Development of Dominant Negative CD40L Antagonists DACD40L

Tech ID: 34281 / UC Case 2018-488-0

ABSTRACT

Researchers at the University of California, Davis have engineered dominant negative CD40L mutant polypeptides that inhibit CD40/CD40L-mediated signaling, offering therapeutic potential for inflammatory, immune disorders, and cancer with improved safety profiles.

FULL DESCRIPTION

The invention relates to isolated polypeptides comprising mutated forms of the CD40 ligand (CD40L) protein, specifically targeting amino acid residues, to reduce or abolish binding to integrin. These dominant negative CD40L mutants selectively inhibit CD40/CD40L signaling pathways responsible for immune cell activation and proliferation. The mutations produce polypeptides defective in integrin binding yet capable of binding CD40, leading to suppression of pathogenic inflammatory and immune responses without the thromboembolic risks associated with prior anti-CD40L therapies. The polypeptides may be further modified to enhance pharmacokinetic properties. Pharmaceutical compositions and gene therapy approaches using nucleic acids encoding these mutants are also provided for treatment and prevention of disorders including autoimmune diseases, systemic lupus erythematosus (SLE), rheumatoid arthritis, transplant rejection, and cancers

APPLICATIONS

- Therapeutics for autoimmune diseases such as systemic lupus erythematosus (SLE), rheumatoid arthritis, psoriasis, and diabetes.
- Treatment of chronic kidney disease and transplant rejection through immune modulation.
- Oncology applications targeting cancers associated with aberrant CD40/CD40L signaling.
- Anti-inflammatory medications for conditions including atherosclerosis and immune-mediated renal diseases.
- Pharmaceutical products comprising recombinant CD40L dominant negative polypeptides, Fc fusion proteins, or gene therapies.
- Research tools for studying CD40/CD40L interactions and integrin functions in immune regulation.

FEATURES/BENEFITS

- Selectively inhibits CD40/CD40L signaling by targeting integrin-binding sites.
- Reduces risk of thromboembolic side effects compared to previous anti-CD40L antibodies.
- Suppresses pathological lymphocyte proliferation and inflammatory responses.
- Enhances pharmacokinetics via PEGylation, myristoylation, or Fc-fusion.
- Versatilely delivers options including protein therapeutics and nucleic acid-based gene therapy. Potential for application in diverse inflammatory, immune-mediated, and cancer

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OTHER INFORMATION

KEYWORDS

autoimmune diseases, cd40/cd40l signaling, dominant negative polypeptides, gene therapy, immune modulation, inflammation, integrin binding, pegylation, rheumatoid arthritis, thromboembolic risk reduction

CATEGORIZED AS

- **Biotechnology**
  - Health
- **Medical**

diseases.

▶ Overcomes safety concerns of prior anti-CD40L monoclonal antibody therapies (e.g., thromboembolic events).

▶ Addresses unmet need for novel therapeutics targeting CD40/CD40L signaling with better efficacy and safety.

▶ Reduces autoimmune inflammation and immune cell proliferation without broadly suppressing immunity.

▶ Enables treatment of chronic inflammatory and immune disorders resistant to existing therapies.

▶ Offers a targeted approach to modulate pathological signaling implicated in cancer cell proliferation.

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Published Application	20220135649	05/05/2022	2018-488

▶ Disease: Autoimmune and Inflammation

▶ Disease: Cancer

▶ Disease: Kidneys and Genito-Urinary System

▶ Gene Therapy

▶ Research Tools

▶ Therapeutics

RELATED CASES

2018-488-0

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- ▶ Suppression of sPLA2-Integrin Binding for Treating an Inflammatory Condition or Suppressing Cell Proliferation
- ▶ Novel Insight into Inhibiting IGF1 Signaling
- ▶ The Isolated Heparin-binding Domain (HBD) of VEGF165 and the Isolated D1 Domain of VEGFR2 (KDR)
- ▶ Novel Fibroblast Growth Factor 1-Derived Peptides for Therapy and Drug Discovery
- ▶ Modulating MD-2-Integrin Interaction for Sepsis Treatment
- ▶ Integrin Binding to P-Selectin as a Treatment for Cancer and Inflammation

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