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Emerging Company Profile

Apexigen: rAbbits hop rodents

By Michael Flanagan
Senior Writer

Looking to exploit antibody generation processes unique to a rabbit's immune system, **Apexigen Inc.** is developing humanized mAbs that it believes will have best-in-class potential by offering better affinity and specificity than humanized murine antibodies. Rabbit mAbs also recognize a greater number of epitopes, which may make it possible to generate mAbs against antigens that have been impossible to target with other types of antibodies.

Earlier this year, the company spun out of service play **Epitomics Inc.**, which had developed a pair of technologies to generate and humanize rabbit-derived mAbs. Apexigen took an exclusive license to the technologies to develop mAbs for therapeutic applications, and has access to Epitomics' antibody generation and screening infrastructure. The parent retained rights to the technologies for diagnostic, research services and reagent purposes.

The first technology, called RabMAb, utilizes hybridomas created by fusing B cells from an immunized rabbit with immortalized myeloma cells to generate selective mAbs.

An early version of RabMAb was developed by researchers at **Loyola University** in the mid-1990s, but Apexigen President and CEO Xiaodong Yang said the resulting compounds were not stable or predictable. Epitomics took over the program in 1997 and "came up with two or three improved versions of the cell line that are highly stable," predictable and flexible in terms of what antigens they can target, he added.

RabMAb "takes advantage of the unique way in which a rabbit's immune system makes antibodies versus rodents and humans," Yang said.

As with humans and mice, antibodies generated in rabbits undergo somatic recombination of the immunoglobulins, a process that produces some diversity. However, he said, the rabbit's immune system features another mechanism called somatic gene conversion, which introduces additional diversity by transferring DNA sequence information from one helix to another while the original helix remains unchanged.

Yang said RabMAb can generate mAbs with 10-100 times the affinity of a comparable mouse or human mAb. Plus, because rabbit-derived mAbs are capable of recognizing a greater variety of epitopes, they can be used to target many peptides and small molecule haptens that do not elicit an immune response in mice and other rodents.

Apexigen's mAbs often are capable of binding to analogous human and mouse targets, which makes preclinical testing straightforward as the mAbs can be tested in human cell lines and in mouse disease models.

Apexigen's second technology is the

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Apexigen Inc.

Burlingame, Calif.
Technology: Humanized mAbs derived from rabbits for therapeutic applications
Disease focus: Cancer, Inflammation
Clinical status: Preclinical
Founded: 2010 by Epitomics Inc.
University collaborators: None
Corporate partners: 3SBio Inc., Simcere Pharmaceutical Group and Jiangsu T-mab Biotechnology Co. Ltd.
Number of employees: 3
Funds raised: Not disclosed
Investors: Epitomics Inc.
CEO: Xiaodong Yang
Patents: 8 issued, covering rabbit mAb and humanization technologies, as well as individual antibody candidates

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Apexigen Inc.,
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mutational lineage guided (MLG) engineering method for humanizing the rabbit-derived mAbs. MLG uses biological and sequence information from a panel of similar, functional rabbit antibodies to identify conserved sequences that are critical for retention of full activity, while also picking out non-critical sequences that can be substituted with human residues.

In contrast, murine mAbs are humanized by grafting or resurfacing the murine complementarity determining region (CDR) onto a human mAb framework, according to Yang. This process often results in the humanized mAb having lower affinity than the murine mAb, thus requiring *in vitro* affinity maturation to regain the affinity.

Yang said Apexigen's immediate priority is validating the therapeutic potential of the RabMAb platform by generating human POC data. To do this, Apexigen has partnered with **Simcere Pharmaceutical Group** and **3SBio Inc.** to develop mAbs against VEGF and tumor necrosis factor (TNF) to treat cancer and autoimmune diseases, respectively.

For these first two products, "we wanted to minimize the amount of risk as much as possible so we selected two well-validated targets," Yang noted. He added that "unique binding epitopes and affinity might translate into better efficacy or lower dosing" for the rabbit-derived mAbs compared with marketed VEGF and TNF antibodies.

Epitomics provided an undisclosed amount of seed funding designed to carry Apexigen into 2H11, at which point Yang hopes to have Phase I data for the anti-VEGF mAb in cancer.

Apexigen's deals with Simcere, 3SBio and a third Chinese partner, **Jiangsu T-mab BioPharma Co. Ltd.**, which has Chinese development rights to an undisclosed number of RabMAb programs, also can be traced back to Epitomics. Soon after Epitomics was founded by President and CEO Guo-Liang Yu in 2001, the company established a wholly owned subsidiary in Hangzhou to manufacture its antibody products.

"Once we have shown that we can develop, humanize and manufacture an antibody that is safe in man," the company will be in a much better position to raise capital and attract partners, Yang said.

Yang hopes to pad the company's bottom line by signing one or two service-type deals over the next couple months to use RabMAb to generate mAbs against targets for pharma partners.

"The potential to offer best-in-class antibodies against conventional antigens" will be one draw for partners, but Apexigen's biggest selling point may turn out to be RabMAb's ability to generate mAbs against otherwise inaccessible targets, Yang noted. Glycosylated or chemically modified antigens, G protein-coupled receptors and conformational epitopes are possible examples, he said.

Apexigen's internal pipeline includes humanized mAbs against six undisclosed targets at various stages of preclinical development. "Once we have the capital to move forward quickly we should be able to file an IND here in the U.S. within 12-15 months," Yang said.

COMPANIES AND INSTITUTIONS MENTIONED

Apexigen Inc., Burlingame, Calif.
Epitomics Inc., Burlingame, Calif.
Jiangsu T-mab BioPharma Co. Ltd., Taizhou, China
Loyola University, Chicago, Ill.
Simcere Pharmaceutical Group (NYE:SCR), Nanjing, China
3SBio Inc. (NASDAQ:SSRX), Shenyang, China