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TRIANNI

Matthias Wabl, *CEO and Chairman, TRIANNI Inc.*

In just a few short years, California-based TRIANNI Inc. has emerged as one of the world's top providers of genetically-engineered mice for the development of antibody-based therapeutics. The TRIANNI mouse, a next-generation antibody discovery and development platform, enables the rapid and reliable isolation of promising therapeutic candidates. Also, contributing to TRIANNI's rapid success is the company's customisable approach to providing cost-effective business agreements tailored to the needs of individual projects, both large and small. TRIANNI CEO Matthias Wabl talks about the TRIANNI mouse™ platform future of drug discovery.

Q: Why are monoclonal antibodies so promising for drug development?

Most therapeutic drugs are small chemicals that while effective against their intended targets, can have poor specificity. Antibodies, on the other hand, are large biological molecules that are highly specific for a particular antigen and bind strongly to their target. So, as a therapeutic, single-target, monoclonal antibodies are almost ideal, with excellent efficacy and safety profiles. With the right platform they are also easy to isolate — the immune system generates a library of billions of different antibodies, each antibody with a unique specificity. For almost any structure, there will be several different antibodies produced. To isolate the antibody-producing cells of interest, we merely need to expose the host to the antigen of interest and then select. So antibodies also offer huge advantages over small chemicals in terms of the efficiency of drug discovery and development.

Q: How are monoclonal antibody therapies developed?

There are various platforms to isolate monoclonal antibodies. What is typically involved is exposing an antigen to an animal, or to an antibody library of bacteriophage, virus or yeast. Then the specific antibody-producing cell is isolated for *in vitro* culturing. Bacterial platforms have the disadvantage of some antibodies so isolated being difficult to scale up for production, while antibodies from yeast platforms scale up well but still lack the mammalian somatic hypermutation mechanism. This mechanism selects better binders from a pool of antigen-specific antibodies. Although the deficiencies of the *in vitro* platforms can be overcome by additional steps, they are time-consuming and do not guarantee an optimal outcome.

Wild type mice can also be used for monoclonal antibody isolation, but the antibodies produced by them are, of course, rejected by humans. By transplanting human antibody genes into the mouse, it is possible to get the mouse to produce human antibodies. Once a specific antibody response has been triggered *in vivo*, the corresponding antibody-producing lymphocytes can be easily isolated from the mouse's spleen and fused *in vitro* with a tumour cell to produce what's called a hybridoma — a monoclonal antibody-producing cell that multiplies indefinitely in the laboratory. But early transgenic mice expressed only a fraction of the normal human antibody diversity. It is only relatively recently that researchers have developed the technology needed to insert very large segments of DNA at the right locations in the mouse genome for this approach to make available the full repertoire of human antibodies. The TRIANNI mouse is one of less than a handful of currently available mouse platforms expressing the full human antibody repertoire.

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Q: What makes the TRIANNI mouse different from other platforms?

Our mission at TRIANNI was to develop a mouse platform that responds to an antigen as efficiently as wild-type mice. In developing the TRIANNI mouse, instead of isolating large sequences of human genes and inserting them into the mouse genome, we computationally constructed loci containing the exons encoding human antibody diversity, while maintaining the native mouse control regions. We made various enhancements to antibody gene segments in order to improve expression and then chemically synthesized these loci and inserted them in place of the corresponding loci in the mouse genome. The result is a chimeric genome that produces fully human antibodies. This approach guarantees very efficient expression of the full human antibody repertoire and at the same time maintains the natural immune response of the wild-type mouse.

Q: Who is the TRIANNI mouse platform for?

We started offering the TRIANNI mouse in 2014, and already have signed agreements with several major pharma clients as well as a number of smaller pharmaceutical / biotech companies. But what's important about TRIANNI is that we want to make it possible for any pharmaceutical / biotech company — be it a global player, a smaller company or even a start-up — to use these mice to develop new, highly-effective biologic therapeutics. TRANNI works closely with discovery partners to define flexible and affordable terms to make sure they can utilize the platform to utmost effectiveness. We have offered our platform from a one-time fee for a perpetual license to an asset by asset deal where upfront payments are minimal and clients pay based on success in milestones and royalties.

Q: What is the future of the TRIANNI mouse and monoclonal antibody therapeutics?

We are about making the best possible mice for developing human monoclonal antibody therapeutics, and both our existing major pharma clients and our own validation studies have provided us data showing how effective these mice are for drug development. But our platform is a dynamic one: we are developing a suite of 'bells and whistles' to make therapeutic antibody discovery even easier and broader. And we have further mice in development, based on the TRIANNI antibody repertoire — for example mice that produce antibodies to epitopes conserved between mice and humans.


The next generation platform for the isolation of fully human monoclonal antibodies:
TRIANNI
Discover why: Trianni.com/discover
TRIANNI is actively seeking to partner with other companies interested in licensing the TRIANNI Platform for the development of their own therapeutic monoclonal antibodies. / Contact us for more information: info@trianni.com.
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