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## (54) Method for predicting immune response to neoplastic disease based on mRNA expression profile in neoplastic cells and stimulated leukocytes

(57) Tumor necrosis factor (TNF) is capable of inducing apoptosis by interacting with specific TNF receptors on the surface of cancer cells. Because multiple members of TNF ligand and receptor are present within each superfamily, over 300 different ligand-receptor combinations exist. Activated blood leukocytes produce TNF as part of the immune response to cancer, as well as producing chemokines to attract other leukocytes to the site. A method is disclosed of detecting significant induction of a variety of TNF superfamily subtype and chemokine mRNAs in blood leukocytes when whole blood is exposed to heat-aggregated IgG or anti-T cell receptor antibodies as a model of immune system interactions. Substantial individual-to-individual variation is observed in TNF subtypes and chemokines induced. Since peripheral blood leukocytes are the supply of anti-cancer immune cells, the quantitation of ex *vivo* inducibility of appropriate TNF ligands and chemokines in blood will be useful in individualized cancer immunotherapy. If the tumor mass is small, such as with early invisible metastatic lesions, appropriate TNF assaults may be sufficient to prevent relapse.

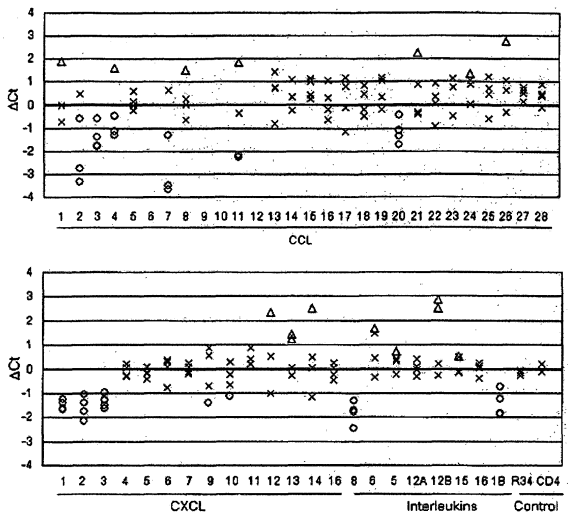


FIGURE 9

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# EUROPEAN SEARCH REPORT

Application Number
EP 08 00 8370

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The present search report has been drawn up for all claims

| Place of search | Date of completion of the search | Examiner |
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CATEGORY OF CITED DOCUMENTS

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Application Number
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## ANNEX TO THE EUROPEAN SEARCH REPORT ON EUROPEAN PATENT APPLICATION NO. EP 08 00 8370

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For more details about this annex : see Official Journal of the European Patent Office, No. 12/82

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| 专利名称(译) | 基于肿瘤细胞和刺激的白细胞中的mRNA表达谱预测对肿瘤疾病的免疫应答的方法 | | |
| 公开(公告)号 | EP1964931A3 | 公开(公告)日 | 2009-01-21 |
| 申请号 | EP2008008370 | 申请日 | 2006-06-08 |
| [标]申请(专利权)人(译) | 日立化成研究中心公司<br>日立化成工业株式会社 | | |
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| [标]发明人 | MITSUHASHI MASATO | | |
| 发明人 | MITSUHASHI, MASATO | | |
| IPC分类号 | C12Q1/68 G01N33/53 G01N33/00 | | |
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| 代理机构(译) | ELSY，DAVID | | |
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摘要(译)

肿瘤坏死因子（TNF）能够通过与癌细胞表面上的特异性TNF受体相互作用来诱导细胞凋亡。因为TNF配体和受体的多个成员存在于每个超家族中，所以存在超过300种不同的配体 - 受体组合。活化的血液白细胞产生TNF作为对癌症的免疫应答的一部分，以及产生趋化因子以吸引其他白细胞到达该位点。公开了一种方法，当全血暴露于热聚集的IgG或抗T细胞受体抗体作为免疫系统相互作用的模型时，检测血液白细胞中各种TNF超家族亚型和趋化因子mRNA的显着诱导。在TNF亚型和诱导的趋化因子中观察到显着的个体间变异。由于外周血白细胞是抗癌免疫细胞的供应，因此血液中适当的TNF配体和趋化因子的离体诱导能力的定量将在个体化的癌症免疫疗法中有用。如果肿瘤块很小，例如早期看不见的转移性病变，适当的TNF攻击可能足以预防复发。


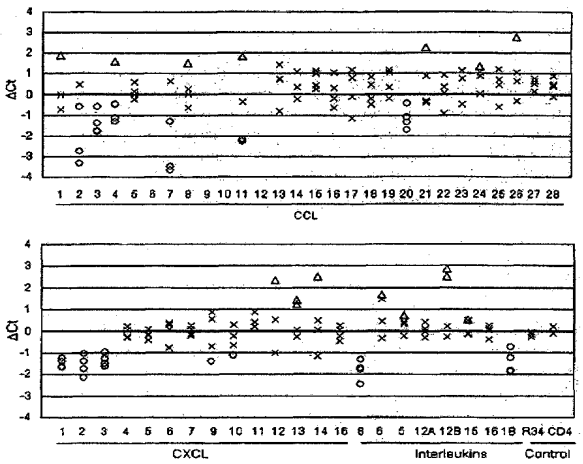


FIGURE 9