Transforming the PRACTICE OF MEDICINE

John Cox, CEO of Repertoire Immune Medicines — a clinical-stage immuno-therapy company — talks about unleashing the curative powers of the immune system to prevent and cure cancer, autoimmune, and infectious diseases.


John Cox

PV: Repertoire Therapeutics was launched late last year, tell us about its genesis.

COX: Our journey began when scientists in Flagship Labs asked themselves a simple question: "What if we could decode the molecular signatures our T-cells respond to every day, and deploy these codes as medicines to prevent and cure disease?" Another Flagship company was asking the question: "What if we could use a person's own T-cells to harness potent cytokines and deliver them to diseased tissues?" Flagship applied its proprietary methodology — hypothesis development, testing, and iteration — to explore these questions, Repertoire Immune Medicines was born.

PV: Repertoire is focused on developing a roadmap from codes to cure, please talk about this mission?

COX: Repertoire is an immune medicines company. There are many companies that are targeting immuno-oncology, and we are as well. But our unique decoding capabilities coupled with our platform puts us in a position to design medicines for areas outside of immuno-oncology.

An example would be infectious diseases. With our technology we can identify the T-cells in a patient who has recovered from an infectious disease. From that we can decode the specific peptides from that virus that would be most reactive to create a set of clones to protect the patient. The long-term, bigger, bolder goal is to understand the T-cell repertoire and support patients with immune medicines based on a person's own natural immune security.

PV: How does the company's name Repertoire reflect the company's mission?

COX: Over the last 20, 30, or actually 40 years much of the research in the biotech industry has tended to focus on B-cells for the production of monoclonal antibody medicines. Immunologists know that we all have literally billions of T-cells, which represent millions of different clones. And each T-cell is unique. Those T-cell clones function as immune surveillance, surveying the body for foreign antigens. That repertoire of T-cells is what provides immune protection. Over time, a person's repertoire of T-cells can change or deteriorate and the level of protection, or ability to fend off cancer or a virus, can be affected.

The complex and elegant code that T-cells, antigen presenting cells, and peptides form and use to create an immune synapse is brilliant. We're in a position to understand this system and to decode it. From that decoding, our belief, is that we can define optimized medicines based on what the immune system tells us is working to protect itself against foreign agents or antigens. This could be an infectious disease, an autoimmune disease, or cancer.

PV: What's your vision for the organization?

COX: Our mission is to develop medicines that are highly rational, highly specific to a person's disease, and that ultimately lead to protection from disease and/or curative solutions. Our immune system protects us and cures us all the time — defending us against cancer mutations for example. Understanding how this works and then defining medicines from that information leads us to believe we can set up a new category of medicines, which we're calling immune medicines.

We have a number of objectives in terms of the platforms we have. Some of this is defining large data sets of what we call antigen TCR pairs. In other words, defining the repertoire. We are also applying the technologies to a clinical trial. We are currently in Phase I/II clinical trial testing for our first generation PRIME IL-15 alone or in combination with Merck's Keytruda. We are also developing PRIME IL-12 and PRIME TLR to target both adaptive and innate immunity, to amplify the immune response for durability and memory. Our next wave of products in immuno-oncology aspire to use cancer antigens selected through our platforms as most likely to activate a person's own T-cells, and then attached to potent immune modulators. We have active discovery programs in autoimmunity and infectious diseases. The strategy in our type I diabetes (T1D) program is to identify novel antigens relevant for initiation and progression of the disease, as well as the specific T-cell clones responding to those antigens. PV

T-Cells: Understanding Curative Potential

At the center of the immune system is a legion of T-cells working to safeguard our health by detecting and acting on danger signals — be those invader pathogens, incipient tumors, or other threats arising either outside or within our bodies. This "immune security system" lexicon comprises some 20 million different, specific groups of T-cells. Each group — or clonotype — is defined by its own unique T-cell receptor (TCR) sequence, and each TCR sequence in turn recognizes a limited set of corresponding target antigens.

Evolved over millions of years, the extraordinary diversity intrinsic to this system shields our bodies against the vast majority of attacks and quickly neutralizes them, with the probability of any one attack breaching the system being exceptionally low. In other words, T-cells are far more effective in preventing and curing disease than any man-made medicine has ever been.

Repertoire Immune Medicines is decoding the universe of TCR-antigen codes that drive health and disease, which represents one of the greatest opportunities for innovation in medical science.

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