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Next-generation animal health vaccines

Angothera marries checkpoint control vaccine technology SnoopVacs with mammalian cell expression system BESTcell to create vaccines for companion animals.

There are many successful examples of treatments that were used in animal health care before being used in humans. Indeed, not soon after the approval of Zoetis' interleukin 31 (IL-31)-targeting antibody Cytopoint (lokivetmab) to treat atopic dermatitis in dogs, Galderma and Chugai Pharmaceutical agreed to co-develop nemolizumab (CIM331), a humanized monoclonal antibody to treat atopic dermatitis and pruritus in hemodialysis patients.

Angothera, an Austrian biotech founded in 2011, is using technologies that were originally devised to solve many of the efficacy and economic challenges of vaccine development to create vaccines for companion animals, such as dogs and cats—a market that was estimated to be worth $2.1 billion in 2015 and that is forecast to grow to $4.5 billion by 2025.

The company is combining a next-generation checkpoint control vaccine technology, SnoopVacs, with a mammalian cell expression system, BESTcell, which is noted for its speed and high yields (**Fig. 1**). This vaccine technology was invented by Geert Mudde and Gottfried Himmler and originally developed and commercialized by S-TARget therapeutics GmbH. In 2014, S-TARget licensed the underlying S-TIR platform to Merck's Allergopharma to develop therapeutic allergy vaccines. This versatile technology can also be used to develop products in other fields, such as oncology, inflammation and infectious diseases. Angothera has an exclusive license for the use of this technology in animal health.

The BESTcell expression system was invented by Emilio Casanova and Anton Bauer and was further developed by The Antibody Lab, a company that is now set to commercialize this powerful expression system. Angothera secured preferred access to BESTcell through a collaboration deal in early 2017.

"Although there is quite some competition in the vaccine field, we believe that our approach can address medical needs other approaches cannot. In combination with the extremely rapid expression and production system, we believe that we have a unique technology set for modern vaccine development," explained Angothera CEO and founder Gottfried Himmler.

No stranger to biotech startups, Himmler was the founding CEO and CSO of antibody technology company F-star Biotechnology. Prior to founding F-star, Himmler developed cancer vaccines and monoclonal antibodies up to clinical phase 2/3 at igeneon GmbH. He is a co-founder of The Antibody Lab and retains strong links with the company as an advisor.

SnoopVacs in action
The SnoopVacs vaccine molecule consists of antigens linked to a species-specific generic section, which directs specific antigens to plasmacytoid dendritic

Figure 1: Schematic showing the creation of animal health vaccines.

cells (pDCs) and B cells through targeting of CD32. This produces large amounts of type 1 helper T (TH1)-cell-inducing cytokines through a specific interaction with Toll-like receptor 9 (TLR9), which acts as an intrinsic adjuvant. The vaccine antigens can be either peptides or recombinant proteins, as both are able to activate antigen-specific T cells and B cells.

Angothera says that this technology has been shown in non-human primates to work effectively with tumor-related antigens and allergens and to have a fast onset of a dose-dependent immune response and extremely high titers.

"SnoopVacs has been shown to break tolerance if necessary and to mount a strong immune response. It can address both the humoral and the cellular side of the immune system. The technology, when combined with the powerful BESTcell expression system, can create a large number of candidate vaccines within a short time frame," explained Himmler.

The underlying S-TIR vaccine technology has been validated by both S-Target's deal with Merck's Allergopharma for allergens and by a commitment from the UK cancer charity Cancer Research UK (CRUK) to fund clinical trials of a vaccine targeting pancreatic cancer that is based on this platform. CRUK and its commercial arm CRT have signed a deal with TYG Oncology Ltd, which had previously licensed the S-TIR platform, to take TYG100, a vaccine that contains gastrin (G17) as the tumor-associated antigen, into clinical trials in patients with advanced solid tumors.

Indeed, in a preclinical trial of the pancreatic cancer vaccine candidate in a non-human primate model, TYG Oncology showed that TYG100 can induce a strong and clinically relevant immune response against gastrin (G17). This response occurred in all treated animals within 2 weeks following a single vaccination.

"Basically, the technology can be applied for classical prophylactic vaccines, such as infectious diseases, as well as more advanced therapeutic vaccine applications, such as allergic diseases and oncology. The technology has been shown to work in non-human primates, [so] we now need to show that it works in various animal species, for example, companion animals such as cats and dogs," added Himmler.

Partnering in animal health
Angothera, which has so far been funded by grants and the company's founders, is looking to partner with animal-health-focused companies to create specific products. Partners are expected to have a clear vision and commitment to developing products, to be willing to make a down payment for access to the technology and to provide milestone-based payments for an FTE cost-based project, with the promise of royalties on sales.

Himmler believes that the company has enough data to sign the first deal. "We want to partner some products with the existing technology early on. This might be via cooperation and license agreements. In parallel, we will further develop the technology base and get selected product candidates towards the market independently from partners," he added.

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