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Emerging Company Profile

Kymab: More mAb diversity

By Stephen Hansen
Senior Writer

Kymab Ltd. is developing its Kymouse transgenic mouse platform to generate a greater repertoire of human mAbs than it says can be done with competing technologies. With the **Wellcome Trust** backing the newco, management plans to build an internal therapeutic pipeline and partner the technology on a non-exclusive basis.

The diversity of mAbs generated by a transgenic mouse platform is determined by three key factors, according to Kymab Chairman and CEO Andrew Sandham.

The first is the size of the human gene set used to encode the mAb variable region, which consists of a heavy chain and one of two types of light chains: kappa or lambda.

Second is having a normal population of B cells. Antibodies are initially displayed on the surface of B cells in the mouse, so a reduced or deficient B cell repertoire can limit the variety of mAbs.

The third key to maximizing mAb diversity is to use the mouse constant region to ensure correct signaling within the B cell. Without a mouse constant region, "B cell signaling is deficient and somatic hypermutation is restricted," Sandham said.

Kymab Ltd.

Cambridge, U.K.
Technology: Kymouse transgenic mouse antibody discovery platform
Disease focus: NA
Clinical status: Discovery
Founded: 2009 by Allan Bradley and the Wellcome Trust Sanger Institute
Corporate partners: None
Number of employees: 30
Funds raised: £20 million ($30.1 million)
Investors: The Wellcome Trust
CEO: Andrew Sandham
Patents: None issued

Additionally, the method of inserting transgenes affects the performance of the mouse. According to Sandham, targeted insertion of human transgenes would be expected to create mice that more efficiently respond to antigenic challenge compared with mice created by transgenesis, which inserts multiple copies of transgenes into random loci.

Kymab has incorporated all of these capabilities into its Kymouse platform.

According to Sandham, platforms that came from Medarex Inc., now owned by **Bristol-Myers Squibb Co.**, and Abgenix Inc., now owned by **Amgen Inc.**, do not have the full human gene set for the mAb variable region, use a human constant region, and the B cell repertoire was half the size of a wild-type mouse — each of which limits diversity. They also were created using transgenesis.

Regeneron Pharmaceuticals Inc.'s VelocImmune mouse is the current gold standard for *in vivo* mAb platforms. The mouse was created with targeted insertion of the human genes into the correct loci, a mouse constant region and functional B cell compartment with normal B cell signaling. But according to Regeneron, VelocImmune's human gene set does not include the lambda light chain genes.

VelocImmune is not widely partnered and is expensive to access. Regeneron has granted non-exclusive rights to the VelocImmune mouse to **Astellas Pharma Inc.** for about $18 million annually, and the biotech has a co-development deal with **Sanofi**.

Ablexis LLC is developing a competing AlivaMab mouse, but details of the technology have not been disclosed *(see BioCentury, Jan. 31, 2011)*.

Kymab plans to develop multiple strains

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of Kymouse, each with its own diversity profile. Immunizing multiple strains of mice against a target thus should provide a broader range of mAbs than immunizing a single mouse strain.

The company's first strain will launch by mid-year. The Kymouse HK contains all the human heavy chain and kappa light chain genes.

Next year, Kymab will launch Kymouse HKL, which will contain all human genes for the heavy chain, and the kappa and lambda light chains.

In addition, the company is developing a portfolio of knock-out (KO) and knock-in (KI) strains. Sandham said some human targets have so much homology to the mouse version that the mouse is unable to mount a strong immune response against the target. By removing the mouse homolog, the KO strain is able generate a robust immune response.

The KI strains contain the human pathway of interest, allowing for preclinical testing of the human mAbs generated by the platform.

Kymab also is developing the Kymouse Supra strain, which Sandham said would provide even greater diversity than the HKL strain. He would not disclose details.

The company aims to license the platform to as many researchers as possible on a non-exclusive basis because of Wellcome's philanthropic mission. While Kymab has not disclosed the expected financial structures of such deals, it will non-exclusively license the technology to corporate partners for an annual access fee.

While Kymab doesn't have any specific therapeutic areas of focus, the company plans to build an internal pipeline of mAbs and retain exclusive options to mAbs generated by academics. Sandham said the company will develop most of its mAbs to preclinical or early clinical development and then find a partner, but it would consider taking a mAb to market in an orphan indication.

The company raised £20 million ($30.1 million) in a series A round in July 2010. Sandham said the cash should last through 2014 and allow Kymab to develop all of the mouse strains and select mAb candidates for two or three projects.

While VCs could join future financings, he cautioned that any new investors would need to have a long investment horizon because Wellcome doesn't want to sell the biotech prior to the technology being fully developed and broadly used.

COMPANIES AND INSTITUTIONS MENTIONED

Ablexis LLC, San Francisco, Calif.
Amgen Inc. (NASDAQ:AMGN), Thousand Oaks, Calif.
Astellas Pharma Inc. (Tokyo:4503), Tokyo, Japan
Bristol-Myers Squibb Co. (NYSE:BMY), New York, N.Y.
Kymab Ltd., Cambridge, U.K.
Regeneron Pharmaceuticals Inc. (NASDAQ:REGN), Tarrytown, N.Y.
Sanofi (Euronext:SAN; NYSE:SNY), Paris, France
Wellcome Trust, London, U.K.