REPRINT FROM OCTOBER 8, 2012

BioCentury

THE BERNSTEIN REPORT ON BIOBUSINESS™

Tools & Techniques

New vista over epitopes

By Meghan Sullivan
Staff Writer

Visterra Inc. came out of stealth mode last month when **Pfizer Inc.** did a deal to use the biotech's protein structure analysis technology to discover antibodies against epitopes of proteins implicated in undisclosed indications. Visterra thinks its platform is a more efficient and effective way to discover antibodies than traditional mAb screening methods.

Under the deal, Visterra will receive an upfront payment and research funding, and will be eligible for R&D milestones plus royalties. Both partners declined to provide details on financial terms, targets or indications in the deal, which is Visterra's first.

Most epitopes of a protein target are conformational epitopes, which arise when a protein is folded in three dimensional space and cause multiple amino acids to closely interact that are otherwise distant from one another in a protein's primary sequence.

Some conformational epitopes are more critical than others to a protein's overall stability. Visterra's platform aims to identify the protein interactions that underlie the critical conformational epitopes and use that information to generate mAbs that potently hit those epitopes.

The company begins with an analysis of the amino acid sequence and interactions between individual amino acids within the same target protein. The goal is to quantify what the company calls the protein's atomic interaction network (AIN), which is the complete set of all amino acid-amino acid interactions that stabilize a protein's 3-D structure.

Once the AIN is calculated, it is possible to determine the significant interaction network (SIN) score of each amino acid and, based on that score, to identify amino acid interactions predicted to be critical to the overall stability of the protein.

"These are the virus' Achilles' heels — the regions that we want to target and disrupt," said Visterra CEO Steven Brugger. Once the target epitope is identified, the same model can be used to design and optimize antibody candidates.

According to Jose Carlos Gutierrez-Ramos, SVP of Pfizer BioTherapeutics R&D, part of the pharma's antibody strategy is to partner with companies like Visterra that are developing disruptive technologies.

> ***"This is a very different approach to the traditional methods of discovering antibodies."***
>
> **Donna Ambrosino, Visterra**

"This is a very different approach to the traditional methods of discovering antibodies," said Visterra CMO Donna Ambrosino. "While most methods find and extract mAbs that have already been made — either by patients' immune systems or transgenic mice — we can instead first identify the optimal area to bind on an antigen and then find the mAb which binds that area."

The platform also includes a scoring scheme for predicting structural regions that are conserved across proteins of the same family.

In its first application of the technology, Visterra developed VIS410, a broad spectrum antibody against the HA protein of influenza A. The company sought to identify a conformational epitope on the stem region of the influenza hemagglutinin (HA) protein that was conserved across all strains of the virus. Visterra then used the identified 3D network to engineer more than 50

See next page

BioCentury®
THE BERNSTEIN REPORT ON BIOBUSINESS

PO Box 1246
San Carlos CA 94070-1246
Voice: 650-595-5333
Fax: 650-595-5589
www.biocentury.com

DAVID FLORES
President & CEO

KAREN BERNSTEIN, Ph.D.
Chairman & Editor-in-Chief

Tools & Techniques,
from previous page

mAbs that bound to and neutralized the strains, including VIS410.

The company thinks VIS410's target is not only conserved across all influenza A strains, but also is resistant to mutation.

Visterra reported preclinical data in September at the **American Society for Microbiology**'s Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) in San Francisco.

In prophylactic studies, 100% of healthy mice that received a single dose of VIS410 survived infection with a lethal dose of either H1N1 or H3N2 influenza A virus. In post-infection studies, 100% of mice survived after treatment with a single dose of VIS410 given up to 72 hours after infection.

Visterra plans to begin Phase I testing in 2014.

"We were able to use the underlying technology of atomic network to identify the epitope that is conserved in all strains," which should give VIS410 the potential to prevent and treat all strains of flu, said Ambrosino.

The company is internally focused on treating seasonal and avian (H5N1) flu infection and will seek partners to develop the mAb as a vaccine to prevent infection during a pandemic outbreak.

Visterra plans to submit grant applications for the program to **NIH**'s National Institute of Allergy and Infectious Diseases (NIAID).

Brugger said Visterra has the capability to develop VIS410 through Phase Ib/IIa proof of concept. The company then hopes to find a partner.

It also is pursuing other infectious diseases, with several undisclosed targets in discovery.

Visterra was founded in 2007 by Ram Sasisekharan, professor of health sciences and technology and biological engineering at **Massachusetts Institute of Technology**.

COMPANIES AND INSTITUTIONS MENTIONED

American Society for Microbiology, Washington, D.C.
Massachusetts Institute of Technology, Cambridge, Mass.
National Institutes of Health (NIH), Bethesda, Md.
Pfizer Inc. (NYSE:PFE), New York, N.Y.
Visterra Inc., Cambridge, Mass.