseases of the blood system, lymph system, cardiovascular system, nervous system, respiratory tract, digestive tract, endocrine system, skin including integumentary appendages, locomotor system and urogenital tract including the kidney.

[0018] The inflammatory processes to be treated are especially selected from the group consisting of asthma bronchiale, chronic inflammatory bowel diseases, organ rejection and further inflammatory processes of the blood system, lymph system, cardiovascular system, nervous system, respiratory tract, digestive tract, endocrine system, skin including integumentary appendages, locomotor system and urogenital tract including the kidney.

[0019] The auto-immune diseases to be treated are especially selected from the group consisting of rheumatoid arthritis, lupus erythematodes and other chronic diseases of the blood system, lymph system, cardiovascular system, nervous system, respiratory tract, digestive tract, endocrine system, skin including integumentary appendages, locomotor system and urogenital tract including the kidney.

[0020] In the diagnosis of organ rejection reactions following organ transplantations, especially performed on leucocytes obtained from the circulation of patients, the use of only at least one chemokine receptor ligand and/or one chemokine receptor is also possible.

[0021] The invention further relates to the use of an inhibitor of a chemokine receptor for preparing a medicament for preventing or alleviating organ rejection reactions following organ transplantations, especially following transplantations of the heart, liver, kidney and pancreas as well as other organs, tissues and cell systems of the gastrointestinal tract, respiratory tract, urogenital tract, cardiovascular system, neuro-endocrine system, and the locomotor system as well as the blood and immune systems.

[0022] In addition to establishing new causalities in a pathological process, the method according to the invention can also be employed for the purpose of diagnosis and therapy. By means of the method according to the invention, for example, the use of chemokines and their corresponding receptors, their antagonists including antibodies was found to inhibit cancer growth including metastatic spread, and to suppress inflammatory and auto-immune diseases. The method according to the invention is based on the finding that chemokines act on specific tumor and inflammation cells via autocrine, paracrine and endocrine routes through the disease-specific constellation of the chemokine receptor proteome. Primary and secondary tumors as well as specific inflammation cells are controlled with respect to their migration and proliferation behavior. By diagnostically detecting the chemokines whose expression and regulation is locally increased and the presence of the chemokine receptor compositions, the possibility arises of critically suppressing or completely preventing cancer growth, metastatic spread of tumors as well as inflammatory and auto-immune diseases.

[0023] The peptides according to the invention having the SEQ ID NOS. 1 to 40 can be employed as epitopes for generating antibodies. These sequences according to the invention are (ID 1-40):

[0024] Amino acid sequences of the N-terminal domains of human chemokine receptors employed for the preparation of specific antibodies

[0025] 1 CXCR1 X-MSNITDPQMWDFDDLNFTGMPPADEDYSPCMLETETLNK-Y

[0026] 2 CXCR2 X-MEDFNMESDSFEDFWKGEDLSNYSYSSTLPPFLLDAAPCEPESLEINK-Y

[0027] 3 CXCR3 X-MVLEVSDHQVLNDAEVAALLENFSSSYDYGENESDSCCTSPPCPQDFSLNFDR-Y

[0028] 4 CXCR4 X-MEGISIYTSDNYTEEMGSGDYDSMKEPCFREENANFNKI-Y

[0029] 5 CXCR5 X-MNYPLTLEMDLENLEDLFWELDRLDNYNDTSLVENHLCPATGPLMASFKAVFVP-Y

[0030] 4 CXCR6 X-MAEHDYHEDYGFSSFNDSSQEEHQDFLQFSKV-Y

[0031] 5 CCR1 X-METPNTTEDYDTTTEFDYGDATPCQKVNERAFGA-Y

[0032] 6 CCR2 X-MLSTSRSRFIRNTNESGEEVTTFFDYDYGAPCHKFDVKQIGA-Y

[0033] 7 CCR3 X-MTTSLDTVETFGTTSYYDDVGLLCEKADTRALMA-Y

[0034] 8 CCR4 X-MNPTDIADTTLDESIYSNYYLYESIPKPCTKEGIKAFGE-Y

[0035] 9 CCR5 X-MDYQVSSPIYDINYYTSEPCQKINVKQIAA-Y

[0036] 10 CCR6a X-MSGESMNFSDVFDSSEDYFVSVNTSYYSVDSEMLLCSLQEVRQFSRL-Y

[0037] 11 CCR6b X-MNFSDVFDSSEDYFVSVNTSYYSVDSEMLLCSLQEVRQFSRL-Y

[0038] 12 CCR7 X-MDLGKPMKSVLVVALLVIFQVCLCQDEVTDDYIGDNTTVDYTLFESLCSKKDVRNFKAW-Y

[0039] 13 CCR8 X-MDYTLDLSVTTVTDYYYPDIFSSPCDAELIQTNGK-Y

[0040] 14 CCR9a X-MTPTDFTSPIPNMADDYGSESTSSMEDYVNFNFTDFYCEKNNVRQFASH-Y

[0041] 15 CCR9b X-MADDYGSESTSSMEDYVNFNFTDFYCEKNNVRQFASH-Y

[0042] 16 CCR10 X-MGTEATEQVSWGHYSGDEEDAYSAEPLPELCYKADVQAFSRAFQPSVSLTVA-Y

[0043] 17 CCR11 X-MALEQNQSTDYYYEENEMNGTYDYSQYELICIKEDVREFAKV-Y

[0044] 18 XCR1 X-MESSGNPESTTFFYYDLQSQPCENQAWVFAT-Y

[0045] 19 CX3CR1 X-MDQFPESVTENFEYDDLAEACYIGDIVVFGT-Y

[0046] 20 D6 X-MAATASPQPLATEDADSENSSFYYYDYLDEVAFMLCRKDAVVSFGKVFL-Y

[0047] Amino acid sequences of the 2nd extracellular loop domains of human chemokine receptors employed for the preparation of specific antibodies

[0048] 21 CXCR1 X-RQAYHPNNSSPVCYEVLGNDTAKWRM-Y, especially CFRQAYHPNNSSPV

[0049] 22 CXCR2 X-RRTVYSSNVSPACYEDMGNNTANWR-Y, especially CFRRTVYSSNVSPA

[0050] 23 CXCR3 X-LSAHHDERLNATHCQYNFPQVGR-Y, especially CLSAHHDERLNATH

[0051] 24 CXCR4 X-NVSEADDRYICDRFYPNDLWVVVFQ-Y, especially DRFYPNDLWVVVFQFC

[0052] 25 CXCR5 X-KVSQGHHNNSLPRCTFSQENQAETHAWFTSR-Y, especially TFSQENQAETHAWFTSRC

[0053] 26 CXCR6 X-PQIIYGNVFNLDKLICGYHDEAI-Y, especially

[0054] 27 CCR1 X-SKTQWEFTHHTCSLHFPHESLREWKL-Y, especially SLHFPHESLREWKLC

[0055] 28 CCR2 X-TKCQKEDSVYVCGPYFPRGWNNFHTIMR-Y, especially GPYFPRGWNNFHTIMRNC

[0056] 29 CCR3 X-YETEELFEETLCSALYPEDTVYSWRHFHTLRM-Y, especially SALYPEDTVYSWRHFHTLRMTC

[0057] 30 CCR4 X-STCYTERNHTYCKTKYSLNSTTWKVLSSLEI-Y, especially KTKYSLNSTTWKVLSSLEINC

[0058] 31 CCR5 X-TRSQKEGLHYTCSSHFPYSQYQFWKNFQTLKI-Y, especially SSHFPYSQYQFWKNFQTLKIVC

[0059] 32 CCR6 X-STFVFNQKYNTQGSDVCEPKYQTVSEPIRW-Y, especially EPKYQTVSEPIRWKC

[0060] 33 CCR7 X-PELLYSDLQRSSSEQAMRCSLITEHVEA-Y, especially CPELLYSDLQRSSSEQAMR

[0061] 34 CCR8 X-YQVASEDGVLQCYSFYNQQTLKWKIFTNFKM-Y, especially YSFYNQQTLKWKIFTNFKMC

[0062] 35 CCR9 X-PEILYSQIKEESGIAICTMVYPSDESTKL-Y, especially CTMVYPSDESTKLK

[0063] 36 CCR10 X-SQDGQREGQRRCRLIFPEGLTQTV-Y, especially FSQDGQREGQRRC

[0064] 37 CCR11 X-TVNDNARCIPIFPRYLGTSMKA-Y, especially CIPIFPRYLGTSMKA

[0065] 38 XCR1 X-HKVLSSGCDYSELTWYLTSVYQH-Y, especially DYSELTWYLTSVYQHC

[0066] 39 CX3CR1 X-TKQKENECLGDYPEVLQEIWPVLRNVET-Y, especially LGDYPEVLQEIWPVLRNVET

[0067] 40 D6 X-QTHENPKGVWNCHADFGGHGTI-WKLFLRFQQNL-Y, especially HADFGGHGTI-WKLFLRFQQNC

[0068] wherein X means an amino acid residue or a peptide residue of up to 30 amino acids, wherein Y means an amino acid residue or a peptide residue of up to 30 amino acids.

[0069] To prepare the antibodies, the peptides according to the invention (sequences according to ID 1-40), which are not normally immunogenic, are coupled to the protein carrier KLH (keyhole limpet hemocyanin). This coupling is effected by means of MBS (m-maleimidobenzoyl-N-hydroxysuccinimide ester) through a cysteine terminally integrated into the peptide, or directly by means of carbodiimide.

[0070] The antibodies are obtained with conventional methods by immunization, preferably of mice, rabbits etc. The methods for the preparation of monoclonal antibodies by molecular-biological methods, such as recombinant preparation, can also be used. The antibodies are purified by the known methods and galenically formulated for use.

[0071] Further, cell preparations, cell extracts and, in particular, membrane isolates from overexpressing, artificially transfected chemokine receptor bearing cells were used for generating such specific antibodies.

[0072] According to the invention, this included the use of proteins based on known sequences as epitopes for generating antibodies. These sequences are known (ID 41-63):

[0073] 41 CCR1 ACCESSION P32246 355aa

[0074] 1 METPNTTEDY DTTTEFDYGD ATPC-QKVNER AFGAQLLPPL YSLVFVIGLV GNIL-VVLVLV

[0075] 61 QYKRLKNMTS IYLLNLAISD LLFLFTLPFW IDYKLKDDWV FGDAMCK-ILS GFYYTGLYSE

[0076] 121 IFFIILLTID RYLAIVHAVF ALRARTVTFG VITSIIIWAL AILASMPGLY FSKTQWEFTH

[0077] 181 HTCSLHFPHE SLREWKLFQA LKLNLFGLVL PLLVMIICYT GIIKILLRRP NEKKSKAVRL

[0078] 241 IFVIMIIFFL FWTPYNLTIL ISVFQDFLFT HECEQSRHLD LAVQVTEVIA YTHCCVNPVI

[0079] 301 YAFVGERFRK YLRQLFHRRV AVHLVKWLPF LSVDRLERVS STSPSTGEHE LSAGF

[0080] 42 CCR2a ACCESSION P41597 374aa

[0081] 1 MLSTSRSRFI RNTNESGEEV TTFFDYDYGA PCHKFDVKQI GAQLLPPLYS LVFIFGFVGN

[0082] 61 MLVVLILINC KKLKCLTDIY LLN-LAISDLL FLITLPLWAH SAANEWVFGN AMCKLFTGLY

[0083] 121 HIGYFGGIFF IILLTIDRYL AIVHAVFALK ARTVTFGVVT SVITWLVAVF ASVPGIIFTK

[0084] 181 CQKEDSVYVC GPYFPRGWNN FHTIMRNILG LVLPLLIMVI CYSGILKTLL RCRNEKKRHR

[0085] 241 AVRVIFTIMI VYFLFWTPYN IVILLNTFQE FFGLSNCEST SQLDQATQVT ETLGMTHCCI

[0086] 301 NPIIYAFVGE KFRSLFHIAL GCRIAPLQKP VCGGPGVRPG KNVKVT-TQGL LDGRGKGKSI

[0087] 361 GRAPEASLQD KEGA

[0088] 43 CCR2b ACCESSION NP_{13}000639 360aa

[0089] 1 MLSTSRSRFI RNTNESGEEV TTFFDYDYGA PCHKFDVKQI GAQLLPPLYS LVFIFGFVGN

[0090] 61 MLVVLILINC KKLKCLTDIY LLN-LAISDLL FLITLPLWAH SAANEWVFGN AMCKLFTGLY

[0091] 121 HIGYFGGIFF IILLTIDRYL AIVHAVFALK ARTVTFGVVT SVITWLVAVF ASVPGIIFTK

[0092] 181 CQKEDSVYVC GPYFPRGWNN FHTIMRNILG LVLPLLIMVI CYSGILKTLL RCRNEKKRHR

[0093] 241 AVRVIFTIMI VYFLFWTPYN IVILLNTFQE FFGLSNCEST SQLDQATQVT ETLGMTHCCI

[0094] 301 NPIIYAFVGE KFRRYLSVFF RKHITKRFCK QCPVFYRETV DGVTSTNTPS TGEQEVSAGL

[0095] 44 CCR3 ACCESSION P51677 355aa

[0096] 1 MTTSLDTVET FGTTSYYDDV GLLCEKADTR ALMAQFVPPL YSLVFTVGLL GNVVVVMILI

[0097] 61 KYRRLRIMTN IYLLNLAISD LLFLVTLPFW IHYVRGHNWV FGHGMCK-LLS GFYHTGLYSE

[0098] 121 IFFIILLTID RYLAIVHAVF ALRARTVTFG VITSIVTWGL AVLAALPEFI FYETEELFEE

[0099] 181 TLCSALYPED TVYSWRHFHT LRMTIFCLVL PLLVMAICYT GIIKTLLRCP SKKKYKAIRL

[0100] 241 IFVIMAVFFI FWTPYNVAIL LSSYQSILFG NDCERSKHLD LVMLVTEVIA YSHCCMNPVI

[0101] 301 YAFVGERFRK YLRHFFHRHL LMHLGRYIPF LPSEKLERTS SVSPSTAEPE LSIVF

[0102] 45 CCR4 ACCESSION P51679 360aa

[0103] 1 MNPTDIADTT LDESIYSNYY LYESIPKPCT KEGIKAFGEL FLPPLYSLVF VFGLLGNSVV

[0104] 61 VLVLFKYKRL RSMTDVYLLN LAISDLLFVF SLPFWGYYAA DQWVF-GLGLC KMISWMYLVG

[0105] 121 FYSGIFFVML MSIDRYLAIV HAVFSLRART LTYGVITSLA TWSVAVFASL PGFLFSTCYT

[0106] 181 ERNHTYCKTK YSLNSTTWKV LSSLEINILG LVIPLGIMLF CYSMIIRTLQ HCKNEKKNKA

[0107] 241 VKMIFAVVVL FLGFWTPYNI VLFLETLVEL EVLQDCTFER YLDYAIQATE TLAFVHCCLN

[0108] 301 PIIYFFLGEK FRKYILQLFK TCR-GLFVLCQ YCGLLQIYSA DTPSSSYTQS TMDHDLHDAL

[0109] 361

[0110] 46 CCR5 ACCESSION P51681 352aa

[0111] 1 MDYQVSSPIY DINYYTSEPC QKIN-VKQIAA RLLPPLYSLV FIFGFVGNML VILIL-INCKR

[0112] 61 LKSMTDIYLL NLAISDLFFL LTVPF-WAHYA AAQWDFGNTM CQLLTGLYFI GFF-SGIFFII

[0113] 121 LLTIDRYLAV VHAVFALKAR TVT-FGVVTSV ITWVVAVFAS LPGIIFTRSQ KEG-LHYTCSS

[0114] 181 HFPYSQYQFW KNFQTLKIVI LGLVLPLLVM VICYSGILKT LLRCRNEKKR HRAVRLIFTI

[0115] 241 MIVYFLFWAP YNIVLLLNTF QEF-FGLNNCS SSNRLDQAMQ VTETLGMTHC CINPIIYAFV

[0116] 301 GEKFRNYLLV FFQKHIAKRF CKCCSIFQQE APERASSVYT RSTGEQEISV GL

[0117] 47 CCR6a ACCESSION P51684 374aa

[0118] 1 MSGESMNFSD VFDSSEDYFV SVNTSYYSVD SEMLLCSLQE VRQFSRLFVP IAYSLICVFG

[0119] 61 LLGNILVVIT FAFYKKARSM TDVYLLNMAI ADILFVLTLP FWAVSHATGA WVFSNATCKL

[0120] 121 LKGIYAINFN CGMLLLTCIS MDRYIAIVQA TKSFRLRSRT LPRSKIICLV VWGLSVIISS

[0121] 181 STFVFNQKYN TQGSDVCEPK YQTVSEPIRW KLLMLGLELL FGFFIPLMFM IFCYTFIVKT

[0122] 241 LVQAQNSKRH KAIRVIIAVV LVFLACQIPH NMVLLVTAAN LGKMNR-SCQS EKLIGYTKTV

[0123] 301 TEVLAFLHCC LNPVLYAFIG QKFRNYFLKI LKDLWCVRRK YKSSGFS-CAG RYSENISRQT

[0124] 361 SETADNDNAS SFTM

[0125] 48 CCR6b 369aa

[0126] 1 MNFSDVFDSS EDYFVSVNTS YYS-VDSEMLL CSLQEVRQFS RLFVPIAYSL ICVFGLLGNI

[0127] 61 LVVITFAFYK KARSMTDVYL LNMAIADILF VLTLPFWAVS HATGAWVFSN ATCKLLKGIY

[0128] 121 AINFNCGMLL LTCISMDRYI AIVQATKSFR LRSRTLPRSK IICLVVWGLS VIISSSTFVF

[0129] 181 NQKYNTQGSD VCEPKYQTVS EPIRWKLLML GLELLFGFFI PLMFMIFCYT FIVKTLVQAQ

[0130] 241 NSKRHKAIRV IIAVVLVFLA CQIPHNMVLL VTAANLGKMN RSCQSEK-LIG YTKTVTEVLA

[0131] 301 FLHCCLNPVL YAFIGQKFRN YFLKILKDLW CVRRKYKSSG FSCAGRY-SEN ISRQTSETAD

[0132] 361 NDNASSFTM

[0133] 49 CCR7 ACCESSION P32248 378aa

[0134] 1 MDLGKPMKSV LVVALLVIFQ VCLCQDEVTD DYIGDNTTVD YTLFESLCSK KDVRNFKAWF

[0135] 61 LPIMYSIICF VGLLGNGLVV LTYIY-FKRLK TMTDTYLLNL AVADILFLLT LPF-WAYSAAK

[0136] 121 SWVFGVHFCK LIFAIYKMSF FSG-MLLLLCI SIDRYVAIVQ AVSAHRHRAR VLLISKLSCV

[0137] 181 GIWILATVLS IPELLYSDLQ RSSSEQAMRC SLITEHVEAF ITIQVAQMVI GFLVPLLAMS

[0138] 241 FCYLVIIRTL LQARNFERNK AIKVIIAVVV VFIVFQLPYN GVVLAQTVAN FNITSSTCEL

[0139] 301 SKQLNIAYDV TYSLACVRCC VNPFLYAFIG VKFRNDLFKL FKDLGCLSQE QLRQWSSCRH

[0140] 361 IRRSSMSVEA ETTTRFSP

[0141] 50 CCR8 ACCESSION P51685 355aa

[0142] 1 MDYTLDLSVT TVTDYYYPDI FSSPCDAELI QTNGKLLLAV FYCLLFVFSL LGNSLVILVL

[0143] 61 VVCKKLRSIT DVYLLNLALS DLL-FVFSFPF QTYYLLDQWV FGTVMCKVVS GFYYIGFYSS

[0144] 121 MFFITLMSVD RYLAVVHAVY ALKVRTIRMG TTLCLAVWLT AIMATIPLLV FYQVASEDGV

[0145] 181 LQCYSFYNQQ TLKWKIFTNF KMNILGLLIP FTIFMFCYIK ILHQLKRCQN HNKTKAIRLV

[0146] 241 LIVVIASLLF WVPFNVVLFL TSLHSMHILD GCSISQQLTY ATHVREIISF THCCVNPVIY

[0147] 301 AFVGEKFKKH LSEIFQKSCS QIFNYLGRQM PRESCEKSSS CQQHSSRSSS VDYIL

[0148] 51 CCR9a ACCESSION $XP_{13}003251$ 369aa

[0149] 1 MTPTDFTSPI PNMADDYGSE STSSMEDYVN FNFTDFYCEK NNVRQFASHF LPPLYWLVFI

[0150] 61 VGALGNSLVI LVYWYCTRVK TMTDMFLLNL AIADLLFLVT LPFWAIAAAD QWKFQTFMCK

[0151] 121 VVNSMYKMNF YSCVLLIMCI SVDRYIAIAQ AMPAHTWREK RLLYSKMVCF TIWVLAAALC

[0152] 181 IPEILYSQIK EESGIAICTM VYPSDESTKL KSAVLTLKVI LGFFLPFVVM ACCYTIIIHT

[0153] 241 LIQAKKSSKH KALKVTITVL TVFVLSQFPY NCILLVQTID AYAMFISNCA VSTNIDICFQ

[0154] 301 VTQTIAFFHS CLNPVLYVFV GERFRRDLVK TLKNLGCISQ AQWVSFTRRE GSLKLSSMLL

[0155] 361 ETTSGALSL

[0156] 52 CCR9b ACCESSION P51686 357aa

[0157] 1 MADDYGSEST SSMEDYVNFN FTDFYCEKNN VRQFASHFLP PLYWLVFIVG ALGNSLVILV

[0158] 61 YWYCTRVKTM TDMFLLNLAI ADLLFLVTLP FWAIAAADQW KFQTFMCKVV NSMYKMNFYS

[0159] 121 CVLLIMCISV DRYIAIAQAM RAHTWREKRL LYSKMVCFTI WVLAAALCIP EILYSQIKEE

[0160] 181 SGIAICTMVY PSDESTKLKS AVLTLKVILG FFLPFVVMAC CYTIIIHTLI QAKKSSKHKA

[0161] 241 LKVTITVLTV FVLSQFPYNC ILLVQTIDAY AMFISNCAVS TNIDICFQVT QTIAFFHSCL

[0162] 301 NPVLYVFVGE RFRRDLVKTL KNLGCISQAQ WVSFTRREGS LKLSSMLLET TSGALSL

[0163] 53 CCR10 ACCESSION P46092 362aa

[0164] 1 MGTEATEQVS WGHYSGDEED AYSAEPLPEL CYKADVQAFS RAFQPSVSLT VAALGLAGNG

[0165] 61 LVLATHLAAR RAARSPTSAH LLQLALADLL LALTLPFAAA GALQGWSLGS ATCRTISGLY

[0166] 121 SASFHAGFLF LACISADRYV AIARALPAGP RPSTPGRAHL VSVIVWLLSL LLALPALLFS

[0167] 181 QDGQREGQRR CRLIFPEGLT QTVKGASAVA QVALGFALPL GVMVACYALL GRTLLAARGP

[0168] 241 ERRRALRVVV ALVAAFVVLQ LPYSLALLLD TADLLAARER SCPASKRKDV ALLVTSGLAL

[0169] 301 ARCGLNPVLY AFLGLRFRQD LRRLLRGGSS PSGPQPRRGC PRRPRLSSCS APTETHSLSW

[0170] 361 DN

[0171] 54 CCR11 ACCESSION AAF61299 350aa

[0172] 1 MALEQNQSTD YYYEENEMNG TYDYSQYELI CIKEDVREFA KVFLPVFLTI VFVIGLAGNS

[0173] 61 MVVAIYAYYK KQRTKTDVYI LNLAVADLLL LFTLPFWAVN AVHGWVLGKI MCKITSALYT

[0174] 121 LNFVSGMQFL ACISIDRYVA VTKVPSQSGV GKPCWIICFC VWMAAILLSI PQLVFYTVND

[0175] 181 NARCIPIFPR YLGTSMKALI QMLEICIGFV VPFLIMGVCY FITARTLMKM PNIKISRPLK

[0176] 241 VLLTVVIVFI VTQLPYNIVK FCRAIDIIYS LITSCNMSKR MDIAIQVTES IALFHSCLNP

[0177] 301 ILYVFMGASF KNYVMKVAKK YGSWRRQRQS VEEFPFDSEG PTEPTSTFSI

[0178] 55 CXCR1 ACCESSION P25024 350aa

[0179] 1 MSNITDPQMW DFDDLNFTGM PPADEDYSPC MLETETLNKY VVIIAYALVF LLSLLGNSLV

[0180] 61 MLVILYSRVG RSVTDVYLLN LALADLLFAL TLPIWAASKV NGWIFGTFLC KVVSLLKEVN

[0181] 121 FYSGILLLAC ISVDRYLAIV HATRTLTQKR HLVKFVCLGC WGLSMNLSLP FFLFRQAYHP

[0182] 181 NNSSPVCYEV LGNDTAKWRM VLRILPHTFG FIVPLFVMLF CYGFTLRTLF KAHMGQKHRA

[0183] 241 MRVIFAVVLI FLLCWLPYNL VLLADTLMRT QVIQETCERR NNIGRALDAT EILGFLHSCL

[0184] 301 NPIIYAFIGQ NFRHGFLKIL AMHGLVSKEF LARHRVTSYT SSSVNVSSNL

[0185] 56 CXCR2 ACCESSION P25025 360aa

[0186] 1 MEDFNMESDS FEDFWKGEDL SNYSYSSTLP PFLLDAAPCE PESLEINKYF VVIIYALVFL

[0187] 61 LSLLGNSLVM LVILYSRVGR SVTD-VYLLNL ALADLLFALT LPIWAASKVN GWIFGTFLCK

[0188] 121 VVSLLKEVNF YSGILLLACI SVDRYLAIVH ATRTLTQKRY LVKFICLSIW GLSLLLALPV

[0189] 181 LLFRRTVYSS NVSPACYEDM GNNTANWRML LRILPQSFGF IVPLLIMLFC YGFTLRTLFK

[0190] 241 AHMGQKHRAM RVIFAWLIF LLCWLPYNLV LLADTLMRTQ VIQET-CERRN HIDRALDATE

[0191] 301 ILGILHSCLN PLIYAFIGQK FRHGLLKILA IHGLISKDSL PKDSRPSFVG SSSGHTSTTL

[0192] 57 CXCR3 ACCESSION P49682 368aa

[0193] 1 MVLEVSDHQV LNDAEVAALL ENF-SSSYDYG ENESDSCCTS PPCPQDFSLN FDRAFLPALY

[0194] 61 SLLFLLGLLG NGAVAAVLLS RRTALSSTDT FLLHLAVADT LLVLTLPLWA VDAAVQWVFG

[0195] 121 SGLCKVAGAL FNINFYAGAL LLA-CISFDRY LNIVHATQLY RRGPPARVTL TCLAVWGLCL

[0196] 181 LFALPDFIFL SAHHDERLNA THC-QYNFPQV GRTALRVLQL VAGFLLPLLV MAYCYAHILA

[0197] 241 VLLVSRGQRR LRAMRLVVVV VVAFALCWTP YHLVVLVDIL MDL-GALARNC GRESRVDVAK

[0198] 301 SVTSGLGYMH CCLNPLLYAF VGVKFRERMW MLLLRLGCPN QRGLQRQPSS SRRDSSWSET

[0199] 361 SEASYSGL

[0200] 58 CXCR4 ACCESSION P30991 352aa

[0201] 1 MEGISIYTSD NYTEEMGSGD YDSMKEPCFR EENANFNKIF LPTIYSIIFL TGIVGNGLVI

[0202] 61 LVMGYQKKLR SMTDKYRLHL SVADLLFVIT LPFWAVDAVA NWYFGNFLCK AVHVIYTVNL

[0203] 121 YSSVLILAFI SLDRYLAIVH ATNSQRPRKL LAEKVVYVGV WIPALLLTIP DFIFANVSEA

[0204] 181 DDRYICDRFY PNDLWVVVFQ FQHIMVGLIL PGIVILSCYC IIISKLSHSK GHQKRKALKT

[0205] 241 TVILILAFFA CWLPYYIGIS IDSFIL-LEII KQGCEFENTV HKWISITEAL AFFHC-CLNPI

[0206] 301 LYAFLGAKFK TSAQHALTSV SRGSSLKILS KGKRGGHSSV STESESSSFH SS

[0207] 59 CXCR5 ACCESSION P32302 372aa

[0208] 1 MNYPLTLEMD LENLEDLFWE LDRLDNYNDT SLVENHLCPA TEGPL-MASFK AVFVPVAYSL

[0209] 61 IFLLGVIGNV LVLVILERHR QTRSSTETFL FHLAVADLLL VFILPFAVAE GSVGWVLGTF

[0210] 121 LCKTVIALHK VNFYCSSLLL ACIAVDRYLA IVHAVHAYRH RRLLSIHITC GTIWLVGFLL

[0211] 181 ALPEILFAKV SQGHHNNSLP RCTFSQENQA ETHAWFTSRF LYHVAGFLLP MLVMGWCYVG

[0212] 241 VVHRLRQAQR RPQRQKAVRV AILVTSIFFL CWSPYHIVIF LDTLARLKAV DNTCKLNGSL

[0213] 301 PVAITMCEFL GLAHCCLNPM LYT-FAGVKFR SDLSRLLTKL GCTGPASLCQ LFPSWRRSSL

[0214] 361 SESENATSLT TF

[0215] 60 CXCR6 ACCESSION NP_{13}006555 342aa

[0216] 1 MAEHDYHEDY GFSSFNDSSQ EEHQDFLQFS KVFLPCMYLV VFVCGLVGNS LVLVISIFYH

[0217] 61 KLQSLTDVFL VNLPLADLVF VCTLPFWAYA GIHEWVFGQV MCK-SLLGIYT INFYTSMLIL

[0218] 121 TCITVDRFIV VVKATKAYNQ QAKRMTWGKV TSLLIWVISL LVSLPQIIYG NVFNLDKLIC

[0219] 181 GYHDEAISTV VLATQMTLGF FLPLLTMIVC YSVIIKTLLH AGGFQKHRSL KIIFLVMAVF

[0220] 241 LLTQMPFNLM KFIRSTHWEY YAMTSFHYTI MVTEAIAYLR ACLNPVLYAF VSLKFRKNFW

[0221] 301 KLVKDIGCLP YLGVSHQWKS SEDNSKTFSA SHNVEATSMF QL

[0222] 61 CX3CR1 ACCESSION P49238 355aa

[0223] 1 MDQFPESVTE NFEYDDLAEA CYIGDIVVFG TVFLSIFYSV IFAIGLVGNL LVVFALTNSK

[0224] 61 KPKSVTDIYL LNLALSDLLF VATLPFWTHY LINEKGLHNA MCKFTTAFFF IGFFGSIFFI

[0225] 121 TVISIDRYLA IVLAANSMNN RTVQHGVTIS LGVWAAAILV AAPQFM-FTKQ KENECLGDYP

[0226] 181 EVLQEIWPVL RNVETNFLGF LLPLLIMSYC YFRIIQTLFS CKNHKKAKAI KLILLVVIVF

[0227] 241 FLFWTPYNVM IFLETLKLYD FFP-SCDMRKD LRLALSVTET VAFSHCCLNP LIYAFAGEKF

[0228] 301 RRYLYHLYGK CLAVLCGRSV HVDFSSSESQ RSRHGSVLSS NFTYHTSDGD ALLLL

[0229] 62 XCR1 ACCESSION P46094 333aa

[0230] 1 MESSGNPEST TFFYYDLQSQ PCEN-QAWVFA TLATTVLYCL VFLLSLVGNS LVL-WVLVKYE

[0231] 61 SLESLTNIFI LNLCLSDLVF ACLL-PVWISP YHWGWVLGDF LCKLLNMIFS ISL-YSSIFFL

[0232] 121 TIMTIHRYLS VVSPLSTLRV PTLR-CRVLVT MAVWVASILS SILDTIFHKV LSS-GCDYSEL

[0233] 181 TWYLTSVYQH NLFFLLSLGI ILF-CYVEILR TLFRSRSKRR HRTVKLIFAI VVAY-FLSWGP

[0234] 241 YNFTLFLQTL FRTQIIRSCE AKQQ-LEYALL ICRNLAFSHC CFNPVLYVFV GVK-FRTHLKH

[0235] 301 VLRQFWFCRL QAPSPASIPH SPGAFAYEGA SFY

[0236] 63 D6 ACCESSION $XP_{13}003126$ 384aa

[0237] 1 MAATASPQPL ATEDADSENS SFYYYDYLDE VAFMLCRKDA VVSFGKV-FLP VFYSLIFVLG

[0238] 61 LSGNLLLLMV LLRYVPRRRM VEIYLLNLAI SNLLFLVTLP FWGISVAWHW VFGSFLCKMV

[0239] 121 STLYTINFYS GIFFISCMSL DKY-LEIVHAQ PYHRLRTRAK SLLLATIVWA VSLAVSIPDM

[0240] 181 VFVQTHENPK GVWNCHADFG GHGTIWKLFL RFQQNLLGFL LPLLAMIFFY SRIGCVLVRL

[0241] 241 RPAGQGRALK IAAALVVAFF VLWFPYNLTL FLHTLLDLQV FGNCEVSQHL DYALQVTESI

[0242] 301 AFLHCCFSPI LYAFSSHRFR QYLKAFLAAV LGWHLAPGTA QASLSSC-SES SILTAQEEMT

[0243] 361 GMNDLGERQS ENYPNKEDVG NKSA

[0244] The medicaments according to the invention can be administered in suitable galenic dosage forms, especially in a lyophilized form taken up with mannitol or similar sugars in sterile ampoules for dissolving in physiological saline and/or infusion solution for repeated single injection and/or permanent infusion in amounts of from 300 mg to 30 mg of pure chemokine receptor ligands, especially chemokines, chemokine agonists or antagonists as well as chemokine and chemokine receptor antibodies, per therapeutic unit. Preferably, the medicament according to the invention is administered in a galenic dosage form in which the medicament is employed in biocompatible microspheres, systemically or topically through an aerosol or through intravenous or subcutaneous administration.

[0245] According to the invention, the following approach may also be used in this method. The tumor cells whose receptor composition is to be examined are grown in parallel in vitro, and the cells obtained therefrom are also examined for their receptor composition and treated with chemokines, preferably of the types HCC-1, HCC-2, MCP-1, RANTES or SDF-1. In addition, the known analogues were also employed. With the modified Boyden migration chamber method, it can be established that the tumor cells display a chemotactic response upon the addition of agonists which bind to the corresponding chemokine receptors. The inhibition of their migration is confirmed by previous incubation with antagonists or receptor antibodies.

[0246] When highly purified antibodies were used, it could be established that these are capable of causing apoptosis of tumor cells in both in-vitro and in-vivo models. When cell lines or removed tumor cells are grown using the usual cell culture methods, their survival time is highly reduced in vitro by the addition of chemokine antibodies whose corresponding receptors were previously detected on the cell surface of these cell types. The apoptosis of a large number of these cultivated cells can be observed.

[0247] Also with in-vivo models, surprisingly, a decrease in tumor cells by apoptosis can be observed.

[0248] Since nude mice have a deficient immune system, the metastatic spread behavior in a host body can be examined in a nude mouse model without the occurrence of the immune reactions which are known between species and without rejection of the foreign cells. Nude mice are inoculated in a per se known manner with tumor cells or tumor cell lines whose chemokine receptor distribution pattern had been analyzed, and the metastatic spread of these cells was checked upon treatment with chemokines and upon treatment with chemokine antagonists and/or receptor antibodies.

[0249] Surprisingly, it is found that chemokine antagonists and receptor antibodies belonging to the receptors found significantly inhibit or prevent metastatic spread while the addition of chemokines results in a modulation of tumor growth. Surprisingly, it is also found that the preparations analyzed by immunohistochemistry exhibit a specific distribution of chemokines and chemokine receptors in the tumor and the tumor-surrounding tissue. Thus, further selective targets have been recognized.

[0250] This intervention in accordance with the method according to the invention consists in additionally extending the proteome analysis of the chemokines and their receptors by the analysis of antitumoral peptides/proteins in the same method. This results in an extension of the diagnostic and therapeutic approach, especially to employ antagonists directed against further clusters of the tumor cell surface proteome. An enhancement of these effects can be achieved by combination with chemokine receptor antagonists and antibodies.

[0251] To confirm these results, tumor cell lines (e.g., preferably, LNCaP-, PC-3-, DU-145, HT-29-, Caco-2-, T-84-) may also be stably transfected with one or more of the chemokine receptors. Upon subsequent injection of these cells into animals in which a chemokine corresponding to the receptor is transgenically overexpressed in the liver, such tumor cells will settle. Thus, such modified cells preferably form metastases in the liver.

[0252] When the method is used in samples of effector cells in inflammatory (acute rejection in kidney transplantation) and auto-immune diseases (rheumatoid arthritis), a specific composition of the chemokine/chemokine receptor proteome, especially the chemokine receptors CXCR4 and CCR5 and/or CXCR3, can also be detected in the rejection of kidney grafts. It has also been demonstrated by in-vitro experiments that a mixture of antibodies and antagonists directed against these receptors strongly inhibits the migration of disease-specific effector cells.

[0253] In the following, the invention is illustrated in more detail by way of Examples.

EXAMPLE 1

[0254] Preparation of specific antibodies against chemokine receptors (preferably CCR and CXCR) and other clusters of the tumor cell surface proteome.

[0255] Surprisingly, for the preparation of specific antibodies against chemokine receptors, it was found that the use of specific amino acid sequences (see Tables 1 and 2), especially against (1) the N-terminal extracellular and (2) the second extracellular loop domains of these 7-TMD receptors (seven transmembrane domains), is especially useful for immunization if the synthesized peptides are coupled to carrier molecules by the usual methods and injected into mice. In addition, multiple antigenic peptides (MAP) connected through lysine to form larger molecules or cell lines transfected with chemokine receptor (sequences according to table 3) are also suitable for preparing these antibodies. The use of immunogens from stably transfected cells bearing chemokin receptors has also proven surprisingly useful as a further method, wherein membrane isolates, cell extracts with complete or fragmented receptors or even lyophilized whole preparations were used.

[0256] The mice (type NZW×NZB) were employed for the preparation of monoclonal antibodies, which is effected with the routine methods of the IPF PharmaCeuticals GmbH. The antibodies checked with Western blot and ELISA can be employed for the diagnostic and therapeutic purposes mentioned when they have been highly purified with the laboratory methods of the IPF PharmaCeuticals GmbH. In detail, the sequences employed for the chemokine receptors are to be selected in accordance with sequences ID 1-63.

EXAMPLE 2

[0257] Detection of chemokines and chemokine receptors in primary tumors, tumor metastases and single tumor cells.

[0258] In the surgical treatment of tumors (e.g., colon, prostate) and their metastases which were removed, for example, from the liver or lymph nodes, the tumor cells could be recovered and analyzed by immunohistochemical methods as well as further molecular-biological methods. In the immunochemical and molecular-biological analyses, it was established that the primary tumor cells, the metastases and circulating single cells (obtained from the blood of patients) contain a specific composition of chemokines and chemokine receptors. The algorithm of this composition is of high specificity individually and depending on the tumor, which surprisingly enables a selective tumor treatment on the basis of the diagnosed proteome clusters by the method according to the invention. Surprisingly, the algorithms of the chemokine receptors are preferably suitable. These algorithms derived from the experiments are defined as follows according to the invention:

[0259] X=chemokine receptors to be newly identified

[0260] n=0 to ∞ further chemokine receptors or chemokine receptors to be newly identified

CCR1 + CCR2 + n	CCR2 + CCR5 + n	CCR3 + CCR8 + n
CCR1 + CCR3 + n	CCR2 + CCR6 + n	CCR3 + CCR9 + n
CCR1 + CCR4 + n	CCR2 + CCR7 + n	CCR3 + CCR10 + n
CCR1 + CCR5 + n	CCR2 + CCR8 + n	CCR3 + CCR11 + n
CCR1 + CCR6 + n	CCR2 + CCR9 + n	CCR3 + CXCR1 + n
CCR1 + CCR7 + n	CCR2 + CCR10 + n	CCR3 + CXCR2 + n
CCR1 + CCR8 + n	CCR2 + CCR11 + n	CCR3 + CXCR3 + n
CCR1 + CCR9 + n	CCR2 + CXCR1 + n	CCR3 + CXCR4 + n
CCR1 + CCR10 + n	CCR2 + CXCR2 + n	CCR3 + CXCR5 + n
CCR1 + CCR11 + n	CCR2 + CXCR3 + n	CCR3 + CXCR6 + n
CCR1 + CXCR1 + n	CCR2 + CXCR4 + n	CCR3 + XCR1 + n
CCR1 + CXCR2 + n	CCR2 + CXCR5 + n	CCR3 + CX3CR1 + n
CCR1 + CXCR3 + n	CCR2 + CXCR6 + n	CCR3 + D6 + n
CCR1 + CXCR4 + n	CCR2 + XCR1 + n	CCR3 + X + n
CCR1 + CXCR5 + n	CCR2 + CX3CR1 + n	
CCR1 + CXCR6 + n	CCR2 + D6 + n	CCR4 + CCR1 + n
CCR1 + XCR1 + n	CCR2 + X + n	CCR4 + CCR2 + n
CCR1 + CX3CR1 + n		CCR4 + CCR3 + n
CCR1 + D6 + n	CCR3 + CCR1 + n	CCR4 + CCR5 + n
CCR1 + X + n	CCR3 + CCR2 + n	CCR4 + CCR6 + n
	CCR3 + CCR4 + n	CCR4 + CCR7 + n
CCR2 + CCR1 + n	CCR3 + CCR5 + n	CCR4 + CCR8 + n
CCR2 + CCR3 + n	CCR3 + CCR6 + n	CCR4 + CCR9 + n
CCR2 + CCR4 + n	CCR3 + CCR7 + n	CCR4 + CCR10 + n
CCR4 + CCR11 + n	CCR6 + CCR9 + n	CCR8 + CCR6 + n
CCR4 + CXCR1 + n	CCR6 + CCR10 + n	CCR8 + CCR7 + n
CCR4 + CXCR2 + n	CCR6 + CCR11 + n	CCR8 + CCR9 + n
CCR4 + CXCR3 + n	CCR6 + CXCR1 + n	CCR8 + CCR10 + n
CCR4 + CXCR4 + n	CCR6 + CXCR2 + n	CCR8 + CCR11 + n
CCR4 + CXCR5 + n	CCR6 + CXCR3 + n	CCR8 + CXCR1 + n
CCR4 + CXCR6 + n	CCR6 + CXCR4 + n	CCR8 + CXCR2 + n
CCR4 + XCR1 + n	CCR6 + CXCR5 + n	CCR8 + CXCR3 + n
CCR4 + CX3CR1 + n	CCR6 + CXCR6 + n	CCR8 + CXCR4 + n
CCR4 + D6 + n	CCR6 + XCR1 + n	CCR8 + CXCR5 + n
CCR4 + X + n	CCR6 + CX3CR1 + n	CCR8 + CXCR6 + n
	CCR6 + D6 + n	CCR8 + XCR1 + n
CCR5 + CCR1 + n	CCR6 + X + n	CCR8 + CX3CR1 + n
CCR5 + CCR2 + n		CCR8 + D6 + n
CCR5 + CCR3 + n	CCR7 + CCR1 + n	CCR8 + X + n
CCR5 + CCR4 + n	CCR7 + CCR2 + n	
CCR5 + CCR6 + n	CCR7 + CCR3 + n	CCR9 + CCR1 + n
CCR5 + CCR7 + n	CCR7 + CCR4 + n	CCR9 + CCR2 + n
CCR5 + CCR8 + n	CCR7 + CCR5 + n	CCR9 + CCR3 + n
CCR5 + CCR9 + n	CCR7 + CCR6 + n	CCR9 + CCR4 + n
CCR5 + CCR10 + n	CCR7 + CCR8 + n	CCR9 + CCRS + n
CCR5 + CCR11 + n	CCR7 + CCR9 + n	CCR9 + CCR6 + n
CCR5 + CXCR1 + n	CCR7 + CCR10 + n	CCR9 + CCR7 + n
CCR5 + CXCR2 + n	CCR7 + CCR11 + n	CCR9 + CCR8 + n
CCR5 + CXCR3 + n	CCR7 + CXCR1 + n	CCR9 + CCR10 + n
CCR5 + CXCR4 + n	CCR7 + CXCR2 + n	CCR9 + CCR11 + n
CCR5 + CXCR5 + n	CCR7 + CXCR3 + n	CCR9 + CXCR1 + n
CCR5 + CXCR6 + n	CCR7 + CXCR4 + n	CCR9 + CXCR2 + n
CCR5 + XCR1 + n	CCR7 + CXCR5 + n	CCR9 + CXCR3 + n
CCR5 + CX3CR1 + n	CCR7 + CXCR6 + n	CCR9 + CXCR4 + n
CCR5 + D6 + n	CCR7 + XCR1 + n	CCR9 + CXCR5 + n
CCR5 + X + n	CCR7 + CX3CR1 + n	CCR9 + CXCR6 + n
	CCR7 + D6 + n	CCR9 + XCR1 + n
CCR6 + CCR1 + n	CCR7 + X + n	CCR9 + CX3CR1 + n
CCR6 + CCR2 + n		CCR9 + D6 + n
CCR6 + CCR3 + n	CCR8 + CCR1 + n	CGR9 + X + n
CCR6 + CCR4 + n	CCR8 + CCR2 + n	
CCR6 + CCR5 + n	CCR8 + CCR3 + n	CCR10 + CCR1 + n
CCR6 + CCR7 + n	CCR8 + CCR4 + n	CCR10 + CCR2 + n
CCR6 + CCR8 + n	CCR8 + CCR5 + n	CCR10 + CCR3 + n
CCR10 + CCR4 + n	CXCR1 + CCR2 + n	
CCR10 + CCR5 + n	CXCR1 + CCR3 + n	CXCR3 + CCR1 + n

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CCR10 + CCR6 + n	CXCR1 + CCR4 + n	CXCR3 + CCR2 + n
CCR10 + CCR7 + n	CXCR1 + CCR5 + n	CXCR3 + CCR3 + n
CCR10 + CCR8 + n	CXCR1 + CCR6 + n	CXCR3 + CCR4 + n
CCR10 + CCR9 + n	CXCR1 + CCR7 + n	CXCR3 + CCR5 + n
CCR10 + CCR11 + n	CXCR1 + CCR8 + n	CXCR3 + CCR6 + n
CCR10 + CXCR1 + n	CXCR1 + CCR9 + n	CXCR3 + CCR7 + n
CCR10 + CXCR2 + n	CXCR1 + CCR10 + n	CXCR3 + CCR8 + n
CCR10 + CXCR3 + n	CXCR1 + CCR11 + n	CXCR3 + CCR9 + n
CCR10 + CXCR4 + n	CXCR1 + CXCR2 + n	CXCR3 + CCR10 + n
CCR10 + CXCR5 + n	CXCR1 + CXCR3 + n	CXGR3 + CCR11 + n
CCR10 + CXCR6 + n	CXCR1 + CXCR4 + n	CXCR3 + CXCR1 + n
CCR10 + XCR1 + n	CXCR1 + CXCR5 + n	CXCR3 + CXCR2 + n
CCR10 + CX3CR1 + n	CXCR1 + CXCR6 + n	CXCR3 + CXCR4 + n
CCR10 + D6 + n	CXCR1 + XCR1 + n	CXCR3 + CXCR5 + n
CCR10 + X + n	CXCR1 + CX3CR1 + n	CXCR3 + CXCR6 + n
	CXCR1 + D6 + n	CXCR3 + XCR1 + n
CCR11 + CCR1 + n	CXCR1 + X + n	CXCR3 + CX3CR1 + n
CCR11 + CCR3 + n		CXCR3 + D6 + n
CCR11 + CCR4 + n	CXCR2 + CCR1 + n	CXCR3 + X + n
CCR11 + CCR5 + n	CXCR2 + CCR2 + n	
CCR11 + CCR6 + n	CXCR2 + CCR3 + n	CXCR4 + CCR1 + n
CCR11 + CCR7 + n	CXCR2 + CCR4 + n	CXCR4 + CCR2 + n
CCR11 + CCR8 + n	CXCR2 + CCR5 + n	CXCR4 + CCR3 + n
CCR11 + CCR9 + n	CXCR2 + CCR6 + n	CXCR4 + CCR4 + n
CCR11 + CCR10 + n	CXCR2 + CCR7 + n	CXCR4 + CCR5 + n
CCR11 + CCR11 + n	CXCR2 + CCR8 + n	CXCR4 + CCR6 + n
CCR11 + CXCR1 + n	CXCR2 + CCR9 + n	CXCR4 + CCR7 + n
CCR11 + CXCR2 + n	CXCR2 + CCR10 + n	CXCR4 + CCR8 + n
CCR11 + CXCR3 + n	CXCR2 + CCR11 + n	CXCR4 + CCR9 + n
CCR11 + CXCR4 + n	CXCR2 + CXCR1 + n	CXCR4 + CCR10 + n
CCR11 + CXCR5 + n	CXCR2 + CXCR3 + n	CXCR4 + CCR11 + n
CCR11 + CXCRG + n	CXCR2 + CXCR4 + n	CXCR4 + CXCR1 + n
CCR11 + XCR1 + n	CXCR2 + CXCR5 + n	CXCR4 + CXCR2 + n
CCR11 + CX3CR1 + n	CXCR2 + CXCR6 + n	CXCR4 + CXCR3 + n
CCR11 + D6 + n	CXCR2 + XCR1 + n	CXCR4 + CXCR5 + n
CCR11 + X + n	CXCR2 + CX3CR1 + n	CXCR4 + CXCR6 + n
	CXCR2 + D6 + n	CXCR4 + XCR1 + n
CXCR1 + CCR1 + n	CXCR2 + X + n	CXCR4 + CX3CR1 + n
CXCR4 + D6 + n	CXCR6 + XCR1 + n	CX3CR1 + CXCR4 + n
CXCR4 + X + n	CXCR6 + CX3CR1 + n	CX3CR1 + CXCR5 + n
	CXCR6 + D6 + n	CX3CR1 + CXCR6 + n
CXCR5 + CCR1 + n	CXCR6 + X + n	CX3CR1 + XCR1 + n

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CXCR5 + CCR2 + n		CX3CR1 + D6 + n
CXCR5 + CCR3 + n	XCR1 + CCR1 + n	CX3CR1 + X + n.
CXCR5 + CCR4 + n	XCR1 + CCR2 + n	
CXCR5 + CCR5 + n	XCR1 + CCR3 + n	
CXCR5 + CCR6 + n	XCR1 + CCR4 + n	
CXCR5 + CCR7 + n	XCR1 + CCR5 + n	
CXCR5 + CCR8 + n	XCR1 + CCR6 + n	
CXCR5 + CCR9 + n	XCR1 + CCR7 + n	
CXCR5 + CCR10 + n	XCR1 + CCR8 + n	
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CXCR5 + CXCR1 + n	XCR1 + CCR10 + n	
CXCR5 + CXCR2 + n	XCR1 + CCR11 + n	
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CXCR5 + CXCR4 + n	XCR1 + CXCR2 + n	
CXCR5 + CXCR6 + n	XCR1 + CXCR3 + n	
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CXCR5 + CX3CR1 + n	XCR1 + CXCR5 + n	
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CXCR5 + X + n	XCR1 + CX3CR1 + n	
	XCR1 + D6 + n	
CXCR6 + CCR1 + n	XCR1 + X + n	
CXCR6 + CCR2 + n		
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CXCR6 + CCR8 + n	CX3CR1 + CCR6 + n	
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CXCR6 + CXCR1 + n	CX3CR1 + CCR10 + n	
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CXCR6 + CXCR3 + n	CX3CR1 + CXCR1 + n	
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[0261]

SEQUENCE LISTING

<160> NUMBER OF SEQ ID NOS: 84

<210> SEQ ID NO 1
<211> LENGTH: 39
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 1

Met Ser Asn Ile Thr Asp Pro Gln Met Trp Asp Phe Asp Asp Leu Asn
1 5 10 15

Phe Thr Gly Met Pro Pro Ala Asp Glu Asp Tyr Ser Pro Cys Met Leu
20 25 30

Glu Thr Glu Thr Leu Asn Lys
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<210> SEQ ID NO 2
<211> LENGTH: 48
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 2

Met Glu Asp Phe Asn Met Glu Ser Asp Ser Phe Glu Asp Phe Trp Lys
1 5 10 15

Gly Glu Asp Leu Ser Asn Tyr Ser Tyr Ser Ser Thr Leu Pro Pro Phe
20 25 30

Leu Leu Asp Ala Ala Pro Cys Glu Pro Glu Ser Leu Glu Ile Asn Lys
35 40 45

<210> SEQ ID NO 3
<211> LENGTH: 53
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 3

Met Val Leu Glu Val Ser Asp His Gln Val Leu Asn Asp Ala Glu Val
1 5 10 15

Ala Ala Leu Leu Glu Asn Phe Ser Ser Ser Tyr Asp Tyr Gly Glu Asn
20 25 30

Glu Ser Asp Ser Cys Cys Thr Ser Pro Pro Cys Pro Gln Asp Phe Ser
35 40 45

Leu Asn Phe Asp Arg
50

<210> SEQ ID NO 4
<211> LENGTH: 39
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 4

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

Gly Ser Gly Asp Tyr Asp Ser Met Lys Glu Pro Cys Phe Arg Glu Glu
20 25 30

Asn Ala Asn Phe Asn Lys Ile
35

<210> SEQ ID NO 5
<211> LENGTH: 54
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 5

Met Asn Tyr Pro Leu Thr Leu Glu Met Asp Leu Glu Asn Leu Glu Asp

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  1               5                  10                  15

Leu Phe Trp Glu Leu Asp Arg Leu Asp Asn Tyr Asn Asp Thr Ser Leu
             20                  25                  30

Val Glu Asn His Leu Cys Pro Ala Thr Gly Pro Leu Met Ala Ser Phe
         35                  40                  45

Lys Ala Val Phe Val Pro
     50


<210> SEQ ID NO 6
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
      Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 6

Met Ala Glu His Asp Tyr His Glu Asp Tyr Gly Phe Ser Ser Phe Asn
  1               5                  10                  15

Asp Ser Ser Gln Glu Glu His Gln Asp Phe Leu Gln Phe Ser Lys Val
             20                  25                  30


<210> SEQ ID NO 7
<211> LENGTH: 34
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
      Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 7

Met Glu Thr Pro Asn Thr Thr Glu Asp Tyr Asp Thr Thr Thr Glu Phe
  1               5                  10                  15

Asp Tyr Gly Asp Ala Thr Pro Cys Gln Lys Val Asn Glu Arg Ala Phe
             20                  25                  30

Gly Ala


<210> SEQ ID NO 8
<211> LENGTH: 42
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
      Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 8

Met Leu Ser Thr Ser Arg Ser Arg Phe Ile Arg Asn Thr Asn Glu Ser
  1               5                  10                  15

Gly Glu Glu Val Thr Thr Phe Phe Asp Tyr Asp Tyr Gly Ala Pro Cys
             20                  25                  30

His Lys Phe Asp Val Lys Gln Ile Gly Ala
         35                  40


<210> SEQ ID NO 9
<211> LENGTH: 34
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
      Amino Acid Sequence for the Generation of Antibodies
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<400> SEQUENCE: 9

Met Thr Thr Ser Leu Asp Thr Val Glu Thr Phe Gly Thr Thr Ser Tyr
1 5 10 15

Tyr Asp Asp Val Gly Leu Leu Cys Glu Lys Ala Asp Thr Arg Ala Leu
20 25 30

Met Ala

<210> SEQ ID NO 10
<211> LENGTH: 39
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 10

Met Asn Pro Thr Asp Ile Ala Asp Thr Thr Leu Asp Glu Ser Ile Tyr
1 5 10 15

Ser Asn Tyr Tyr Leu Tyr Glu Ser Ile Pro Lys Pro Cys Thr Lys Glu
20 25 30

Gly Ile Lys Ala Phe Gly Glu
35

<210> SEQ ID NO 11
<211> LENGTH: 30
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 11

Met Asp Tyr Gln Val Ser Ser Pro Ile Tyr Asp Ile Asn Tyr Tyr Thr
1 5 10 15

Ser Glu Pro Cys Gln Lys Ile Asn Val Lys Gln Ile Ala Ala
20 25 30

<210> SEQ ID NO 12
<211> LENGTH: 47
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 12

Met Ser Gly Glu Ser Met Asn Phe Ser Asp Val Phe Asp Ser Ser Glu
1 5 10 15

Asp Tyr Phe Val Ser Val Asn Thr Ser Tyr Tyr Ser Val Asp Ser Glu
20 25 30

Met Leu Leu Cys Ser Leu Gln Glu Val Arg Gln Phe Ser Arg Leu
35 40 45

<210> SEQ ID NO 13
<211> LENGTH: 42
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

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<400> SEQUENCE: 13

Met Asn Phe Ser Asp Val Phe Asp Ser Ser Glu Asp Tyr Phe Val Ser
1 5 10 15

Val Asn Thr Ser Tyr Tyr Ser Val Asp Ser Glu Met Leu Leu Cys Ser
20 25 30

Leu Gln Glu Val Arg Gln Phe Ser Arg Leu
35 40

<210> SEQ ID NO 14
<211> LENGTH: 59
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 14

Met Asp Leu Gly Lys Pro Met Lys Ser Val Leu Val Val Ala Leu Leu
1 5 10 15

Val Ile Phe Gln Val Cys Leu Cys Gln Asp Glu Val Thr Asp Asp Tyr
20 25 30

Ile Gly Asp Asn Thr Thr Val Asp Tyr Thr Leu Phe Glu Ser Leu Cys
35 40 45

Ser Lys Lys Asp Val Arg Asn Phe Lys Ala Trp
50 55

<210> SEQ ID NO 15
<211> LENGTH: 35
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 15

Met Asp Tyr Thr Leu Asp Leu Ser Val Thr Thr Val Thr Asp Tyr Tyr
1 5 10 15

Tyr Pro Asp Ile Phe Ser Ser Pro Cys Asp Ala Glu Leu Ile Gln Thr
20 25 30

Asn Gly Lys
35

<210> SEQ ID NO 16
<211> LENGTH: 49
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 16

Met Thr Pro Thr Asp Phe Thr Ser Pro Ile Pro Asn Met Ala Asp Asp
1 5 10 15

Tyr Gly Ser Glu Ser Thr Ser Ser Met Glu Asp Tyr Val Asn Phe Asn
20 25 30

Phe Thr Asp Phe Tyr Cys Glu Lys Asn Asn Val Arg Gln Phe Ala Ser
35 40 45

His

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<210> SEQ ID NO 17
<211> LENGTH: 37
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 17

Met Ala Asp Asp Tyr Gly Ser Glu Ser Thr Ser Ser Met Glu Asp Tyr
1 5 10 15

Val Asn Phe Asn Phe Thr Asp Phe Tyr Cys Glu Lys Asn Asn Val Arg
20 25 30

Gln Phe Ala Ser His
35

<210> SEQ ID NO 18
<211> LENGTH: 52
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 18

Met Gly Thr Glu Ala Thr Glu Gln Val Ser Trp Gly His Tyr Ser Gly
1 5 10 15

Asp Glu Glu Asp Ala Tyr Ser Ala Glu Pro Leu Pro Glu Leu Cys Tyr
20 25 30

Lys Ala Asp Val Gln Ala Phe Ser Arg Ala Phe Gln Pro Ser Val Ser
35 40 45

Leu Thr Val Ala
50

<210> SEQ ID NO 19
<211> LENGTH: 42
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 19

Met Ala Leu Glu Gln Asn Gln Ser Thr Asp Tyr Tyr Tyr Glu Glu Asn
1 5 10 15

Glu Met Asn Gly Thr Tyr Asp Tyr Ser Gln Tyr Glu Leu Ile Cys Ile
20 25 30

Lys Glu Asp Val Arg Glu Phe Ala Lys Val
35 40

<210> SEQ ID NO 20
<211> LENGTH: 31
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 20

Met Glu Ser Ser Gly Asn Pro Glu Ser Thr Thr Phe Phe Tyr Tyr Asp
1 5 10 15

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Leu Gln Ser Gln Pro Cys Glu Asn Gln Ala Trp Val Phe Ala Thr
20 25 30

<210> SEQ ID NO 21
<211> LENGTH: 31
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 21

Met Asp Gln Phe Pro Glu Ser Val Thr Glu Asn Phe Glu Tyr Asp Asp
1 5 10 15

Leu Ala Glu Ala Cys Tyr Ile Gly Asp Ile Val Val Phe Gly Thr
20 25 30

<210> SEQ ID NO 22
<211> LENGTH: 49
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 22

Met Ala Ala Thr Ala Ser Pro Gln Pro Leu Ala Thr Glu Asp Ala Asp
1 5 10 15

Ser Glu Asn Ser Ser Phe Tyr Tyr Tyr Asp Tyr Leu Asp Glu Val Ala
20 25 30

Phe Met Leu Cys Arg Lys Asp Ala Val Val Ser Phe Gly Lys Val Phe
35 40 45

Leu

<210> SEQ ID NO 23
<211> LENGTH: 26
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 23

Arg Gln Ala Tyr His Pro Asn Asn Ser Ser Pro Val Cys Tyr Glu Val
1 5 10 15

Leu Gly Asn Asp Thr Ala Lys Trp Arg Met
20 25

<210> SEQ ID NO 24
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 24

Cys Phe Arg Gln Ala Tyr His Pro Asn Asn Ser Ser Pro Val
1 5 10

<210> SEQ ID NO 25

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<211> LENGTH: 25
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 25

Arg Arg Thr Val Tyr Ser Ser Asn Val Ser Pro Ala Cys Tyr Glu Asp
1 5 10 15

Met Gly Asn Asn Thr Ala Asn Trp Arg
20 25

<210> SEQ ID NO 26
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 26

Cys Phe Arg Arg Thr Val Tyr Ser Ser Asn Val Ser Pro Ala
1 5 10

<210> SEQ ID NO 27
<211> LENGTH: 23
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 27

Leu Ser Ala His His Asp Glu Arg Leu Asn Ala Thr His Cys Gln Tyr
1 5 10 15

Asn Phe Pro Gln Val Gly Arg
20

<210> SEQ ID NO 28
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 28

Cys Leu Ser Ala His His Asp Glu Arg Leu Asn Ala Thr His
1 5 10

<210> SEQ ID NO 29
<211> LENGTH: 25
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 29

Asn Val Ser Glu Ala Asp Asp Arg Tyr Ile Cys Asp Arg Phe Tyr Pro
1 5 10 15

Asn Asp Leu Trp Val Val Val Phe Gln
20 25

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<210> SEQ ID NO 30
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 30

Asp Arg Phe Tyr Pro Asn Asp Leu Trp Val Val Val Phe Gln Phe Cys
1 5 10 15

<210> SEQ ID NO 31
<211> LENGTH: 31
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 31

Lys Val Ser Gln Gly His His Asn Asn Ser Leu Pro Arg Cys Thr Phe
1 5 10 15

Ser Gln Glu Asn Gln Ala Glu Thr His Ala Trp Phe Thr Ser Arg
20 25 30

<210> SEQ ID NO 32
<211> LENGTH: 18
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 32

Thr Phe Ser Gln Glu Asn Gln Ala Glu Thr His Ala Trp Phe Thr Ser
1 5 10 15

Arg Cys

<210> SEQ ID NO 33
<211> LENGTH: 23
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 33

Pro Gln Ile Ile Tyr Gly Asn Val Phe Asn Leu Asp Lys Leu Ile Cys
1 5 10 15

Gly Tyr His Asp Glu Ala Ile
20

<210> SEQ ID NO 34
<211> LENGTH: 26
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 34

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Ser Lys Thr Gln Trp Glu Phe Thr His His Thr Cys Ser Leu His Phe
1 5 10 15

Pro His Glu Ser Leu Arg Glu Trp Lys Leu
20 25

<210> SEQ ID NO 35
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 35

Ser Leu His Phe Pro His Glu Ser Leu Arg Glu Trp Lys Leu Cys
1 5 10 15

<210> SEQ ID NO 36
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 36

Thr Lys Cys Gln Lys Glu Asp Ser Val Tyr Val Cys Gly Pro Tyr Phe
1 5 10 15

Pro Arg Gly Trp Asn Asn Phe His Thr Ile Met Arg
20 25

<210> SEQ ID NO 37
<211> LENGTH: 18
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 37

Gly Pro Tyr Phe Pro Arg Gly Trp Asn Asn Phe His Thr Ile Met Arg
1 5 10 15

Asn Cys

<210> SEQ ID NO 38
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 38

Tyr Glu Thr Glu Glu Leu Phe Glu Glu Thr Leu Cys Ser Ala Leu Tyr
1 5 10 15

Pro Glu Asp Thr Val Tyr Ser Trp Arg His Phe His Thr Leu Arg Met
20 25 30

<210> SEQ ID NO 39
<211> LENGTH: 22
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:

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<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 39

Ser Ala Leu Tyr Pro Glu Asp Thr Val Tyr Ser Trp Arg His Phe His
1 5 10 15

Thr Leu Arg Met Thr Cys
20

<210> SEQ ID NO 40
<211> LENGTH: 31
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 40

Ser Thr Cys Tyr Thr Glu Arg Asn His Thr Tyr Cys Lys Thr Lys Tyr
1 5 10 15

Ser Leu Asn Ser Thr Thr Trp Lys Val Leu Ser Ser Leu Glu Ile
20 25 30

<210> SEQ ID NO 41
<211> LENGTH: 21
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 41

Lys Thr Lys Tyr Ser Leu Asn Ser Thr Thr Trp Lys Val Leu Ser Ser
1 5 10 15

Leu Glu Ile Asn Cys
20

<210> SEQ ID NO 42
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 42

Thr Arg Ser Gln Lys Glu Gly Leu His Tyr Thr Cys Ser Ser His Phe
1 5 10 15

Pro Tyr Ser Gln Tyr Gln Phe Trp Lys Asn Phe Gln Thr Leu Lys Ile
20 25 30

<210> SEQ ID NO 43
<211> LENGTH: 22
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 43

Ser Ser His Phe Pro Tyr Ser Gln Tyr Gln Phe Trp Lys Asn Phe Gln
1 5 10 15

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Thr Leu Lys Ile Val Cys
20

<210> SEQ ID NO 44
<211> LENGTH: 30
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 44

Ser Thr Phe Val Phe Asn Gln Lys Tyr Asn Thr Gln Gly Ser Asp Val
1 5 10 15

Cys Glu Pro Lys Tyr Gln Thr Val Ser Glu Pro Ile Arg Trp
20 25 30

<210> SEQ ID NO 45
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 45

Glu Pro Lys Tyr Gln Thr Val Ser Glu Pro Ile Arg Trp Lys Cys
1 5 10 15

<210> SEQ ID NO 46
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 46

Pro Glu Leu Leu Tyr Ser Asp Leu Gln Arg Ser Ser Ser Glu Gln Ala
1 5 10 15

Met Arg Cys Ser Leu Ile Thr Glu His Val Glu Ala
20 25

<210> SEQ ID NO 47
<211> LENGTH: 19
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 47

Cys Pro Glu Leu Leu Tyr Ser Asp Leu Gln Arg Ser Ser Ser Glu Gln
1 5 10 15

Ala Met Arg

<210> SEQ ID NO 48
<211> LENGTH: 31
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

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<400> SEQUENCE: 48

Tyr Gln Val Ala Ser Glu Asp Gly Val Leu Gln Cys Tyr Ser Phe Tyr
1 5 10 15

Asn Gln Gln Thr Leu Lys Trp Lys Ile Phe Thr Asn Phe Lys Met
20 25 30

<210> SEQ ID NO 49
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 49

Tyr Ser Phe Tyr Asn Gln Gln Thr Leu Lys Trp Lys Ile Phe Thr Asn
1 5 10 15

Phe Lys Met Cys
20

<210> SEQ ID NO 50
<211> LENGTH: 29
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 50

Pro Glu Ile Leu Tyr Ser Gln Ile Lys Glu Glu Ser Gly Ile Ala Ile
1 5 10 15

Cys Thr Met Val Tyr Pro Ser Asp Glu Ser Thr Lys Leu
20 25

<210> SEQ ID NO 51
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 51

Cys Thr Met Val Tyr Pro Ser Asp Glu Ser Thr Lys Leu Lys
1 5 10

<210> SEQ ID NO 52
<211> LENGTH: 24
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 52

Ser Gln Asp Gly Gln Arg Glu Gly Gln Arg Arg Cys Arg Leu Ile Phe
1 5 10 15

Pro Glu Gly Leu Thr Gln Thr Val
20

<210> SEQ ID NO 53
<211> LENGTH: 13

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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 53

Phe Ser Gln Asp Gly Gln Arg Glu Gly Gln Arg Arg Cys
1 5 10

<210> SEQ ID NO 54
<211> LENGTH: 22
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 54

Thr Val Asn Asp Asn Ala Arg Cys Ile Pro Ile Phe Pro Arg Tyr Leu
1 5 10 15

Gly Thr Ser Met Lys Ala
20

<210> SEQ ID NO 55
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 55

Cys Ile Pro Ile Phe Pro Arg Tyr Leu Gly Thr Ser Met Lys Ala
1 5 10 15

<210> SEQ ID NO 56
<211> LENGTH: 23
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 56

His Lys Val Leu Ser Ser Gly Cys Asp Tyr Ser Glu Leu Thr Trp Tyr
1 5 10 15

Leu Thr Ser Val Tyr Gln His
20

<210> SEQ ID NO 57
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 57

Asp Tyr Ser Glu Leu Thr Trp Tyr Leu Thr Ser Val Tyr Gln His Cys
1 5 10 15

<210> SEQ ID NO 58
<211> LENGTH: 28

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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 58

Thr Lys Gln Lys Glu Asn Glu Cys Leu Gly Asp Tyr Pro Glu Val Leu
1 5 10 15

Gln Glu Ile Trp Pro Val Leu Arg Asn Val Glu Thr
20 25

<210> SEQ ID NO 59
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 59

Leu Gly Asp Tyr Pro Glu Val Leu Gln Glu Ile Trp Pro Val Leu Arg
1 5 10 15

Asn Val Glu Thr
20

<210> SEQ ID NO 60
<211> LENGTH: 33
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 60

Gln Thr His Glu Asn Pro Lys Gly Val Trp Asn Cys His Ala Asp Phe
1 5 10 15

Gly Gly His Gly Thr Ile Trp Lys Leu Phe Leu Arg Phe Gln Gln Asn
20 25 30

Leu

<210> SEQ ID NO 61
<211> LENGTH: 21
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 61

His Ala Asp Phe Gly Gly His Gly Thr Ile Trp Lys Leu Phe Leu Arg
1 5 10 15

Phe Gln Gln Asn Cys
20

<210> SEQ ID NO 62
<211> LENGTH: 355
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

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<400> SEQUENCE: 62

Met Glu Thr Pro Asn Thr Thr Glu Asp Tyr Asp Thr Thr Thr Glu Phe
1 5 10 15

Asp Tyr Gly Asp Ala Thr Pro Cys Gln Lys Val Asn Glu Arg Ala Phe
20 25 30

Gly Ala Gln Leu Leu Pro Pro Leu Tyr Ser Leu Val Phe Val Ile Gly
35 40 45

Leu Val Gly Asn Ile Leu Val Val Leu Val Leu Val Gln Tyr Lys Arg
50 55 60

Leu Lys Asn Met Thr Ser Ile Tyr Leu Leu Asn Leu Ala Ile Ser Asp
65 70 75 80

Leu Leu Phe Leu Phe Thr Leu Pro Phe Trp Ile Asp Tyr Lys Leu Lys
85 90 95

Asp Asp Trp Val Phe Gly Asp Ala Met Cys Lys Ile Leu Ser Gly Phe
100 105 110

Tyr Tyr Thr Gly Leu Tyr Ser Glu Ile Phe Phe Ile Ile Leu Leu Thr
115 120 125

Ile Asp Arg Tyr Leu Ala Ile Val His Ala Val Phe Ala Leu Arg Ala
130 135 140

Arg Thr Val Thr Phe Gly Val Ile Thr Ser Ile Ile Ile Trp Ala Leu
145 150 155 160

Ala Ile Leu Ala Ser Met Pro Gly Leu Tyr Phe Ser Lys Thr Gln Trp
165 170 175

Glu Phe Thr His His Thr Cys Ser Leu His Phe Pro His Glu Ser Leu
180 185 190

Arg Glu Trp Lys Leu Phe Gln Ala Leu Lys Leu Asn Leu Phe Gly Leu
195 200 205

Val Leu Pro Leu Leu Val Met Ile Ile Cys Tyr Thr Gly Ile Ile Lys
210 215 220

Ile Leu Leu Arg Arg Pro Asn Glu Lys Lys Ser Lys Ala Val Arg Leu
225 230 235 240

Ile Phe Val Ile Met Ile Ile Phe Phe Leu Phe Trp Thr Pro Tyr Asn
245 250 255

Leu Thr Ile Leu Ile Ser Val Phe Gln Asp Phe Leu Phe Thr His Glu
260 265 270

Cys Glu Gln Ser Arg His Leu Asp Leu Ala Val Gln Val Thr Glu Val
275 280 285

Ile Ala Tyr Thr His Cys Cys Val Asn Pro Val Ile Tyr Ala Phe Val
290 295 300

Gly Glu Arg Phe Arg Lys Tyr Leu Arg Gln Leu Phe His Arg Arg Val
305 310 315 320

Ala Val His Leu Val Lys Trp Leu Pro Phe Leu Ser Val Asp Arg Leu
325 330 335

Glu Arg Val Ser Ser Thr Ser Pro Ser Thr Gly Glu His Glu Leu Ser
340 345 350

Ala Gly Phe
355

<210> SEQ ID NO 63
<211> LENGTH: 374
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence

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<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 63

Met Leu Ser Thr Ser Arg Ser Arg Phe Ile Arg Asn Thr Asn Glu Ser
1 5 10 15

Gly Glu Glu Val Thr Thr Phe Phe Asp Tyr Asp Tyr Gly Ala Pro Cys
20 25 30

His Lys Phe Asp Val Lys Gln Ile Gly Ala Gln Leu Leu Pro Pro Leu
35 40 45

Tyr Ser Leu Val Phe Ile Phe Gly Phe Val Gly Asn Met Leu Val Val
50 55 60

Leu Ile Leu Ile Asn Cys Lys Lys Leu Lys Cys Leu Thr Asp Ile Tyr
65 70 75 80

Leu Leu Asn Leu Ala Ile Ser Asp Leu Leu Phe Leu Ile Thr Leu Pro
85 90 95

Leu Trp Ala His Ser Ala Ala Asn Glu Trp Val Phe Gly Asn Ala Met
100 105 110

Cys Lys Leu Phe Thr Gly Leu Tyr His Ile Gly Tyr Phe Gly Gly Ile
115 120 125

Phe Phe Ile Ile Leu Leu Thr Ile Asp Arg Tyr Leu Ala Ile Val His
130 135 140

Ala Val Phe Ala Leu Lys Ala Arg Thr Val Thr Phe Gly Val Val Thr
145 150 155 160

Ser Val Ile Thr Trp Leu Val Ala Val Phe Ala Ser Val Pro Gly Ile
165 170 175

Ile Phe Thr Lys Cys Gln Lys Glu Asp Ser Val Tyr Val Cys Gly Pro
180 185 190

Tyr Phe Pro Arg Gly Trp Asn Asn Phe His Thr Ile Met Arg Asn Ile
195 200 205

Leu Gly Leu Val Leu Pro Leu Leu Ile Met Val Ile Cys Tyr Ser Gly
210 215 220

Ile Leu Lys Thr Leu Leu Arg Cys Arg Asn Glu Lys Lys Arg His Arg
225 230 235 240

Ala Val Arg Val Ile Phe Thr Ile Met Ile Val Tyr Phe Leu Phe Trp
245 250 255

Thr Pro Tyr Asn Ile Val Ile Leu Leu Asn Thr Phe Gln Glu Phe Phe
260 265 270

Gly Leu Ser Asn Cys Glu Ser Thr Ser Gln Leu Asp Gln Ala Thr Gln
275 280 285

Val Thr Glu Thr Leu Gly Met Thr His Cys Cys Ile Asn Pro Ile Ile
290 295 300

Tyr Ala Phe Val Gly Glu Lys Phe Arg Ser Leu Phe His Ile Ala Leu
305 310 315 320

Gly Cys Arg Ile Ala Pro Leu Gln Lys Pro Val Cys Gly Gly Pro Gly
325 330 335

Val Arg Pro Gly Lys Asn Val Lys Val Thr Thr Gln Gly Leu Leu Asp
340 345 350

Gly Arg Gly Lys Gly Lys Ser Ile Gly Arg Ala Pro Glu Ala Ser Leu
355 360 365

Gln Asp Lys Glu Gly Ala

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370

<210> SEQ ID NO 64
<211> LENGTH: 360
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 64

Met Leu Ser Thr Ser Arg Ser Arg Phe Ile Arg Asn Thr Asn Glu Ser
1 5 10 15

Gly Glu Glu Val Thr Thr Phe Phe Asp Tyr Asp Tyr Gly Ala Pro Cys
20 25 30

His Lys Phe Asp Val Lys Gln Ile Gly Ala Gln Leu Leu Pro Pro Leu
35 40 45

Tyr Ser Leu Val Phe Ile Phe Gly Phe Val Gly Asn Met Leu Val Val
50 55 60

Leu Ile Leu Ile Asn Cys Lys Lys Leu Lys Cys Leu Thr Asp Ile Tyr
65 70 75 80

Leu Leu Asn Leu Ala Ile Ser Asp Leu Leu Phe Leu Ile Thr Leu Pro
85 90 95

Leu Trp Ala His Ser Ala Ala Asn Glu Trp Val Phe Gly Asn Ala Met
100 105 110

Cys Lys Leu Phe Thr Gly Leu Tyr His Ile Gly Tyr Phe Gly Gly Ile
115 120 125

Phe Phe Ile Ile Leu Leu Thr Ile Asp Arg Tyr Leu Ala Ile Val His
130 135 140

Ala Val Phe Ala Leu Lys Ala Arg Thr Val Thr Phe Gly Val Val Thr
145 150 155 160

Ser Val Ile Thr Trp Leu Val Ala Val Phe Ala Ser Val Pro Gly Ile
165 170 175

Ile Phe Thr Lys Cys Gln Lys Glu Asp Ser Val Tyr Val Cys Gly Pro
180 185 190

Tyr Phe Pro Arg Gly Trp Asn Asn Phe His Thr Ile Met Arg Asn Ile
195 200 205

Leu Gly Leu Val Leu Pro Leu Leu Ile Met Val Ile Cys Tyr Ser Gly
210 215 220

Ile Leu Lys Thr Leu Leu Arg Cys Arg Asn Glu Lys Lys Arg His Arg
225 230 235 240

Ala Val Arg Val Ile Phe Thr Ile Met Ile Val Tyr Phe Leu Phe Trp
245 250 255

Thr Pro Tyr Asn Ile Val Ile Leu Leu Asn Thr Phe Gln Glu Phe Phe
260 265 270

Gly Leu Ser Asn Cys Glu Ser Thr Ser Gln Leu Asp Gln Ala Thr Gln
275 280 285

Val Thr Glu Thr Leu Gly Met Thr His Cys Cys Ile Asn Pro Ile Ile
290 295 300

Tyr Ala Phe Val Gly Glu Lys Phe Arg Arg Tyr Leu Ser Val Phe Phe
305 310 315 320

Arg Lys His Ile Thr Lys Arg Phe Cys Lys Gln Cys Pro Val Phe Tyr
325 330 335

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Arg Glu Thr Val Asp Gly Val Thr Ser Thr Asn Thr Pro Ser Thr Gly
            340                 345                 350

Glu Gln Glu Val Ser Ala Gly Leu
        355                 360


<210> SEQ ID NO 65
<211> LENGTH: 355
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
      Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 65

Met Thr Thr Ser Leu Asp Thr Val Glu Thr Phe Gly Thr Thr Ser Tyr
  1               5                  10                  15

Tyr Asp Asp Val Gly Leu Leu Cys Glu Lys Ala Asp Thr Arg Ala Leu
             20                  25                  30

Met Ala Gln Phe Val Pro Pro Leu Tyr Ser Leu Val Phe Thr Val Gly
         35                  40                  45

Leu Leu Gly Asn Val Val Val Val Met Ile Leu Ile Lys Tyr Arg Arg
     50                  55                  60

Leu Arg Ile Met Thr Asn Ile Tyr Leu Leu Asn Leu Ala Ile Ser Asp
 65                  70                  75                  80

Leu Leu Phe Leu Val Thr Leu Pro Phe Trp Ile His Tyr Val Arg Gly
                 85                  90                  95

His Asn Trp Val Phe Gly His Gly Met Cys Lys Leu Leu Ser Gly Phe
            100                 105                 110

Tyr His Thr Gly Leu Tyr Ser Glu Ile Phe Phe Ile Ile Leu Leu Thr
        115                 120                 125

Ile Asp Arg Tyr Leu Ala Ile Val His Ala Val Phe Ala Leu Arg Ala
    130                 135                 140

Arg Thr Val Thr Phe Gly Val Ile Thr Ser Ile Val Thr Trp Gly Leu
145                 150                 155                 160

Ala Val Leu Ala Ala Leu Pro Glu Phe Ile Phe Tyr Glu Thr Glu Glu
                165                 170                 175

Leu Phe Glu Glu Thr Leu Cys Ser Ala Leu Tyr Pro Glu Asp Thr Val
            180                 185                 190

Tyr Ser Trp Arg His Phe His Thr Leu Arg Met Thr Ile Phe Cys Leu
        195                 200                 205

Val Leu Pro Leu Leu Val Met Ala Ile Cys Tyr Thr Gly Ile Ile Lys
    210                 215                 220

Thr Leu Leu Arg Cys Pro Ser Lys Lys Lys Tyr Lys Ala Ile Arg Leu
225                 230                 235                 240

Ile Phe Val Ile Met Ala Val Phe Phe Ile Phe Trp Thr Pro Tyr Asn
                245                 250                 255

Val Ala Ile Leu Leu Ser Ser Tyr Gln Ser Ile Leu Phe Gly Asn Asp
            260                 265                 270

Cys Glu Arg Ser Lys His Leu Asp Leu Val Met Leu Val Thr Glu Val
        275                 280                 285

Ile Ala Tyr Ser His Cys Cys Met Asn Pro Val Ile Tyr Ala Phe Val
    290                 295                 300

Gly Glu Arg Phe Arg Lys Tyr Leu Arg His Phe Phe His Arg His Leu
305                 310                 315                 320
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Leu Met His Leu Gly Arg Tyr Ile Pro Phe Leu Pro Ser Glu Lys Leu
                325                 330                 335

Glu Arg Thr Ser Ser Val Ser Pro Ser Thr Ala Glu Pro Glu Leu Ser
            340                 345                 350

Ile Val Phe
        355


<210> SEQ ID NO 66
<211> LENGTH: 360
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
      Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 66

Met Asn Pro Thr Asp Ile Ala Asp Thr Thr Leu Asp Glu Ser Ile Tyr
  1               5                  10                  15

Ser Asn Tyr Tyr Leu Tyr Glu Ser Ile Pro Lys Pro Cys Thr Lys Glu
             20                  25                  30

Gly Ile Lys Ala Phe Gly Glu Leu Phe Leu Pro Pro Leu Tyr Ser Leu
         35                  40                  45

Val Phe Val Phe Gly Leu Leu Gly Asn Ser Val Val Val Leu Val Leu
     50                  55                  60

Phe Lys Tyr Lys Arg Leu Arg Ser Met Thr Asp Val Tyr Leu Leu Asn
 65                  70                  75                  80

Leu Ala Ile Ser Asp Leu Leu Phe Val Phe Ser Leu Pro Phe Trp Gly
                 85                  90                  95

Tyr Tyr Ala Ala Asp Gln Trp Val Phe Gly Leu Gly Leu Cys Lys Met
            100                 105                 110

Ile Ser Trp Met Tyr Leu Val Gly Phe Tyr Ser Gly Ile Phe Phe Val
        115                 120                 125

Met Leu Met Ser Ile Asp Arg Tyr Leu Ala Ile Val His Ala Val Phe
    130                 135                 140

Ser Leu Arg Ala Arg Thr Leu Thr Tyr Gly Val Ile Thr Ser Leu Ala
145                 150                 155                 160

Thr Trp Ser Val Ala Val Phe Ala Ser Leu Pro Gly Phe Leu Phe Ser
                165                 170                 175

Thr Cys Tyr Thr Glu Arg Asn His Thr Tyr Cys Lys Thr Lys Tyr Ser
            180                 185                 190

Leu Asn Ser Thr Thr Trp Lys Val Leu Ser Ser Leu Glu Ile Asn Ile
        195                 200                 205

Leu Gly Leu Val Ile Pro Leu Gly Ile Met Leu Phe Cys Tyr Ser Met
    210                 215                 220

Ile Ile Arg Thr Leu Gln His Cys Lys Asn Glu Lys Lys Asn Lys Ala
225                 230                 235                 240

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

Pro Tyr Asn Ile Val Leu Phe Leu Glu Thr Leu Val Glu Leu Glu Val
            260                 265                 270

Leu Gln Asp Cys Thr Phe Glu Arg Tyr Leu Asp Tyr Ala Ile Gln Ala
        275                 280                 285

Thr Glu Thr Leu Ala Phe Val His Cys Cys Leu Asn Pro Ile Ile Tyr
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    290                 295                 300

Phe Phe Leu Gly Glu Lys Phe Arg Lys Tyr Ile Leu Gln Leu Phe Lys
305                 310                 315                 320

Thr Cys Arg Gly Leu Phe Val Leu Cys Gln Tyr Cys Gly Leu Leu Gln
                325                 330                 335

Ile Tyr Ser Ala Asp Thr Pro Ser Ser Ser Tyr Thr Gln Ser Thr Met
            340                 345                 350

Asp His Asp Leu His Asp Ala Leu
        355                 360


<210> SEQ ID NO 67
<211> LENGTH: 352
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
      Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 67

Met Asp Tyr Gln Val Ser Ser Pro Ile Tyr Asp Ile Asn Tyr Tyr Thr
  1               5                  10                  15

Ser Glu Pro Cys Gln Lys Ile Asn Val Lys Gln Ile Ala Ala Arg Leu
             20                  25                  30

Leu Pro Pro Leu Tyr Ser Leu Val Phe Ile Phe Gly Phe Val Gly Asn
         35                  40                  45

Met Leu Val Ile Leu Ile Leu Ile Asn Cys Lys Arg Leu Lys Ser Met
     50                  55                  60

Thr Asp Ile Tyr Leu Leu Asn Leu Ala Ile Ser Asp Leu Phe Phe Leu
 65                  70                  75                  80

Leu Thr Val Pro Phe Trp Ala His Tyr Ala Ala Ala Gln Trp Asp Phe
                 85                  90                  95

Gly Asn Thr Met Cys Gln Leu Leu Thr Gly Leu Tyr Phe Ile Gly Phe
            100                 105                 110

Phe Ser Gly Ile Phe Phe Ile Ile Leu Leu Thr Ile Asp Arg Tyr Leu
        115                 120                 125

Ala Val Val His Ala Val Phe Ala Leu Lys Ala Arg Thr Val Thr Phe
    130                 135                 140

Gly Val Val Thr Ser Val Ile Thr Trp Val Val Ala Val Phe Ala Ser
145                 150                 155                 160

Leu Pro Gly Ile Ile Phe Thr Arg Ser Gln Lys Glu Gly Leu His Tyr
                165                 170                 175

Thr Cys Ser Ser His Phe Pro Tyr Ser Gln Tyr Gln Phe Trp Lys Asn
            180                 185                 190

Phe Gln Thr Leu Lys Ile Val Ile Leu Gly Leu Val Leu Pro Leu Leu
        195                 200                 205

Val Met Val Ile Cys Tyr Ser Gly Ile Leu Lys Thr Leu Leu Arg Cys
    210                 215                 220

Arg Asn Glu Lys Lys Arg His Arg Ala Val Arg Leu Ile Phe Thr Ile
225                 230                 235                 240

Met Ile Val Tyr Phe Leu Phe Trp Ala Pro Tyr Asn Ile Val Leu Leu
                245                 250                 255

Leu Asn Thr Phe Gln Glu Phe Phe Gly Leu Asn Asn Cys Ser Ser Ser
            260                 265                 270
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```
Asn Arg Leu Asp Gln Ala Met Gln Val Thr Glu Thr Leu Gly Met Thr
        275                 280                 285

His Cys Cys Ile Asn Pro Ile Ile Tyr Ala Phe Val Gly Glu Lys Phe
    290                 295                 300

Arg Asn Tyr Leu Leu Val Phe Phe Gln Lys His Ile Ala Lys Arg Phe
305                 310                 315                 320

Cys Lys Cys Cys Ser Ile Phe Gln Gln Glu Ala Pro Glu Arg Ala Ser
                325                 330                 335

Ser Val Tyr Thr Arg Ser Thr Gly Glu Gln Glu Ile Ser Val Gly Leu
            340                 345                 350


<210> SEQ ID NO 68
<211> LENGTH: 374
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
      Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 68

Met Ser Gly Glu Ser Met Asn Phe Ser Asp Val Phe Asp Ser Ser Glu
  1               5                  10                  15

Asp Tyr Phe Val Ser Val Asn Thr Ser Tyr Tyr Ser Val Asp Ser Glu
             20                  25                  30

Met Leu Leu Cys Ser Leu Gln Glu Val Arg Gln Phe Ser Arg Leu Phe
         35                  40                  45

Val Pro Ile Ala Tyr Ser Leu Ile Cys Val Phe Gly Leu Leu Gly Asn
     50                  55                  60

Ile Leu Val Val Ile Thr Phe Ala Phe Tyr Lys Lys Ala Arg Ser Met
 65                  70                  75                  80

Thr Asp Val Tyr Leu Leu Asn Met Ala Ile Ala Asp Ile Leu Phe Val
                 85                  90                  95

Leu Thr Leu Pro Phe Trp Ala Val Ser His Ala Thr Gly Ala Trp Val
            100                 105                 110

Phe Ser Asn Ala Thr Cys Lys Leu Leu Lys Gly Ile Tyr Ala Ile Asn
        115                 120                 125

Phe Asn Cys Gly Met Leu Leu Leu Thr Cys Ile Ser Met Asp Arg Tyr
    130                 135                 140

Ile Ala Ile Val Gln Ala Thr Lys Ser Phe Arg Leu Arg Ser Arg Thr
145                 150                 155                 160

Leu Pro Arg Ser Lys Ile Ile Cys Leu Val Val Trp Gly Leu Ser Val
                165                 170                 175

Ile Ile Ser Ser Ser Thr Phe Val Phe Asn Gln Lys Tyr Asn Thr Gln
            180                 185                 190

Gly Ser Asp Val Cys Glu Pro Lys Tyr Gln Thr Val Ser Glu Pro Ile
        195                 200                 205

Arg Trp Lys Leu Leu Met Leu Gly Leu Glu Leu Leu Phe Gly Phe Phe
    210                 215                 220

Ile Pro Leu Met Phe Met Ile Phe Cys Tyr Thr Phe Ile Val Lys Thr
225                 230                 235                 240

Leu Val Gln Ala Gln Asn Ser Lys Arg His Lys Ala Ile Arg Val Ile
                245                 250                 255

Ile Ala Val Val Leu Val Phe Leu Ala Cys Gln Ile Pro His Asn Met
            260                 265                 270
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```
Val Leu Leu Val Thr Ala Ala Asn Leu Gly Lys Met Asn Arg Ser Cys
        275                 280                 285

Gln Ser Glu Lys Leu Ile Gly Tyr Thr Lys Thr Val Thr Glu Val Leu
    290                 295                 300

Ala Phe Leu His Cys Cys Leu Asn Pro Val Leu Tyr Ala Phe Ile Gly
305                 310                 315                 320

Gln Lys Phe Arg Asn Tyr Phe Leu Lys Ile Leu Lys Asp Leu Trp Cys
                325                 330                 335

Val Arg Arg Lys Tyr Lys Ser Ser Gly Phe Ser Cys Ala Gly Arg Tyr
            340                 345                 350

Ser Glu Asn Ile Ser Arg Gln Thr Ser Glu Thr Ala Asp Asn Asp Asn
        355                 360                 365

Ala Ser Ser Phe Thr Met
    370


<210> SEQ ID NO 69
<211> LENGTH: 369
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
      Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 69

Met Asn Phe Ser Asp Val Phe Asp Ser Ser Glu Asp Tyr Phe Val Ser
  1               5                  10                  15

Val Asn Thr Ser Tyr Tyr Ser Val Asp Ser Glu Met Leu Leu Cys Ser
             20                  25                  30

Leu Gln Glu Val Arg Gln Phe Ser Arg Leu Phe Val Pro Ile Ala Tyr
         35                  40                  45

Ser Leu Ile Cys Val Phe Gly Leu Leu Gly Asn Ile Leu Val Val Ile
     50                  55                  60

Thr Phe Ala Phe Tyr Lys Lys Ala Arg Ser Met Thr Asp Val Tyr Leu
 65                  70                  75                  80

Leu Asn Met Ala Ile Ala Asp Ile Leu Phe Val Leu Thr Leu Pro Phe
                 85                  90                  95

Trp Ala Val Ser His Ala Thr Gly Ala Trp Val Phe Ser Asn Ala Thr
            100                 105                 110

Cys Lys Leu Leu Lys Gly Ile Tyr Ala Ile Asn Phe Asn Cys Gly Met
        115                 120                 125

Leu Leu Leu Thr Cys Ile Ser Met Asp Arg Tyr Ile Ala Ile Val Gln
    130                 135                 140

Ala Thr Lys Ser Phe Arg Leu Arg Ser Arg Thr Leu Pro Arg Ser Lys
145                 150                 155                 160

Ile Ile Cys Leu Val Val Trp Gly Leu Ser Val Ile Ile Ser Ser Ser
                165                 170                 175

Thr Phe Val Phe Asn Gln Lys Tyr Asn Thr Gln Gly Ser Asp Val Cys
            180                 185                 190

Glu Pro Lys Tyr Gln Thr Val Ser Glu Pro Ile Arg Trp Lys Leu Leu
        195                 200                 205

Met Leu Gly Leu Glu Leu Leu Phe Gly Phe Phe Ile Pro Leu Met Phe
    210                 215                 220

Met Ile Phe Cys Tyr Thr Phe Ile Val Lys Thr Leu Val Gln Ala Gln
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225                 230                 235                 240

Asn Ser Lys Arg His Lys Ala Ile Arg Val Ile Ile Ala Val Val Leu
                245                 250                 255

Val Phe Leu Ala Cys Gln Ile Pro His Asn Met Val Leu Leu Val Thr
            260                 265                 270

Ala Ala Asn Leu Gly Lys Met Asn Arg Ser Cys Gln Ser Glu Lys Leu
        275                 280                 285

Ile Gly Tyr Thr Lys Thr Val Thr Glu Val Leu Ala Phe Leu His Cys
    290                 295                 300

Cys Leu Asn Pro Val Leu Tyr Ala Phe Ile Gly Gln Lys Phe Arg Asn
305                 310                 315                 320

Tyr Phe Leu Lys Ile Leu Lys Asp Leu Trp Cys Val Arg Arg Lys Tyr
                325                 330                 335

Lys Ser Ser Gly Phe Ser Cys Ala Gly Arg Tyr Ser Glu Asn Ile Ser
            340                 345                 350

Arg Gln Thr Ser Glu Thr Ala Asp Asn Asp Asn Ala Ser Ser Phe Thr
        355                 360                 365

Met
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<210> SEQ ID NO 70
<211> LENGTH: 378
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 70

```
Met Asp Leu Gly Lys Pro Met Lys Ser Val Leu Val Val Ala Leu Leu
  1               5                  10                  15

Val Ile Phe Gln Val Cys Leu Cys Gln Asp Glu Val Thr Asp Asp Tyr
             20                  25                  30

Ile Gly Asp Asn Thr Thr Val Asp Tyr Thr Leu Phe Glu Ser Leu Cys
         35                  40                  45

Ser Lys Lys Asp Val Arg Asn Phe Lys Ala Trp Phe Leu Pro Ile Met
     50                  55                  60

Tyr Ser Ile Ile Cys Phe Val Gly Leu Leu Gly Asn Gly Leu Val Val
 65                  70                  75                  80

Leu Thr Tyr Ile Tyr Phe Lys Arg Leu Lys Thr Met Thr Asp Thr Tyr
                 85                  90                  95

Leu Leu Asn Leu Ala Val Ala Asp Ile Leu Phe Leu Leu Thr Leu Pro
            100                 105                 110

Phe Trp Ala Tyr Ser Ala Ala Lys Ser Trp Val Phe Gly Val His Phe
        115                 120                 125

Cys Lys Leu Ile Phe Ala Ile Tyr Lys Met Ser Phe Phe Ser Gly Met
    130                 135                 140

Leu Leu Leu Leu Cys Ile Ser Ile Asp Arg Tyr Val Ala Ile Val Gln
145                 150                 155                 160

Ala Val Ser Ala His Arg His Arg Ala Arg Val Leu Leu Ile Ser Lys
                165                 170                 175

Leu Ser Cys Val Gly Ile Trp Ile Leu Ala Thr Val Leu Ser Ile Pro
            180                 185                 190

Glu Leu Leu Tyr Ser Asp Leu Gln Arg Ser Ser Ser Glu Gln Ala Met
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        195                 200                 205

Arg Cys Ser Leu Ile Thr Glu His Val Glu Ala Phe Ile Thr Ile Gln
    210                 215                 220

Val Ala Gln Met Val Ile Gly Phe Leu Val Pro Leu Leu Ala Met Ser
225                 230                 235                 240

Phe Cys Tyr Leu Val Ile Ile Arg Thr Leu Leu Gln Ala Arg Asn Phe
                245                 250                 255

Glu Arg Asn Lys Ala Ile Lys Val Ile Ile Ala Val Val Val Val Phe
            260                 265                 270

Ile Val Phe Gln Leu Pro Tyr Asn Gly Val Val Leu Ala Gln Thr Val
        275                 280                 285

Ala Asn Phe Asn Ile Thr Ser Ser Thr Cys Glu Leu Ser Lys Gln Leu
    290                 295                 300

Asn Ile Ala Tyr Asp Val Thr Tyr Ser Leu Ala Cys Val Arg Cys Cys
305                 310                 315                 320

Val Asn Pro Phe Leu Tyr Ala Phe Ile Gly Val Lys Phe Arg Asn Asp
                325                 330                 335

Leu Phe Lys Leu Phe Lys Asp Leu Gly Cys Leu Ser Gln Glu Gln Leu
            340                 345                 350

Arg Gln Trp Ser Ser Cys Arg His Ile Arg Arg Ser Ser Met Ser Val
        355                 360                 365

Glu Ala Glu Thr Thr Thr Thr Phe Ser Pro
    370                 375


<210> SEQ ID NO 71
<211> LENGTH: 355
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
      Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 71

Met Asp Tyr Thr Leu Asp Leu Ser Val Thr Thr Val Thr Asp Tyr Tyr
  1               5                  10                  15

Tyr Pro Asp Ile Phe Ser Ser Pro Cys Asp Ala Glu Leu Ile Gln Thr
             20                  25                  30

Asn Gly Lys Leu Leu Leu Ala Val Phe Tyr Cys Leu Leu Phe Val Phe
         35                  40                  45

Ser Leu Leu Gly Asn Ser Leu Val Ile Leu Val Leu Val Val Cys Lys
     50                  55                  60

Lys Leu Arg Ser Ile Thr Asp Val Tyr Leu Leu Asn Leu Ala Leu Ser
 65                  70                  75                  80

Asp Leu Leu Phe Val Phe Ser Phe Pro Phe Gln Thr Tyr Tyr Leu Leu
                 85                  90                  95

Asp Gln Trp Val Phe Gly Thr Val Met Cys Lys Val Val Ser Gly Phe
            100                 105                 110

Tyr Tyr Ile Gly Phe Tyr Ser Ser Met Phe Phe Ile Thr Leu Met Ser
        115                 120                 125

Val Asp Arg Tyr Leu Ala Val Val His Ala Val Tyr Ala Leu Lys Val
    130                 135                 140

Arg Thr Ile Arg Met Gly Thr Thr Leu Cys Leu Ala Val Trp Leu Thr
145                 150                 155                 160
```

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```
Ala Ile Met Ala Thr Ile Pro Leu Leu Val Phe Tyr Gln Val Ala Ser
                165                 170                 175

Glu Asp Gly Val Leu Gln Cys Tyr Ser Phe Tyr Asn Gln Gln Thr Leu
            180                 185                 190

Lys Trp Lys Ile Phe Thr Asn Phe Lys Met Asn Ile Leu Gly Leu Leu
        195                 200                 205

Ile Pro Phe Thr Ile Phe Met Phe Cys Tyr Ile Lys Ile Leu His Gln
    210                 215                 220

Leu Lys Arg Cys Gln Asn His Asn Lys Thr Lys Ala Ile Arg Leu Val
225                 230                 235                 240

Leu Ile Val Val Ile Ala Ser Leu Leu Phe Trp Val Pro Phe Asn Val
                245                 250                 255

Val Leu Phe Leu Thr Ser Leu His Ser Met His Ile Leu Asp Gly Cys
            260                 265                 270

Ser Ile Ser Gln Gln Leu Thr Tyr Ala Thr His Val Thr Glu Ile Ile
        275                 280                 285

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

Glu Lys Phe Lys Lys His Leu Ser Glu Ile Phe Gln Lys Ser Cys Ser
305                 310                 315                 320

Gln Ile Phe Asn Tyr Leu Gly Arg Gln Met Pro Arg Glu Ser Cys Glu
                325                 330                 335

Lys Ser Ser Ser Cys Gln Gln His Ser Ser Arg Ser Ser Ser Val Asp
            340                 345                 350

Tyr Ile Leu
        355


<210> SEQ ID NO 72
<211> LENGTH: 369
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
      Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 72

Met Thr Pro Thr Asp Phe Thr Ser Pro Ile Pro Asn Met Ala Asp Asp
  1               5                  10                  15

Tyr Gly Ser Glu Ser Thr Ser Ser Met Glu Asp Tyr Val Asn Phe Asn
             20                  25                  30

Phe Thr Asp Phe Tyr Cys Glu Lys Asn Asn Val Arg Gln Phe Ala Ser
         35                  40                  45

His Phe Leu Pro Pro Leu Tyr Trp Leu Val Phe Ile Val Gly Ala Leu
     50                  55                  60

Gly Asn Ser Leu Val Ile Leu Val Tyr Trp Tyr Cys Thr Arg Val Lys
 65                  70                  75                  80

Thr Met Thr Asp Met Phe Leu Leu Asn Leu Ala Ile Ala Asp Leu Leu
                 85                  90                  95

Phe Leu Val Thr Leu Pro Phe Trp Ala Ile Ala Ala Ala Asp Gln Trp
            100                 105                 110

Lys Phe Gln Thr Phe Met Cys Lys Val Val Asn Ser Met Tyr Lys Met
        115                 120                 125

Asn Phe Tyr Ser Cys Val Leu Leu Ile Met Cys Ile Ser Val Asp Arg
    130                 135                 140
```

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```
Tyr Ile Ala Ile Ala Gln Ala Met Arg Ala His Thr Trp Arg Glu Lys
145                 150                 155                 160

Arg Leu Leu Tyr Ser Lys Met Val Cys Phe Thr Ile Trp Val Leu Ala
                165                 170                 175

Ala Ala Leu Cys Ile Pro Glu Ile Leu Tyr Ser Gln Ile Lys Glu Glu
            180                 185                 190

Ser Gly Ile Ala Ile Cys Thr Met Val Tyr Pro Ser Asp Glu Ser Thr
        195                 200                 205

Lys Leu Lys Ser Ala Val Leu Thr Leu Lys Val Ile Leu Gly Phe Phe
    210                 215                 220

Leu Pro Phe Val Val Met Ala Cys Cys Tyr Thr Ile Ile Ile His Thr
225                 230                 235                 240

Leu Ile Gln Ala Lys Lys Ser Ser Lys His Lys Ala Leu Lys Val Thr
                245                 250                 255

Ile Thr Val Leu Thr Val Phe Val Leu Ser Gln Phe Pro Tyr Asn Cys
            260                 265                 270

Ile Leu Leu Val Gln Thr Ile Asp Ala Tyr Ala Met Phe Ile Ser Asn
        275                 280                 285

Cys Ala Val Ser Thr Asn Ile Asp Ile Cys Phe Gln Val Thr Gln Thr
    290                 295                 300

Ile Ala Phe Phe His Ser Cys Leu Asn Pro Val Leu Tyr Val Phe Val
305                 310                 315                 320

Gly Glu Arg Phe Arg Arg Asp Leu Val Lys Thr Leu Lys Asn Leu Gly
                325                 330                 335

Cys Ile Ser Gln Ala Gln Trp Val Ser Phe Thr Arg Arg Glu Gly Ser
            340                 345                 350

Leu Lys Leu Ser Ser Met Leu Leu Glu Thr Thr Ser Gly Ala Leu Ser
        355                 360                 365

Leu
```

<210> SEQ ID NO 73
<211> LENGTH: 357
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 73

```
Met Ala Asp Asp Tyr Gly Ser Glu Ser Thr Ser Ser Met Glu Asp Tyr
  1               5                  10                  15

Val Asn Phe Asn Phe Thr Asp Phe Tyr Cys Glu Lys Asn Asn Val Arg
             20                  25                  30

Gln Phe Ala Ser His Phe Leu Pro Pro Leu Tyr Trp Leu Val Phe Ile
         35                  40                  45

Val Gly Ala Leu Gly Asn Ser Leu Val Ile Leu Val Tyr Trp Tyr Cys
     50                  55                  60

Thr Arg Val Lys Thr Met Thr Asp Met Phe Leu Leu Asn Leu Ala Ile
 65                  70                  75                  80

Ala Asp Leu Leu Phe Leu Val Thr Leu Pro Phe Trp Ala Ile Ala Ala
                 85                  90                  95

Ala Asp Gln Trp Lys Phe Gln Thr Phe Met Cys Lys Val Val Asn Ser
            100                 105                 110
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```
Met Tyr Lys Met Asn Phe Tyr Ser Cys Val Leu Leu Ile Met Cys Ile
        115                 120                 125

Ser Val Asp Arg Tyr Ile Ala Ile Ala Gln Ala Met Arg Ala His Thr
    130                 135                 140

Trp Arg Glu Lys Arg Leu Leu Tyr Ser Lys Met Val Cys Phe Thr Ile
145                 150                 155                 160

Trp Val Leu Ala Ala Ala Leu Cys Ile Pro Glu Ile Leu Tyr Ser Gln
                165                 170                 175

Ile Lys Glu Glu Ser Gly Ile Ala Ile Cys Thr Met Val Tyr Pro Ser
            180                 185                 190

Asp Glu Ser Thr Lys Leu Lys Ser Ala Val Leu Thr Leu Lys Val Ile
        195                 200                 205

Leu Gly Phe Phe Leu Pro Phe Val Val Met Ala Cys Cys Tyr Thr Ile
    210                 215                 220

Ile Ile His Thr Leu Ile Gln Ala Lys Lys Ser Ser Lys His Lys Ala
225                 230                 235                 240

Leu Lys Val Thr Ile Thr Val Leu Thr Val Phe Val Leu Ser Gln Phe
                245                 250                 255

Pro Tyr Asn Cys Ile Leu Leu Val Gln Thr Ile Asp Ala Tyr Ala Met
            260                 265                 270

Phe Ile Ser Asn Cys Ala Val Ser Thr Asn Ile Asp Ile Cys Phe Gln
        275                 280                 285

Val Thr Gln Thr Ile Ala Phe Phe His Ser Cys Leu Asn Pro Val Leu
    290                 295                 300

Tyr Val Phe Val Gly Glu Arg Phe Arg Arg Asp Leu Val Lys Thr Leu
305                 310                 315                 320

Lys Asn Leu Gly Cys Ile Ser Gln Ala Gln Trp Val Ser Phe Thr Arg
                325                 330                 335

Arg Glu Gly Ser Leu Lys Leu Ser Ser Met Leu Leu Glu Thr Thr Ser
            340                 345                 350

Gly Ala Leu Ser Leu
        355


<210> SEQ ID NO 74
<211> LENGTH: 362
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
      Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 74

Met Gly Thr Glu Ala Thr Glu Gln Val Ser Trp Gly His Tyr Ser Gly
  1               5                  10                  15

Asp Glu Glu Asp Ala Tyr Ser Ala Glu Pro Leu Pro Glu Leu Cys Tyr
             20                  25                  30

Lys Ala Asp Val Gln Ala Phe Ser Arg Ala Phe Gln Pro Ser Val Ser
         35                  40                  45

Leu Thr Val Ala Ala Leu Gly Leu Ala Gly Asn Gly Leu Val Leu Ala
     50                  55                  60

Thr His Leu Ala Ala Arg Arg Ala Ala Arg Ser Pro Thr Ser Ala His
 65                  70                  75                  80

Leu Leu Gln Leu Ala Leu Ala Asp Leu Leu Leu Ala Leu Thr Leu Pro
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                85                  90                  95

Phe Ala Ala Ala Gly Ala Leu Gln Gly Trp Ser Leu Gly Ser Ala Thr
            100                 105                 110

Cys Arg Thr Ile Ser Gly Leu Tyr Ser Ala Ser Phe His Ala Gly Phe
        115                 120                 125

Leu Phe Leu Ala Cys Ile Ser Ala Asp Arg Tyr Val Ala Ile Ala Arg
    130                 135                 140

Ala Leu Pro Ala Gly Pro Arg Pro Ser Thr Pro Gly Arg Ala His Leu
145                 150                 155                 160

Val Ser Val Ile Val Trp Leu Leu Ser Leu Leu Leu Ala Leu Pro Ala
                165                 170                 175

Leu Leu Phe Ser Gln Asp Gly Gln Arg Glu Gly Gln Arg Arg Cys Arg
            180                 185                 190

Leu Ile Phe Pro Glu Gly Leu Thr Gln Thr Val Lys Gly Ala Ser Ala
        195                 200                 205

Val Ala Gln Val Ala Leu Gly Phe Ala Leu Pro Leu Gly Val Met Val
    210                 215                 220

Ala Cys Tyr Ala Leu Leu Gly Arg Thr Leu Leu Ala Ala Arg Gly Pro
225                 230                 235                 240

Glu Arg Arg Arg Ala Leu Arg Val Val Val Ala Leu Val Ala Ala Phe
                245                 250                 255

Val Val Leu Gln Leu Pro Tyr Ser Leu Ala Leu Leu Leu Asp Thr Ala
            260                 265                 270

Asp Leu Leu Ala Ala Arg Glu Arg Ser Cys Pro Ala Ser Lys Arg Lys
        275                 280                 285

Asp Val Ala Leu Leu Val Thr Ser Gly Leu Ala Leu Ala Arg Cys Gly
    290                 295                 300

Leu Asn Pro Val Leu Tyr Ala Phe Leu Gly Leu Arg Phe Arg Gln Asp
305                 310                 315                 320

Leu Arg Arg Leu Leu Arg Gly Gly Ser Ser Pro Ser Gly Pro Gln Pro
                325                 330                 335

Arg Arg Gly Cys Pro Arg Arg Pro Arg Leu Ser Ser Cys Ser Ala Pro
            340                 345                 350

Thr Glu Thr His Ser Leu Ser Trp Asp Asn
        355                 360


<210> SEQ ID NO 75
<211> LENGTH: 350
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
      Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 75

Met Ala Leu Glu Gln Asn Gln Ser Thr Asp Tyr Tyr Tyr Glu Glu Asn
  1               5                  10                  15

Glu Met Asn Gly Thr Tyr Asp Tyr Ser Gln Tyr Glu Leu Ile Cys Ile
             20                  25                  30

Lys Glu Asp Val Arg Glu Phe Ala Lys Val Phe Leu Pro Val Phe Leu
         35                  40                  45

Thr Ile Val Phe Val Ile Gly Leu Ala Gly Asn Ser Met Val Val Ala
     50                  55                  60
```

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```
Ile Tyr Ala Tyr Tyr Lys Lys Gln Arg Thr Lys Thr Asp Val Tyr Ile
 65                  70                  75                  80

Leu Asn Leu Ala Val Ala Asp Leu Leu Leu Leu Phe Thr Leu Pro Phe
                85                  90                  95

Trp Ala Val Asn Ala Val His Gly Trp Val Leu Gly Lys Ile Met Cys
            100                 105                 110

Lys Ile Thr Ser Ala Leu Tyr Thr Leu Asn Phe Val Ser Gly Met Gln
        115                 120                 125

Phe Leu Ala Cys Ile Ser Ile Asp Arg Tyr Val Ala Val Thr Lys Val
    130                 135                 140

Pro Ser Gln Ser Gly Val Gly Lys Pro Cys Trp Ile Ile Cys Phe Cys
145                 150                 155                 160

Val Trp Met Ala Ala Ile Leu Leu Ser Ile Pro Gln Leu Val Phe Tyr
                165                 170                 175

Thr Val Asn Asp Asn Ala Arg Cys Ile Pro Ile Phe Pro Arg Tyr Leu
            180                 185                 190

Gly Thr Ser Met Lys Ala Leu Ile Gln Met Leu Glu Ile Cys Ile Gly
        195                 200                 205

Phe Val Val Pro Phe Leu Ile Met Gly Val Cys Tyr Phe Ile Thr Ala
    210                 215                 220

Arg Thr Leu Met Lys Met Pro Asn Ile Lys Ile Ser Arg Pro Leu Lys
225                 230                 235                 240

Val Leu Leu Thr Val Val Ile Val Phe Ile Val Thr Gln Leu Pro Tyr
                245                 250                 255

Asn Ile Val Lys Phe Cys Arg Ala Ile Asp Ile Ile Tyr Ser Leu Ile
            260                 265                 270

Thr Ser Cys Asn Met Ser Lys Arg Met Asp Ile Ala Ile Gln Val Thr
        275                 280                 285

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

Phe Met Gly Ala Ser Phe Lys Asn Tyr Val Met Lys Val Ala Lys Lys
305                 310                 315                 320

Tyr Gly Ser Trp Arg Arg Gln Arg Gln Ser Val Glu Glu Phe Pro Phe
                325                 330                 335

Asp Ser Glu Gly Pro Thr Glu Pro Thr Ser Thr Phe Ser Ile
            340                 345                 350


<210> SEQ ID NO 76
<211> LENGTH: 350
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
      Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 76

Met Ser Asn Ile Thr Asp Pro Gln Met Trp Asp Phe Asp Asp Leu Asn
  1               5                  10                  15

Phe Thr Gly Met Pro Pro Ala Asp Glu Asp Tyr Ser Pro Cys Met Leu
             20                  25                  30

Glu Thr Glu Thr Leu Asn Lys Tyr Val Val Ile Ile Ala Tyr Ala Leu
         35                  40                  45

Val Phe Leu Leu Ser Leu Leu Gly Asn Ser Leu Val Met Leu Val Ile
     50                  55                  60
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```
Leu Tyr Ser Arg Val Gly Arg Ser Val Thr Asp Val Tyr Leu Leu Asn
 65                  70                  75                  80

Leu Ala Leu Ala Asp Leu Leu Phe Ala Leu Thr Leu Pro Ile Trp Ala
                 85                  90                  95

Ala Ser Lys Val Asn Gly Trp Ile Phe Gly Thr Phe Leu Cys Lys Val
            100                 105                 110

Val Ser Leu Leu Lys Glu Val Asn Phe Tyr Ser Gly Ile Leu Leu Leu
        115                 120                 125

Ala Cys Ile Ser Val Asp Arg Tyr Leu Ala Ile Val His Ala Thr Arg
    130                 135                 140

Thr Leu Thr Gln Lys Arg His Leu Val Lys Phe Val Cys Leu Gly Cys
145                 150                 155                 160

Trp Gly Leu Ser Met Asn Leu Ser Leu Pro Phe Phe Leu Phe Arg Gln
                165                 170                 175

Ala Tyr His Pro Asn Asn Ser Ser Pro Val Cys Tyr Glu Val Leu Gly
            180                 185                 190

Asn Asp Thr Ala Lys Trp Arg Met Val Leu Arg Ile Leu Pro His Thr
        195                 200                 205

Phe Gly Phe Ile Val Pro Leu Phe Val Met Leu Phe Cys Tyr Gly Phe
    210                 215                 220

Thr Leu Arg Thr Leu Phe Lys Ala His Met Gly Gln Lys His Arg Ala
225                 230                 235                 240

Met Arg Val Ile Phe Ala Val Val Leu Ile Phe Leu Leu Cys Trp Leu
                245                 250                 255

Pro Tyr Asn Leu Val Leu Leu Ala Asp Thr Leu Met Arg Thr Gln Val
            260                 265                 270

Ile Gln Glu Thr Cys Glu Arg Arg Asn Asn Ile Gly Arg Ala Leu Asp
        275                 280                 285

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

Tyr Ala Phe Ile Gly Gln Asn Phe Arg His Gly Phe Leu Lys Ile Leu
305                 310                 315                 320

Ala Met His Gly Leu Val Ser Lys Glu Phe Leu Ala Arg His Arg Val
                325                 330                 335

Thr Ser Tyr Thr Ser Ser Ser Val Asn Val Ser Ser Asn Leu
            340                 345                 350


<210> SEQ ID NO 77
<211> LENGTH: 360
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
      Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 77

Met Glu Asp Phe Asn Met Glu Ser Asp Ser Phe Glu Asp Phe Trp Lys
  1               5                  10                  15

Gly Glu Asp Leu Ser Asn Tyr Ser Tyr Ser Ser Thr Leu Pro Pro Phe
             20                  25                  30

Leu Leu Asp Ala Ala Pro Cys Glu Pro Glu Ser Leu Glu Ile Asn Lys
         35                  40                  45

Tyr Phe Val Val Ile Ile Tyr Ala Leu Val Phe Leu Leu Ser Leu Leu
```

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```
     50                  55                  60

Gly Asn Ser Leu Val Met Leu Val Ile Leu Tyr Ser Arg Val Gly Arg
 65                  70                  75                  80

Ser Val Thr Asp Val Tyr Leu Leu Asn Leu Ala Leu Ala Asp Leu Leu
                 85                  90                  95

Phe Ala Leu Thr Leu Pro Ile Trp Ala Ala Ser Lys Val Asn Gly Trp
            100                 105                 110

Ile Phe Gly Thr Phe Leu Cys Lys Val Val Ser Leu Leu Lys Glu Val
        115                 120                 125

Asn Phe Tyr Ser Gly Ile Leu Leu Leu Ala Cys Ile Ser Val Asp Arg
    130                 135                 140

Tyr Leu Ala Ile Val His Ala Thr Arg Thr Leu Thr Gln Lys Arg Tyr
145                 150                 155                 160

Leu Val Lys Phe Ile Cys Leu Ser Ile Trp Gly Leu Ser Leu Leu Leu
                165                 170                 175

Ala Leu Pro Val Leu Leu Phe Arg Arg Thr Val Tyr Ser Ser Asn Val
            180                 185                 190

Ser Pro Ala Cys Tyr Glu Asp Met Gly Asn Asn Thr Ala Asn Trp Arg
        195                 200                 205

Met Leu Leu Arg Ile Leu Pro Gln Ser Phe Gly Phe Ile Val Pro Leu
    210                 215                 220

Leu Ile Met Leu Phe Cys Tyr Gly Phe Thr Leu Arg Thr Leu Phe Lys
225                 230                 235                 240

Ala His Met Gly Gln Lys His Arg Ala Met Arg Val Ile Phe Ala Val
                245                 250                 255

Val Leu Ile Phe Leu Leu Cys Trp Leu Pro Tyr Asn Leu Val Leu Leu
            260                 265                 270

Ala Asp Thr Leu Met Arg Thr Gln Val Ile Gln Glu Thr Cys Glu Arg
        275                 280                 285

Arg Asn His Ile Asp Arg Ala Leu Asp Ala Thr Glu Ile Leu Gly Ile
    290                 295                 300

Leu His Ser Cys Leu Asn Pro Leu Ile Tyr Ala Phe Ile Gly Gln Lys
305                 310                 315                 320

Phe Arg His Gly Leu Leu Lys Ile Leu Ala Ile His Gly Leu Ile Ser
                325                 330                 335

Lys Asp Ser Leu Pro Lys Asp Ser Arg Pro Ser Phe Val Gly Ser Ser
            340                 345                 350

Ser Gly His Thr Ser Thr Thr Leu
        355                 360


<210> SEQ ID NO 78
<211> LENGTH: 368
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
      Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 78

Met Val Leu Glu Val Ser Asp His Gln Val Leu Asn Asp Ala Glu Val
  1               5                  10                  15

Ala Ala Leu Leu Glu Asn Phe Ser Ser Ser Tyr Asp Tyr Gly Glu Asn
             20                  25                  30
```

-continued

```
Glu Ser Asp Ser Cys Cys Thr Ser Pro Pro Cys Pro Gln Asp Phe Ser
         35                  40                  45

Leu Asn Phe Asp Arg Ala Phe Leu Pro Ala Leu Tyr Ser Leu Leu Phe
     50                  55                  60

Leu Leu Gly Leu Leu Gly Asn Gly Ala Val Ala Ala Val Leu Leu Ser
 65                  70                  75                  80

Arg Arg Thr Ala Leu Ser Ser Thr Asp Thr Phe Leu Leu His Leu Ala
                 85                  90                  95

Val Ala Asp Thr Leu Leu Val Leu Thr Leu Pro Leu Trp Ala Val Asp
            100                 105                 110

Ala Ala Val Gln Trp Val Phe Gly Ser Gly Leu Cys Lys Val Ala Gly
        115                 120                 125

Ala Leu Phe Asn Ile Asn Phe Tyr Ala Gly Ala Leu Leu Leu Ala Cys
    130                 135                 140

Ile Ser Phe Asp Arg Tyr Leu Asn Ile Val His Ala Thr Gln Leu Tyr
145                 150                 155                 160

Arg Arg Gly Pro Pro Ala Arg Val Thr Leu Thr Cys Leu Ala Val Trp
                165                 170                 175

Gly Leu Cys Leu Leu Phe Ala Leu Pro Asp Phe Ile Phe Leu Ser Ala
            180                 185                 190

His His Asp Glu Arg Leu Asn Ala Thr His Cys Gln Tyr Asn Phe Pro
        195                 200                 205

Gln Val Gly Arg Thr Ala Leu Arg Val Leu Gln Leu Val Ala Gly Phe
    210                 215                 220

Leu Leu Pro Leu Leu Val Met Ala Tyr Cys Tyr Ala His Ile Leu Ala
225                 230                 235                 240

Val Leu Leu Val Ser Arg Gly Gln Arg Arg Leu Arg Ala Met Arg Leu
                245                 250                 255

Val Val Val Val Val Val Ala Phe Ala Leu Cys Trp Thr Pro Tyr His
            260                 265                 270

Leu Val Val Leu Val Asp Ile Leu Met Asp Leu Gly Ala Leu Ala Arg
        275                 280                 285

Asn Cys Gly Arg Glu Ser Arg Val Asp Val Ala Lys Ser Val Thr Ser
    290                 295                 300

Gly Leu Gly Tyr Met His Cys Cys Leu Asn Pro Leu Leu Tyr Ala Phe
305                 310                 315                 320

Val Gly Val Lys Phe Arg Glu Arg Met Trp Met Leu Leu Leu Arg Leu
                325                 330                 335

Gly Cys Pro Asn Gln Arg Gly Leu Gln Arg Gln Pro Ser Ser Ser Arg
            340                 345                 350

Arg Asp Ser Ser Trp Ser Glu Thr Ser Glu Ala Ser Tyr Ser Gly Leu
        355                 360                 365


<210> SEQ ID NO 79
<211> LENGTH: 352
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
      Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 79

Met Glu Gly Ile Ser Ile Tyr Thr Ser Asp Asn Tyr Thr Glu Glu Met
  1               5                  10                  15
```

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```
Gly Ser Gly Asp Tyr Asp Ser Met Lys Glu Pro Cys Phe Arg Glu Glu
            20                  25                  30

Asn Ala Asn Phe Asn Lys Ile Phe Leu Pro Thr Ile Tyr Ser Ile Ile
        35                  40                  45

Phe Leu Thr Gly Ile Val Gly Asn Gly Leu Val Ile Leu Val Met Gly
    50                  55                  60

Tyr Gln Lys Lys Leu Arg Ser Met Thr Asp Lys Tyr Arg Leu His Leu
65                  70                  75                  80

Ser Val Ala Asp Leu Leu Phe Val Ile Thr Leu Pro Phe Trp Ala Val
                85                  90                  95

Asp Ala Val Ala Asn Trp Tyr Phe Gly Asn Phe Leu Cys Lys Ala Val
            100                 105                 110

His Val Ile Tyr Thr Val Asn Leu Tyr Ser Ser Val Leu Ile Leu Ala
        115                 120                 125

Phe Ile Ser Leu Asp Arg Tyr Leu Ala Ile Val His Ala Thr Asn Ser
    130                 135                 140

Gln Arg Pro Arg Lys Leu Leu Ala Glu Lys Val Val Tyr Val Gly Val
145                 150                 155                 160

Trp Ile Pro Ala Leu Leu Leu Thr Ile Pro Asp Phe Ile Phe Ala Asn
                165                 170                 175

Val Ser Glu Ala Asp Asp Arg Tyr Ile Cys Asp Arg Phe Tyr Pro Asn
            180                 185                 190

Asp Leu Trp Val Val Val Phe Gln Phe Gln His Ile Met Val Gly Leu
        195                 200                 205

Ile Leu Pro Gly Ile Val Ile Leu Ser Cys Tyr Cys Ile Ile Ile Ser
    210                 215                 220

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

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

Ile Gly Ile Ser Ile Asp Ser Phe Ile Leu Leu Glu Ile Ile Lys Gln
            260                 265                 270

Gly Cys Glu Phe Glu Asn Thr Val His Lys Trp Ile Ser Ile Thr Glu
        275                 280                 285

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

Leu Gly Ala Lys Phe Lys Thr Ser Ala Gln His Ala Leu Thr Ser Val
305                 310                 315                 320

Ser Arg Gly Ser Ser Leu Lys Ile Leu Ser Lys Gly Lys Arg Gly Gly
                325                 330                 335

His Ser Ser Val Ser Thr Glu Ser Glu Ser Ser Ser Phe His Ser Ser
            340                 345                 350


<210> SEQ ID NO 80
<211> LENGTH: 372
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
      Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 80

Met Asn Tyr Pro Leu Thr Leu Glu Met Asp Leu Glu Asn Leu Glu Asp
```

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```
  1               5                  10                  15

Leu Phe Trp Glu Leu Asp Arg Leu Asp Asn Tyr Asn Asp Thr Ser Leu
            20                  25                  30

Val Glu Asn His Leu Cys Pro Ala Thr Glu Gly Pro Leu Met Ala Ser
         35                  40                  45

Phe Lys Ala Val Phe Val Pro Val Ala Tyr Ser Leu Ile Phe Leu Leu
     50                  55                  60

Gly Val Ile Gly Asn Val Leu Val Leu Val Ile Leu Glu Arg His Arg
 65                  70                  75                  80

Gln Thr Arg Ser Ser Thr Glu Thr Phe Leu Phe His Leu Ala Val Ala
                85                  90                  95

Asp Leu Leu Leu Val Phe Ile Leu Pro Phe Ala Val Ala Glu Gly Ser
            100                 105                 110

Val Gly Trp Val Leu Gly Thr Phe Leu Cys Lys Thr Val Ile Ala Leu
        115                 120                 125

His Lys Val Asn Phe Tyr Cys Ser Ser Leu Leu Leu Ala Cys Ile Ala
    130                 135                 140

Val Asp Arg Tyr Leu Ala Ile Val His Ala Val His Ala Tyr Arg His
145                 150                 155                 160

Arg Arg Leu Leu Ser Ile His Ile Thr Cys Gly Thr Ile Trp Leu Val
                165                 170                 175

Gly Phe Leu Leu Ala Leu Pro Glu Ile Leu Phe Ala Lys Val Ser Gln
            180                 185                 190

Gly His His Asn Asn Ser Leu Pro Arg Cys Thr Phe Ser Gln Glu Asn
        195                 200                 205

Gln Ala Glu Thr His Ala Trp Phe Thr Ser Arg Phe Leu Tyr His Val
    210                 215                 220

Ala Gly Phe Leu Leu Pro Met Leu Val Met Gly Trp Cys Tyr Val Gly
225                 230                 235                 240

Val Val His Arg Leu Arg Gln Ala Gln Arg Arg Pro Gln Arg Gln Lys
                245                 250                 255

Ala Val Arg Val Ala Ile Leu Val Thr Ser Ile Phe Phe Leu Cys Trp
            260                 265                 270

Ser Pro Tyr His Ile Val Ile Phe Leu Asp Thr Leu Ala Arg Leu Lys
        275                 280                 285

Ala Val Asp Asn Thr Cys Lys Leu Asn Gly Ser Leu Pro Val Ala Ile
    290                 295                 300

Thr Met Cys Glu Phe Leu Gly Leu Ala His Cys Cys Leu Asn Pro Met
305                 310                 315                 320

Leu Tyr Thr Phe Ala Gly Val Lys Phe Arg Ser Asp Leu Ser Arg Leu
                325                 330                 335

Leu Thr Lys Leu Gly Cys Thr Gly Pro Ala Ser Leu Cys Gln Leu Phe
            340                 345                 350
Pro Ser Trp Arg Arg Ser Ser Leu Ser Glu Ser Glu Asn Ala Thr Ser
        355                 360                 365

Leu Thr Thr Phe
    370


<210> SEQ ID NO 81
<211> LENGTH: 342
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
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<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 81

Met Ala Glu His Asp Tyr His Glu Asp Tyr Gly Phe Ser Ser Phe Asn
1 5 10 15

Asp Ser Ser Gln Glu Glu His Gln Asp Phe Leu Gln Phe Ser Lys Val
20 25 30

Phe Leu Pro Cys Met Tyr Leu Val Val Phe Val Cys Gly Leu Val Gly
35 40 45

Asn Ser Leu Val Leu Val Ile Ser Ile Phe Tyr His Lys Leu Gln Ser
50 55 60

Leu Thr Asp Val Phe Leu Val Asn Leu Pro Leu Ala Asp Leu Val Phe
65 70 75 80

Val Cys Thr Leu Pro Phe Trp Ala Tyr Ala Gly Ile His Glu Trp Val
85 90 95

Phe Gly Gln Val Met Cys Lys Ser Leu Leu Gly Ile Tyr Thr Ile Asn
100 105 110

Phe Tyr Thr Ser Met Leu Ile Leu Thr Cys Ile Thr Val Asp Arg Phe
115 120 125

Ile Val Val Val Lys Ala Thr Lys Ala Tyr Asn Gln Gln Ala Lys Arg
130 135 140

Met Thr Trp Gly Lys Val Thr Ser Leu Leu Ile Trp Val Ile Ser Leu
145 150 155 160

Leu Val Ser Leu Pro Gln Ile Ile Tyr Gly Asn Val Phe Asn Leu Asp
165 170 175

Lys Leu Ile Cys Gly Tyr His Asp Glu Ala Ile Ser Thr Val Val Leu
180 185 190

Ala Thr Gln Met Thr Leu Gly Phe Phe Leu Pro Leu Leu Thr Met Ile
195 200 205

Val Cys Tyr Ser Val Ile Ile Lys Thr Leu Leu His Ala Gly Gly Phe
210 215 220

Gln Lys His Arg Ser Leu Lys Ile Ile Phe Leu Val Met Ala Val Phe
225 230 235 240

Leu Leu Thr Gln Met Pro Phe Asn Leu Met Lys Phe Ile Arg Ser Thr
245 250 255

His Trp Glu Tyr Tyr Ala Met Thr Ser Phe His Tyr Thr Ile Met Val
260 265 270

Thr Glu Ala Ile Ala Tyr Leu Arg Ala Cys Leu Asn Pro Val Leu Tyr
275 280 285

Ala Phe Val Ser Leu Lys Phe Arg Lys Asn Phe Trp Lys Leu Val Lys
290 295 300

Asp Ile Gly Cys Leu Pro Tyr Leu Gly Val Ser His Gln Trp Lys Ser
305 310 315 320

Ser Glu Asp Asn Ser Lys Thr Phe Ser Ala Ser His Asn Val Glu Ala
325 330 335

Thr Ser Met Phe Gln Leu
340

<210> SEQ ID NO 82
<211> LENGTH: 355
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence

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<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 82

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Met Asp Gln Phe Pro Glu Ser Val Thr Glu Asn Phe Glu Tyr Asp Asp
  1               5                  10                  15

Leu Ala Glu Ala Cys Tyr Ile Gly Asp Ile Val Val Phe Gly Thr Val
             20                  25                  30

Phe Leu Ser Ile Phe Tyr Ser Val Ile Phe Ala Ile Gly Leu Val Gly
         35                  40                  45

Asn Leu Leu Val Val Phe Ala Leu Thr Asn Ser Lys Lys Pro Lys Ser
     50                  55                  60

Val Thr Asp Ile Tyr Leu Leu Asn Leu Ala Leu Ser Asp Leu Leu Phe
 65                  70                  75                  80

Val Ala Thr Leu Pro Phe Trp Thr His Tyr Leu Ile Asn Glu Lys Gly
                 85                  90                  95

Leu His Asn Ala Met Cys Lys Phe Thr Thr Ala Phe Phe Phe Ile Gly
            100                 105                 110

Phe Phe Gly Ser Ile Phe Phe Ile Thr Val Ile Ser Ile Asp Arg Tyr
        115                 120                 125

Leu Ala Ile Val Leu Ala Ala Asn Ser Met Asn Asn Arg Thr Val Gln
    130                 135                 140

His Gly Val Thr Ile Ser Leu Gly Val Trp Ala Ala Ala Ile Leu Val
145                 150                 155                 160

Ala Ala Pro Gln Phe Met Phe Thr Lys Gln Lys Glu Asn Glu Cys Leu
                165                 170                 175

Gly Asp Tyr Pro Glu Val Leu Gln Glu Ile Trp Pro Val Leu Arg Asn
            180                 185                 190

Val Glu Thr Asn Phe Leu Gly Phe Leu Leu Pro Leu Leu Ile Met Ser
        195                 200                 205

Tyr Cys Tyr Phe Arg Ile Ile Gln Thr Leu Phe Ser Cys Lys Asn His
    210                 215                 220

Lys Lys Ala Lys Ala Ile Lys Leu Ile Leu Leu Val Val Ile Val Phe
225                 230                 235                 240

Phe Leu Phe Trp Thr Pro Tyr Asn Val Met Ile Phe Leu Glu Thr Leu
                245                 250                 255

Lys Leu Tyr Asp Phe Phe Pro Ser Cys Asp Met Arg Lys Asp Leu Arg
            260                 265                 270

Leu Ala Leu Ser Val Thr Glu Thr Val Ala Phe Ser His Cys Cys Leu
        275                 280                 285

Asn Pro Leu Ile Tyr Ala Phe Ala Gly Glu Lys Phe Arg Arg Tyr Leu
    290                 295                 300

Tyr His Leu Tyr Gly Lys Cys Leu Ala Val Leu Cys Gly Arg Ser Val
305                 310                 315                 320

His Val Asp Phe Ser Ser Ser Glu Ser Gln Arg Ser Arg His Gly Ser
                325                 330                 335

Val Leu Ser Ser Asn Phe Thr Tyr His Thr Ser Asp Gly Asp Ala Leu
            340                 345                 350

Leu Leu Leu
        355
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<210> SEQ ID NO 83
<211> LENGTH: 333
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 83

Met Glu Ser Ser Gly Asn Pro Glu Ser Thr Thr Phe Phe Tyr Tyr Asp
1 5 10 15

Leu Gln Ser Gln Pro Cys Glu Asn Gln Ala Trp Val Phe Ala Thr Leu
20 25 30

Ala Thr Thr Val Leu Tyr Cys Leu Val Phe Leu Leu Ser Leu Val Gly
35 40 45

Asn Ser Leu Val Leu Trp Val Leu Val Lys Tyr Glu Ser Leu Glu Ser
50 55 60

Leu Thr Asn Ile Phe Ile Leu Asn Leu Cys Leu Ser Asp Leu Val Phe
65 70 75 80

Ala Cys Leu Leu Pro Val Trp Ile Ser Pro Tyr His Trp Gly Trp Val
85 90 95

Leu Gly Asp Phe Leu Cys Lys Leu Leu Asn Met Ile Phe Ser Ile Ser
100 105 110

Leu Tyr Ser Ser Ile Phe Phe Leu Thr Ile Met Thr Ile His Arg Tyr
115 120 125

Leu Ser Val Val Ser Pro Leu Ser Thr Leu Arg Val Pro Thr Leu Arg
130 135 140

Cys Arg Val Leu Val Thr Met Ala Val Trp Val Ala Ser Ile Leu Ser
145 150 155 160

Ser Ile Leu Asp Thr Ile Phe His Lys Val Leu Ser Ser Gly Cys Asp
165 170 175

Tyr Ser Glu Leu Thr Trp Tyr Leu Thr Ser Val Tyr Gln His Asn Leu
180 185 190

Phe Phe Leu Leu Ser Leu Gly Ile Ile Leu Phe Cys Tyr Val Glu Ile
195 200 205

Leu Arg Thr Leu Phe Arg Ser Arg Ser Lys Arg Arg His Arg Thr Val
210 215 220

Lys Leu Ile Phe Ala Ile Val Val Ala Tyr Phe Leu Ser Trp Gly Pro
225 230 235 240

Tyr Asn Phe Thr Leu Phe Leu Gln Thr Leu Phe Arg Thr Gln Ile Ile
245 250 255

Arg Ser Cys Glu Ala Lys Gln Gln Leu Glu Tyr Ala Leu Leu Ile Cys
260 265 270

Arg Asn Leu Ala Phe Ser His Cys Cys Phe Asn Pro Val Leu Tyr Val
275 280 285

Phe Val Gly Val Lys Phe Arg Thr His Leu Lys His Val Leu Arg Gln
290 295 300

Phe Trp Phe Cys Arg Leu Gln Ala Pro Ser Pro Ala Ser Ile Pro His
305 310 315 320

Ser Pro Gly Ala Phe Ala Tyr Glu Gly Ala Ser Phe Tyr
325 330

<210> SEQ ID NO 84
<211> LENGTH: 384

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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence:
Amino Acid Sequence for the Generation of Antibodies

<400> SEQUENCE: 84

Met Ala Ala Thr Ala Ser Pro Gln Pro Leu Ala Thr Glu Asp Ala Asp
1 5 10 15

Ser Glu Asn Ser Ser Phe Tyr Tyr Tyr Asp Tyr Leu Asp Glu Val Ala
20 25 30

Phe Met Leu Cys Arg Lys Asp Ala Val Val Ser Phe Gly Lys Val Phe
35 40 45

Leu Pro Val Phe Tyr Ser Leu Ile Phe Val Leu Gly Leu Ser Gly Asn
50 55 60

Leu Leu Leu Leu Met Val Leu Leu Arg Tyr Val Pro Arg Arg Arg Met
65 70 75 80

Val Glu Ile Tyr Leu Leu Asn Leu Ala Ile Ser Asn Leu Leu Phe Leu
85 90 95

Val Thr Leu Pro Phe Trp Gly Ile Ser Val Ala Trp His Trp Val Phe
100 105 110

Gly Ser Phe Leu Cys Lys Met Val Ser Thr Leu Tyr Thr Ile Asn Phe
115 120 125

Tyr Ser Gly Ile Phe Phe Ile Ser Cys Met Ser Leu Asp Lys Tyr Leu
130 135 140

Glu Ile Val His Ala Gln Pro Tyr His Arg Leu Arg Thr Arg Ala Lys
145 150 155 160

Ser Leu Leu Leu Ala Thr Ile Val Trp Ala Val Ser Leu Ala Val Ser
165 170 175

Ile Pro Asp Met Val Phe Val Gln Thr His Glu Asn Pro Lys Gly Val
180 185 190

Trp Asn Cys His Ala Asp Phe Gly Gly His Gly Thr Ile Trp Lys Leu
195 200 205

Phe Leu Arg Phe Gln Gln Asn Leu Leu Gly Phe Leu Leu Pro Leu Leu
210 215 220

Ala Met Ile Phe Phe Tyr Ser Arg Ile Gly Cys Val Leu Val Arg Leu
225 230 235 240

Arg Pro Ala Gly Gln Gly Arg Ala Leu Lys Ile Ala Ala Ala Leu Val
245 250 255

Val Ala Phe Phe Val Leu Trp Phe Pro Tyr Asn Leu Thr Leu Phe Leu
260 265 270

His Thr Leu Leu Asp Leu Gln Val Phe Gly Asn Cys Glu Val Ser Gln
275 280 285

His Leu Asp Tyr Ala Leu Gln Val Thr Glu Ser Ile Ala Phe Leu His
290 295 300

Cys Cys Phe Ser Pro Ile Leu Tyr Ala Phe Ser Ser His Arg Phe Arg
305 310 315 320

Gln Tyr Leu Lys Ala Phe Leu Ala Ala Val Leu Gly Trp His Leu Ala
325 330 335

Pro Gly Thr Ala Gln Ala Ser Leu Ser Ser Cys Ser Glu Ser Ser Ile
340 345 350

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Leu Thr Ala Gln Glu Glu Met Thr Gly Met Asn Asp Leu Gly Glu Arg
        355                 360                 365

Gln Ser Glu Asn Tyr Pro Asn Lys Glu Asp Val Gly Asn Lys Ser Ala
    370                 375                 380
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1. A diagnostic agent containing at least two different ligands of receptors involved in a pathological process.

2. A diagnostic agent containing at least two different chemokine receptor ligands.

3. The diagnostic agent according to claim 2, wherein said chemokine receptor ligands are chemokines, chemokine derivatives, agonists or antagonists of chemokine receptors, antibodies or antibody fragments which at least partially block the binding site of the chemokine receptor.

4. The diagnostic agent according to claims **2** and **3**, wherein said chemokines are selected from the group consisting of C, CC, CXC, CX_3C chemokines, their pharmacological analogues, binding proteins and antibodies which bind to the specific receptors in accordance with the chemokines mentioned.

5. Use of at least two different ligands of receptors involved in a pathological process for the diagnosis of diseases.

6. The use according to claim 5, wherein at least two chemokine receptor ligands and/or two different chemokine receptors are employed for the diagnosis of tumors.

7. The use according to claim 6, wherein said tumors are selected from the group consisting of colorectal tumors and prostatic tumors.

8. Use of at least two different chemokine receptor ligands and/or two different chemokine receptors for the diagnosis of organ rejection reactions.

9. Use of at least two different chemokine receptor ligands and/or two different chemokine receptors for the diagnosis of inflammatory processes.

10. Use of at least two different chemokine receptor ligands and/or two different chemokine receptors for the diagnosis of auto-immune diseases.

11. A medicament containing at least one inhibitor of at least two different ligands of receptors involved in a pathological process.

12. The medicament according to claim 11, containing at least one inhibitor of at least two chemokine receptors.

13. The medicament according to claim 12, containing antagonists of chemokine receptors, antibodies or antibody fragments which at least partially block the binding site of the chemokine receptor.

14. Use of inhibitors of at least two different ligands of receptors involved in a pathological process for the treatment of such diseases.

15. The use according to claim 14, wherein at least two chemokine receptors are used for preparing a medicament for the treatment of tumors, inflammatory processes, auto-immune diseases, diseases of the bone marrow.

16. The use according to claim 14, wherein tumors, inflammatory processes, auto-immune diseases of the vascular system, lymph system, respiratory tract, digestive tract and urogenital tract including the kidney are involved.

17. The use according to claims **15** and **16**, wherein said inhibitors are selected from the group antagonists of chemokine receptors, antibodies or antibody fragments which at least partially block the binding sites of the chemokine receptor and thus modulate their function.

18. The use according to any of claims 15 to 17, wherein said tumors are selected from the group consisting of colorectal tumors, prostatic tumors and other tumor diseases of the blood system, lymph system, cardiovascular system, nervous system, respiratory tract, digestive tract, endocrine system, skin including integumentary appendages, locomotor system and urogenital tract including the kidney.

19. The use according to any of claims 15 to 17, wherein said inflammatory processes are selected from the group consisting of asthma bronchiale, chronic inflammatory bowel diseases, organ rejection and further inflammatory processes of the blood system, lymph system, cardiovascular system, nervous system, respiratory tract, digestive tract, endocrine system, skin including integumentary appendages, locomotor system and urogenital tract including the kidney.

20. The use according to any of claims 15 to 17, wherein said auto-immune diseases are selected from the group consisting of rheumatoid arthritis, lupus erythematodes and other chronic diseases of the blood system, lymph system, cardiovascular system, nervous system, respiratory tract, digestive tract, endocrine system, skin including integumentary appendages, locomotor system and urogenital tract including the kidney.

21. Use of at least one chemokine receptor ligand and/or chemokine receptor for the diagnosis of organ rejection reactions following organ transplantations.

22. Use of an inhibitor of a chemokine receptor for preparing a medicament for preventing or alleviating organ rejection reactions following organ transplantations.

23. The use according to claim 22, following transplantations of the liver, kidney, pancreas, small intestine, as well as other organs, tissues and cell systems of the gastrointestinal tract, respiratory tract, urogenital tract, cardiovascular system, neuro-endocrine system, and the locomotor system as well as the blood and immune systems.

24. Peptides having the SEQ ID NOS. 1 to 40.

25. Use of the peptides according to claim 24 for preparing antibodies against a chemokine receptor.

26. A method for recognizing receptors involved in pathological processes, wherein expression profiles are examined on the proteome level using cell-biological or cytochemical methods, especially by immunochemical methods, immunohistochemistry using serial sections or multiple successive or simultaneous single sections, FACS analysis and/or the expression of receptors on the transcriptional level by molecular-biological methods, especially PCR, Northern analysis and/or in-situ hybridization methods.

27. The method according to claim 26, wherein a diagnostic agent according to any of claims 1 to 4 is employed.

* * * * *

专利名称(译)	用于分析肿瘤和炎性细胞的细胞表面蛋白质组以及用于治疗肿瘤和炎性疾病的诊断和药物，优选使用特异性趋化因子受体分析和趋化因子受体 - 配体相互作用

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IPC分类号	G01N33/53 A61K38/00 A61K39/395 A61K45/00 A61P1/00 A61P5/00 A61P9/00 A61P11/00 A61P11/06 A61P13/00 A61P13/12 A61P17/00 A61P19/02 A61P21/00 A61P25/00 A61P29/00 A61P35/00 A61P37/02 A61P37/06 A61P43/00 C07K14/52 C07K16/28 C12P21/08 C12Q1/68 G01N33/574 A61K38/10
CPC分类号	A61K38/00 C07K16/2866 C07K14/522 A61P1/00 A61P11/00 A61P11/06 A61P13/00 A61P13/12 A61P17/00 A61P19/02 A61P21/00 A61P25/00 A61P29/00
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摘要(译)

本发明涉及通过蛋白质组分析获得的药物和诊断剂的提供，优选含有至少两种不同的趋化因子受体配体或趋化因子受体抗体，并且还涉及至少两种不同的趋化因子受体配体，趋化因子受体的用途。抗体和/或两种不同的趋化因子受体。作为抑制剂，药物优选含有至少两种趋化因子受体的配体或抗体或表面趋化因子受体蛋白质组的相关算法，以及至少一种趋化因子受体配体和/或趋化因子受体，肽和抗体的用途及其用途肿瘤疾病和炎症性疾病的诊断和治疗。作为类比，也可以使用分析的肿瘤细胞表面蛋白质组的簇，例如外蛋白酶，粘附分子或各种受体类型。本发明涉及一种方法诊断和治疗的目的以及趋化因子及其相应受体的医学和工业用途，发现其包括抗体的拮抗剂抑制癌症生长，包括转移性扩散，并抑制炎症和自身免疫疾病。该方法基于以下发现：趋化因子通过自分泌，旁分泌和内分泌途径通过趋化因子受体蛋白质组的疾病特异性星座作用于特定肿瘤和炎症细胞。在其迁移和增殖行为方面控制原发性和继发性肿瘤以及特定炎症细胞。通过诊断检测其表达和调节局部增加的趋化因子和趋化因子受体组合物的存在，可能出现

严重抑制或完全预防癌症生长，肿瘤转移性扩散以及炎症和自身免疫的可能性。疾病。