Chimeric receptor molecules with innate receptors for immunotherapy.

KEYWORDS

- CAR
- CHIMERIC ANTIGEN RECEPTORS
- Fcγ-CR
- IMMUNOTHERAPY
- SOLID TUMORS
- HEMATOLOGIC MALIGNANCIES
- ANTITUMOR ACTIVITY

AREA

- CHEMISTRY & BIOTECHNOLOGY

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Patent Type
Patent for invention.

Co-Ownership
Sapienza University of Rome 50%, National Research Council (CNR) 50%.

Inventors
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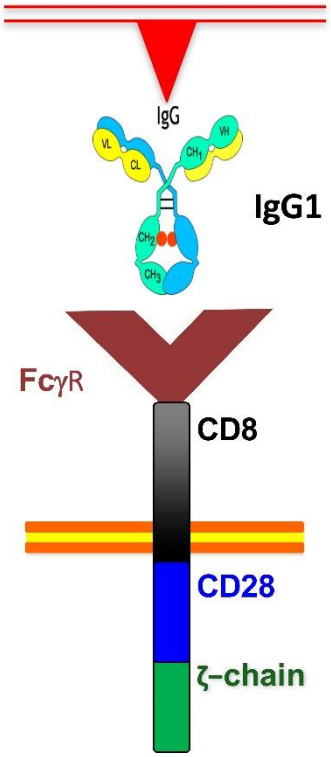
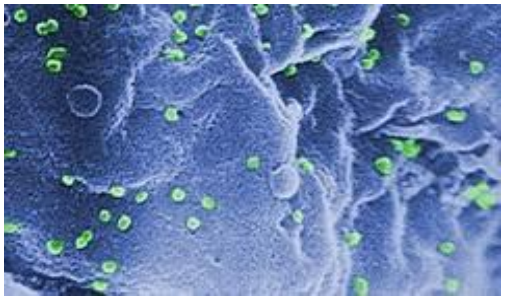
Industrial & Commercial Reference
Pharmaceutical and Biotechnology Industries. Industries involved in the development of immunological therapies and mAbs.

Time to Market
18 months.

Availability
Cession, Licensing, Research, Development, Experimentation, Collaboration, Start-up and Spin-off.





Abstract
The Fcγ-CRs are designed to redirect T cells functions against opsonized target cells.
This is made possible by the presence of an extracellular module of the FcγRs capable of binding monoclonal antibodies, and by the presence of signal transduction elements (CD28/ζ-chain) in the intracellular portion.
These "universal Fcγ-CRs" implement the activity of the immune system by recruiting a T-dependent ADCC-like response, while maintaining the clinically relevant effects of the therapeutic antibodies available for the treatment of tumors that can be administered differently to patients during therapy.

Publications

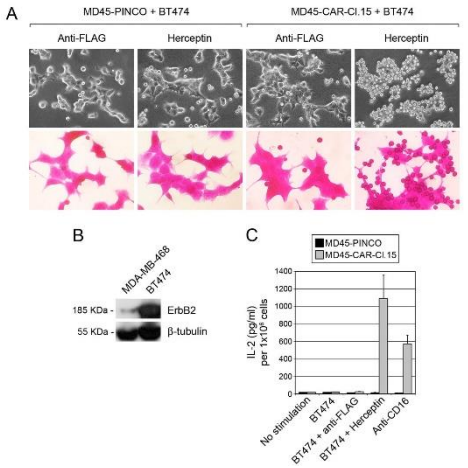
- Fcγ Chimeric Receptor-Engineered T Cells: Methodology, Advantages, Limitations and Clinical Relevance. https://doi.org/10.3389/fimmu.2017.00457
- T lymphocytes engineered to express a CD16-chimeric antigen receptor re-direct T-cell immune responses against immunoglobulin G-opsonized target cells. doi:10.1016/j.fob.2015.08 .012
- http://www.promab.com/index.php?main_page=page&id=57

Chimeric receptor molecules with innate receptors for immunotherapy.

Technical Description

The Fcγ-CRs code for transmembrane chimeric molecules with dual functions:
a) Binding to the Fc fragment of IgG via the extracellular portion of the FcγIII fragment of CD16 (CD16-CR); FcγRIRI CD64 (CD32-CR FcγRIIb CD32 (CD32-CR).
b) Activation of the lithic machinery in the immune effector cells, via the intracellular portions of CD28 and ζ-chain embedded in the Fcγ-CR.

The mechanism of activation involves the formation of a bridge between the "target cell" and the "reprogrammed T lymphocyte" mediated by monoclonal antibodies directed against the antigens present on the surface of the target cell.



Technologies & Advantages

The Fcγ-CRs are "Universal CR" specifically designed to wider the immunotherapeutic options through the use of mAbs and to overcome resistance due to the selection of antigen-negative tumor cells.

T lymphocytes expressing the Fcγ-CRs improve the efficacy of the therapeutic Abs normally used in cancer therapy.

The Fcγ-CRs may limit the "off-target toxicity" because of the possibility to choose the monoclonal antibodies with the suitable affinity for any antigen.

Fcγ-CR T cell therapies can be optimized based on administrations of monoclonal antibodies targeting different antigens, simultaneously or in different moments of the therapy.

The natural half-life of the antibodies in the blood stream (about three weeks) provides an additional level of control of the CR-T cell responses and adverse immune reactions, by modulating frequencies and doses of the antibody administration

Applications

The adoptive therapy with Fcγ-CR lymphocytes can be utilized in several fields. The areas of application are tumor immunotherapy, infectious diseases and autoimmune diseases.
Oncology is the main area of application for these immunotherapeutic strategies. T lymphocytes expressing Fcγ-CRs can be used in the treatment of solid or hematological tumors, for which a monoclonal antibody of proven therapeutic efficacy is available.

Fcγ-CR T lymphocytes can be used to eliminate virally-infected cells (eg EBV, CMV, HPV, HSV1 and HSV-2 and HIV) opsonized by a specific antibody, or to redirect an immune response to autoreactive lymphocytes in autoimmune diseases (e.g. type I diabetes, systemic lupus erythematosus, myelodysplastic syndromes).

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