**Fig. 1. Chimeric Receptors**

![Chimeric Receptors Diagram]

**Figure 1A**

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**Abstract:** A fusion protein, when displayed on a cell can convert a negative signal into a positive signal in the cell. The fusion protein is a chimeric protein in that the protein comprises at least two domains, wherein the first domain is a polypeptide that is associated with a negative signal and the second domain is a polypeptide that is associated with a positive signal. Thus, these switch receptors are able to switch negative signals to positive signals for enhancement of an immune response.

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A. CLASSIFICATION OF SUBJECT MATTER

| IPC(8) | A61 P 37/04, A61 P 35/00, A61 K 39/00 (2012.01) |

USPC - 435/69.7, 424/192.1

According to International Patent Classification (IPC) or to both national classification and IPC.

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC(8) - A61P 37/04, A61P 35/00, A61K 39/00 (2012.01)

USPC - 435/69.7, 424/192.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

IPC(8) - A61P 37/04, A61P 35/00, A61K 39/00 (2012.01), USPC - 435/69.7, 424/192.1, 424/185.1, 435/372.3, 424/93.71: keyword search, as below

Electronic database consulted during the international search (name of data base and, where practicable, search terms used)

USPTO PubWest (databases: PGPB,USPT,USOC,EPAB,JPAB), PubMed, Google Scholar - Search Terms: chimeric, chimera, chimaera, fused, fusion, cd28, icos, cta4, pd-1, btl, cd152, npl17, npl23, intracellular, extracellular, internal, cytosolic, cytoplasmic, transmembrane, positive, stimulatory, activate, negative, repress, suppress, upregulate, downreg

C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
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<tbody>
<tr>
<td>X</td>
<td>DENNEHY et al., Cutting Edge: Monovalency of CD28 Maintains the Antigen Dependence of the T Cell Costimulatory Responses. J. Immunol., 15 May 2006, Vol. 176, No 10, pg. 5725-5729. Especially abstract; pg 5725, col 1, para 1-2; pg. 5726, col 2, para 2; pg. 5726, col 1, para 2</td>
<td>1-7, 9</td>
</tr>
<tr>
<td>Y</td>
<td>ZHAO et al., Multiple Injections of Electroporated Autologous T Cells Expressing a Chimeric Antigen Receptor Mediate Regression of Human Disseminated Tumor. Cancer Res, 5 October 2010, Vol. 70, No 22, pg. 9053-9061. Especially abstract; pg. 9054, col 1, para 2; pg. 9054, col 1, para 1</td>
<td>8, 11, 12</td>
</tr>
<tr>
<td>Y</td>
<td>CARPENITO et al., Control of large, established tumor xenografts with genetically retargeted human T cells containing CD28 and CD137 domains. PNAS USA, 3 March 2009, Vol. 106, No. 9, pg. 3360-3365. Especially abstract</td>
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