agenusnews

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Designing Cures for Cancers…

…and Innovation across Disciplines

While we are mindful of the current challenges faced by us and the world, and have deliberately slowed down select development programs, we continue to pursue our more advanced clinical development candidates and our in-house research projects with a high level of rigor. This week's Agenus News features our Molecular and Information Science team, led by our expert Dr. Dennis Underwood, and highlights how this team rapidly designs new cancer therapies entering our company's pipeline. Recently, we repurposed some of these capabilities to address the challenges posed by today's pandemic. By fostering creativity among our scientists and bringing together multiple basic and data science disciplines, we have created an in-house discovery capability that sets us apart from our larger peers. **This creativity is exemplified by our agility in mobilizing our pipeline of immune modulating candidates, like balstilimab, QS-21, and our unmodified iNKT cells, for applications beyond cancer including COVID-19.**

An interview with Dennis Underwood, Ph.D., our Head of Molecular and Information Science

Dr. Underwood spent 35 years in the pharmaceutical and biotech industries leading Structural Biology and Molecular Design teams at Merck, DuPont Pharmaceuticals, Bristol Myers Squibb, and Infinity Pharmaceuticals. He founded Praxeon (part of the Google health initiative) and developed social outreach approaches to connect patients with clinical trials for Quintiles. He was trained as an organic chemist at the University of Adelaide in Australia and was a post-doctoral fellow at prestigious labs including Rockefeller, Cornell, Commonwealth Scientific and Industrial Research Organisation (Australia's national science research agency), and Australian National University. Dr. Underwood describes himself as, "a scientist at heart -- excited about drug discovery and development and hungry for new approaches to treat cancer." Across Agenus we share this enthusiasm for developing new therapies to help patients defeat cancer.

Where do you see opportunities to innovate in immuno-oncology drug discovery?

Understanding the function of biological structures, biochemistry, and signaling has been and will be transformative. I worked on the first protein structure developed at Merck in 1985 (human leukocyte elastase) studying the binding of drug candidates and discovering new ways to interact with this enzyme. Using this structure was transformative: it was the first time in Merck's history that chemists and biochemists understood in real-time how the compounds that they worked on fit and inhibited the enzyme. From this point forward, every drug discovery and development program used structural biology to help guide their efforts, including developing many new drugs for HIV and heart disease. **I believe that we are at the same transformative moment in I-O and immunology – understanding structural function, biochemistry and signaling will open up creative new opportunities for therapies, new technologies for improved discovery, and increase the rate of new discoveries.**

Why did you choose to work at Agenus?

What attracted me to Agenus was the quality of the people and the freedom to "think big." We have

integrated multiple Agenus teams including: molecular biology, biochemistry, bioinformatics, data visualization, and information technology. My teams have a highly collaborative culture and each member understands that they bring unique and essential experience to the table. They are spread across all 3 Agenus sites which nucleates a dynamic cross-site interaction that is an essential feature of the Agen(T)us research culture.

Harboring and breeding innovation is not just about coming up with great ideas – it's about creating an environment and culture to allow this to occur. Agenus is unique in how it enables and empowers creativity and innovation through a strong mentorship infrastructure where scientists are encouraged to show their creativity – this is rare to see in biotech. Not allowing scientists to think broadly and to "think big" results in top-down organizations that are "brittle," not adaptable, and slow. **At Agenus, teams are given the freedom to run how they see best and bring out the best in people which means everyone becomes an innovator.**

How do you and your team drive forward drug discovery at Agenus?

My team works on every antibody discovery and development program at Agenus and has been instrumental in the development of our bispecific antibody programs, such as AGEN1223 and AGEN1777. Our approach is to apply cutting-edge technologies such as epitope mapping, structural biology, biochemistry, affinity maturation, to both identifying and optimizing antibody candidates.

We were the first in the industry to recognize that there is an exciting class of new targets important in immune recognition of cancer – these were the phosphopeptide tumor targets or "PTTs." We developed a group at the cutting edge of a technology known as ligandomics (mapping disease targets on cells) to industrialize the process of identifying these targets. The result is the identification of thousands of tumor-associated antigens from cancer patient tissues --dozens of which are potential tumor-specific targets to use for developing immunotherapies. These PTTs, for example, are the basis of new, first-in-class T-cell receptor discovery programs at AgenTus.

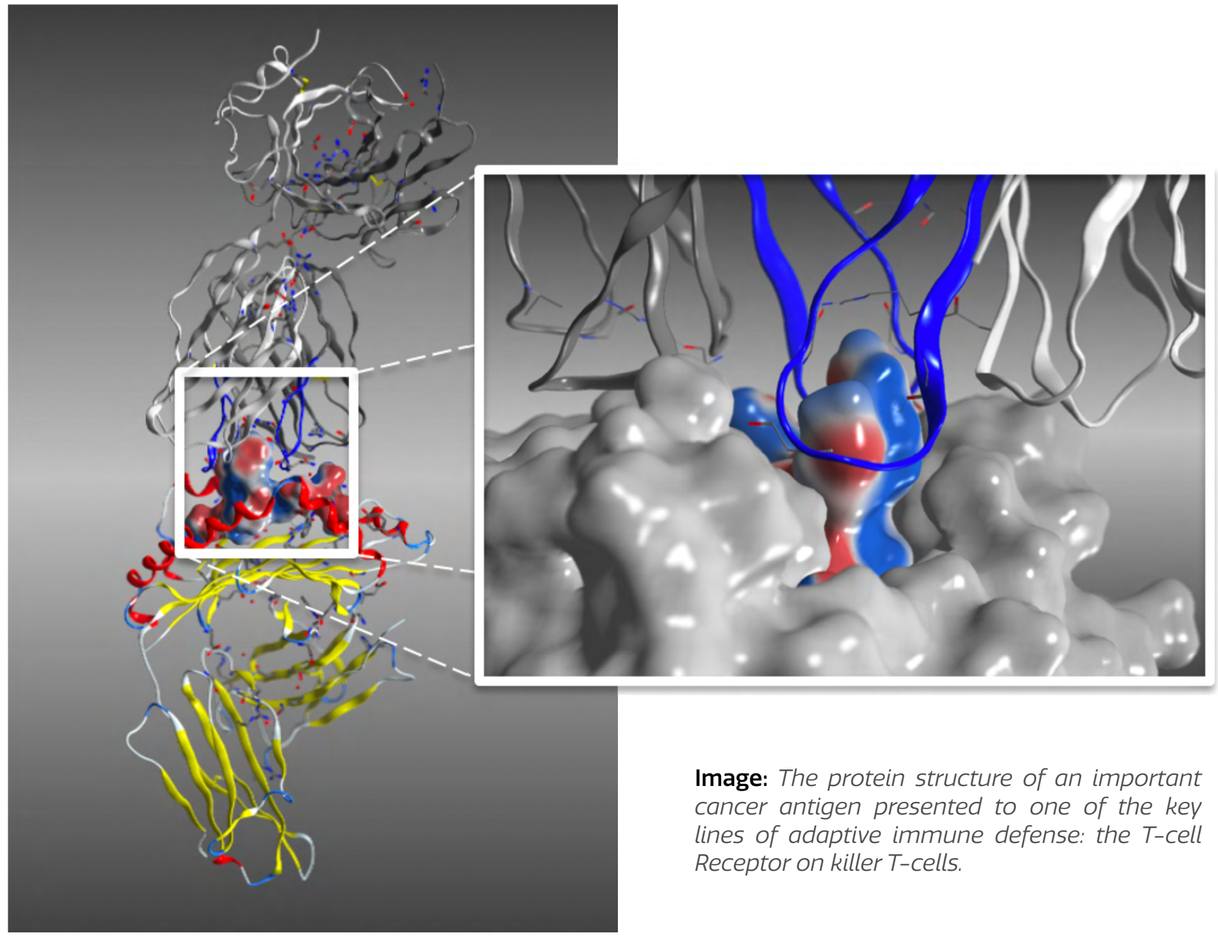

Image: *The protein structure of an important cancer antigen presented to one of the key lines of adaptive immune defense: the T-cell Receptor on killer T-cells.*