



BIOLOGIC

Novel Bispecific to Alter the Immunosuppressive Tumor Microenvironment

Brief Technology Description

Compositions and methods of treatment of a novel bispecific reagent that targets Notch ligand to tumor sites

BUSINESS OPPORTUNITY

Exclusive licence
Sponsored research
Start-up opportunity

TECHNOLOGY TYPE

Therapeutic

STAGE OF DEVELOPMENT

Preclinical in vivo

PATENT INFORMATION

[US20190248894](#)

[WO2021021825](#)

INVESTIGATOR OVERVIEW

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Technology Overview

The tumor microenvironment (TME) consists of the complex ecosystem where cancerous cells reside and interact with their non-malignant neighbors, including immunosuppressive myeloid cells that hinder immune control of tumors. In particular, immunosuppressive macrophages lead to the resistance of tumors to immunotherapy, a valuable treatment against many different types of cancers. Although numerous approaches are under development to eliminate, or modify specific pathways within immunosuppressive myeloid cells, methods that alter the TME from an immunosuppressive to anti-tumor state could present additional therapeutic benefits. Notch signaling has been shown to polarize macrophages towards a pro-inflammatory (anti-tumor) state and away from an immunosuppressive state. However, development of a Notch activation approach to elicit this anti-tumor effect has not been considered, likely due to the lack of selective in vivo targeting. Hutch researchers have developed a bispecific protein which targets a high affinity Notch ligand to tumor cells, activating Notch receptors expressed on surrounding immunosuppressive macrophages, thereby shifting the TME from a pro-tumor to anti-tumor state; alterations which we believe will increase the penetrance and efficacies of various immunotherapies.

Applications

- Combination therapy with checkpoint inhibitors and other immune-oncology treatments

Potential Advantages

- Targeted activation minimizes the risk of off-target toxicities potentially caused by Notch activation
- May be used in a variety of solid tumor settings
- Preclinical in vivo proof of concept demonstrating priming TME with bi-specific could lead to improved treatment efficacy of immune checkpoint inhibitors when used in combination

Market Overview

Worldwide new cancer cases are projected to increase from 14M (2012) to 21M (2030). Worldwide cancer deaths projected to increase 60% from 8M in 2012 to 13M in 2030. Global sales for immune checkpoint inhibitors are forecast to reach \$54.39B by 2025, growing at a 14.67% compounds annual growth rate.