NATIONAL CANCER INSTITUTE
Technology Transfer Center

Human Monoclonal Antibodies Cross-reacting to Insulin-like Growth Factors IGF-I and IGF-II as Potential Anti-tumor Agents

Summary

The National Cancer Institute's Cancer and Inflammation Program is seeking statements of capability or interest from parties interested in licensing monoclonal antibodies to IGF-1 and IGF-II for the treatment of cancer.

NIH Reference Number

E-068-2011

Product Type

- Therapeutics

Keywords

- Dimitrov
- monoclonal antibody
- insulin-like growth factor
- IGF-I
- IGF-II

Collaboration Opportunity

This invention is available for licensing.

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Description of Technology

The National Cancer Institute's Cancer and Inflammation Program is seeking statements of capability or interest from parties interested in licensing this technology.

The type 1 insulin-like growth factor (IGF) receptor (IGF1R) is over-expressed by many tumors and mediates proliferation, motility, and protection from apoptosis. Agents that inhibit IGF1R expression or function can potentially block tumor growth and metastasis. Its major ligands, IGF-I, and IGF-II are over-expressed by multiple tumor types. Previous studies indicate that inhibition of IGF-I, and/or IGF-II binding to its cognizant receptor negatively modulates signal transduction through the IGF pathway and concomitant cell

proliferation and growth. Therefore, use of humanized or fully human antibodies against IGFs represents a valid approach to inhibit tumor growth.

The present invention discloses the identification and characterization of a fully human monoclonal antibody designated m708.5 that has been affinity maturated against IGF-I and IGF-II and displays extremely high affinities for IGF-I and IGF-II in the picoM range. The m708.5 antibody potently inhibited signal transduction mediated by the IGF-1R interaction with IGF-I and IGF-II and blocked phosphorylation of IGF-IR and the insulin receptor. Further, this antibody inhibited migration in the MCF-7 breast cancer cell line at the picoM range. Therefore, this antibody can be used to prevent binding of IGF-I and/or IGF-II to its concomitant receptor IGFIR, consequently, modulating diseases such as cancer.

Potential Commercial Applications

- Therapeutic for the treatment of various human diseases associated with aberrant cell growth and motility such as breast, prostate, and leukemia carcinomas.
- Research regent to study IGF-I and/or IGF-II binding and its association with tumor growth.

Competitive Advantages

- Antibodies against the ligands IGF-I and IGF-II, such as this invention, inhibit the interaction with IGF-IR yet likely do not have the type of toxicity associated with IGF-1R antibodies.
- High concentrations of IGF-II are found in cancer patients, on average several fold higher than IGF-I, thus this cross-reacting IGF-I/IGF-II antibody could be more effective than existing IGF-IR and/or IGF-I currently in the clinic.
- This novel IGF antibody may provide therapeutic intervention for multiple carcinomas.

Inventor(s)

Dimiter Dimitrov (NCI)

Development Stage

- Discovery (Lead Identification)

Publications

Zhao Q, et al.; Human monoclonal antibody fragments binding to insulin-like growth factors 1 and 2 with picomolar affinity. [PMID 21750218]

Feng Y, et al.; Novel human monoclonal antibodies to insulin-like growth factor (IGF)-II that potently inhibit the IGF receptor type I signal transduction function. [PMID 18283605]

Kimura T, et al.; Targeting of bone-derived insulin-like growth factor-II by a human neutralizing antibody suppresses the growth of prostate cancer cells in a human bone environment. [PMID 20028742]

Patent Status

- **U.S. Patent Issued:** U.S. Patent Number 9676846, Filed 12 Apr 2011, Issued 13 Jun 2017

Related Technologies

- E-217-2005
- E-336-2005

Therapeutic Area

- Cancer/Neoplasm

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