

Single-domain monoclonal antibodies for the treatment of hepatocellular carcinoma

Summary

The National Cancer Institute seeks parties to license human monoclonal antibodies and immunoconjugates and co-develop, evaluate, and/or commercialize large-scale antibody production and hepatocellular carcinoma (HCC) xenograft mouse models.

NIH Reference Number

E-130-2011

Product Type

- Therapeutics

Keywords

- Liver cancer
- hepatocellular carcinoma
- HCC
- immunotoxins
- antibody-drug conjugate
- chimeric antigen receptor

Collaboration Opportunity

This invention is available for licensing and co-development.

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Description of Technology

The National Cancer Institute seeks parties to license human monoclonal antibodies and immunoconjugates and co-develop, evaluate, and/or commercialize large-scale antibody production and hepatocellular carcinoma (HCC) xenograft mouse models. An advantage of these monoclonal antibodies as a potential therapeutic is their specificity, which would reduce deleterious side-effects. HCC is the most common form of liver cancer, and is among the more deadly cancers in the world. There is a need for new treatments that can be successfully applied to a large population of patients.

Glypican-3 (GPC3) is a cell surface protein that is preferentially expressed on HCC cells. Researchers at the [NCI Laboratory of Molecular Biology](#) demonstrated that a soluble form of GPC3 that is incapable of cell signaling can inhibit the growth of HCC cells. This suggests that blocking GPC3 signaling could serve as a therapeutic approach for treating HCC.

This opportunity to collaborate with NCI researchers or license the technology covers monoclonal antibodies (mAb) against GPC3 and their use, either by themselves or as the targeting domain for an immunotoxin, antibody drug conjugate (ADC) or chimeric antigen receptors (CARs), for the treatment of GPC3-expressing cancers such as HCC. Specifically, this involves two distinct monoclonal antibodies to GPC3 generated by the researchers. The first monoclonal antibody (HN3) binds to a conformational epitope on the cell surface domain of GPC3. The second monoclonal antibody (HS20) binds specifically to heparin sulfate chains on GPC3. By blocking GPC3 function, these antibodies can inhibit the growth of HCC cells, thereby decreasing the ability of tumors to grow and metastasize. Furthermore, by using the antibodies to target a toxin to only those cells that express GPC3, cancer cells can be eliminated while healthy, essential cells remain unharmed. Thus, monoclonal antibodies to GPC3 (and corresponding immunotoxins) represent a novel therapeutic candidate for treatment of HCC, as well as other cancers associated with the differential expression of GPC3.

Potential Commercial Applications

- Therapeutic candidates against cancers that overexpress GPC3
- Antibodies for killing cancer cells by inhibiting GPC3-based cell signaling, thereby inhibiting tumor cell growth
- CARs, immunotoxins and ADCs for killing cancer cells
- Diagnostics for detecting cancers associated with GPC3 overexpression
- Specific cancers include hepatocellular cancer (HCC), melanoma, thyroid cancer, lung squamous cell carcinoma, Wilms tumor, neuroblastoma, hepatoblastoma, and testicular germ-cell tumors

Competitive Advantages

- Monoclonal antibodies create a level of specificity that can reduce deleterious side-effects
- Multiple treatment strategies available including the killing of cancer cells with a toxic agent or by inhibiting cell signaling
- Non-invasive and potentially non-liver toxic alternative to current HCC treatment strategies

Inventor(s)

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Development Stage

- Pre-clinical (in vivo)

Publications

M Feng, M Ho et al. [PMID: 23471984]

M Feng, M Ho et al. [PMID: 20617511]

SI Zitterman, M Ho et al. [PMID:19816934]

Patent Status

- **U.S. Patent Issued:** U.S. Patent Number 9,394,364, Issued 19 Jul 2016
- **U.S. Patent Issued:** U.S. Patent Number 9,206,257, Issued 08 Dec 2015
- **U.S. Patent Filed:** U.S. Patent Application Number PCT/US2012/034186, Filed 19 Apr 2012
- **Foreign Filed:** Chinese - Patent Application 201280029201.3
- **Foreign Filed:** EP - Patent Application 12717009
- **Foreign Filed:** EP - Patent Application 15188264.4

Related Technologies

- [E-136-2012 - High-Affinity Mouse Monoclonal Antibodies to GPC-3 for Liver Cancer Research](#)
- [E-198-2012 - High-Affinity Rabbit Monoclonal Antibodies for Cancer Treatment](#)
- [E-236-2012 - Anti-Mesothelin Monoclonal Antibodies for the Treatment of Cancer](#)
- [E-302-2009 - Mouse Xenograft Model for Mesothelioma](#)
- [E-176-2010](#)

Therapeutic Area

- Cancer/Neoplasm

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