EXPERT OPINION:

Multispecific and Bispecific Antibodies for Immuno-Oncology

With increased expertise in molecular design, companies have begun to develop multiple antigen binding domains into a single antibody molecule. These bispecific or multispecific antibodies have great ability to generate novel biological responses, and potentially have success in challenging tumour models. Invenra Inc. has a pipeline of multispecific anitbodies that are advancing towards the clinic, and we sat down with Bryan Glaser, a founding member of the Invenra scientific team, to hear more about why they chose this immuno-oncology strategy.

BRYAN GLASER

Vice President, Business Development, Invenra Inc.

Dr. Glaser was a founding member of the Invenra scientific team and was the Vice President of Research responsible for overseeing the development of its B-Body™ multispecific technologies as well as early discovery efforts for internal and partnered programs in immuno-oncology. Dr. Glaser is now Vice President of Business Development, responsible for leading efforts in partnering Invenra pipeline assets as well as establishing new strategic collaborations. Dr. Glaser received his Ph.D. in Molecular and Cellular Pharmacology from the University of Wisconsin and was a postdoctoral fellow/Senior Scientist at the non-profit, SRI International.

Your company works on multispecific antibodies. Why do you think this therapeutic strategy will have such an impact on immuno-oncology?

Multispecific antibodies have the ability to generate novel biological responses that are not seen using standard monoclonal antibodies. Multispecific antibodies have the potential to deliver more than the results that are achieved through the combination of two monoclonal antibodies. New first-in-class molecules can be generated when multispecifics are optimized to find the right combination of epitope, affinity, and geometry such that novel biological responses are generated.

Could you explain a bit more about your multispecific platform?

Our platform, the B-Body™, has been designed to enable high throughput functional discovery while maintaining good biophysical properties needed for manufacturing. We think it is critical to screen candidates in their final format in biologically relevant assays to generate first-in-class molecules. To accomplish this goal, we focused our technology on high fidelity Heavy Chain/Light Chain pairing through a domain substitution strategy. We have removed the CH1/CL from one fab arm and replaced it with another human antibody domain pair. This substitution provides the asymmetry needed for proper assembly. We have also paired the technology with a proprietary purification strategy that enables the rapid generation of 1000's of Fab arm combinations without the need for optimization. Our discovery strategy uses this purification scheme to empirically test combinations of fabs binding to different epitopes, various KDs, and multiple geometries in reporter and primary assay systems.

What are the recurrent challenges you come against in your research?

The biggest challenge we face is in the understanding of the disease biology. We are able to create 1000's of candidates per program but we must understand the proper screening assays and the proper animal models for candidate selection. Animal models become increasingly difficult with multispecifics as the ability to generate cross-reactive molecules can limit the animal system that can be used for testing.

What are your main priorities across the next year?

Our main priority across the next year is supporting the clinical validation of the B-Body™ platform. We believe strongly in the design of the platform but are still waiting for our first programs to advance to the clinic. We expect significant advances in our first programs in cell line development.

What are the most important technologies impacting immuno-oncology currently?

T cell engagers, T-cell therapies and related approaches are of growing importance in the field. The issues are being worked out, and many companies of all sizes have active programs. An interesting side note is the more recent work in recruiting and engaging other effector cells such as NK cells or neutrophils. We are interested in following these new approaches combining the adaptive and innate immune systems to see if they can bring enhanced efficacy.

In addition, we are very interested in the work exploring combining multiple therapies for the induction of an in situ vaccination. We work closely with Paul Sondel, from the University of Wisconsin. His group, along with others, are generating very interesting data in which the use of standard chemotherapy or low dose radiation in combination with different I-O approaches are having success in very challenging tumor models. We think this approach can have a broad therapeutic impact if the correct dosing schedule is determined.

Outside of multispecific and bispecific approaches, what therapeutic modalities do you think have the most potential in immuno-oncology currently?

We have been very interested in following the advances in cell therapy approaches for oncology. In particular, we have been interested in approaches that combine antibody-based therapies with cell therapies to improve efficacy. We think there are interesting ways in which bispecific approaches can complement rather than compete with cell therapies.

Find out more about Bryan and his involvement with the Immuno-Oncology Congress HERE