nature research
custom media

[insideview]

HIGH THROUGHPUT TECHNOLOGY DRIVES DEVELOPMENTS IN PERSONALIZED CANCER IMMUNO-THERAPIES

A conversation with **MARVIN GEE**, Co-Founder and Head of Target Discovery at 3T Biosciences

Developing effective cancer immunotherapies for solid tumors can be extremely challenging, primarily because they have physical barriers the immune response must overcome. 3T Biosciences identifies novel targets of T cell receptors for personalized therapy that enable immune responses to penetrate solid tumors and kill cancer cells. Using a high throughput platform with more than 100 billion different targets, 3T Biosciences quickly and comprehensively identifies novel targets relevant for developing cell therapies. These novel targets include neoantigen peptides, which are derived from tumor-specific mutations, as well as self-antigens and various other targets that produce effective immune responses. Marvin Gee, co-Founder of 3T Biosciences, describes how their platform facilitates the development of safer, more effective cancer therapies for solid tumors.

What are the current challenges in developing cancer immunotherapies?

A lot of the focus now is on how we tackle some of the more severe cancer types, like solid tumors that have difficult biology to overcome. Compared to blood cancers, solid tumors have a physical barrier. In a natural immune response, even if you generate T cells to a solid tumor, they often won't penetrate into the tissue to begin killing the cancer cells.

One of the major challenges with cell therapies, in which live cells are transplanted into patients to help treat their cancers, is identifying novel targets on the surface of tumor cells that can be accessible for large patient populations. These targets come in multiple flavors, including neoantigens, which are peptides derived from mutations specific to tumors, as well as self-antigens, which are overexpressed in the tumor. Our goal is to identify novel targets of all types that can generate strong immune responses and are shared across patient populations.

Another compounding difficulty is accessing reliable materials. Because immune responses are very specific, it's important to use high-quality peptides so you can feel confident that the targets you identify for cell therapies can elicit an immune response. We work with GenScript to synthesize thousands of high-quality peptides, including neoantigens, for our assays.

How are you addressing these challenges?

Most companies and academics rely on technologies such as mass spectrometry, which are limited to a small set of targets. As a result, it's very challenging to capture the entire repertoire of targets on a cancer cell and it's often unclear whether those targets can elicit an immune response, which is the end goal of therapy. In contrast, we take samples from patients that are responding to therapy, so we know they're having productive T cell responses. We developed a platform that displays more than 100 billion targets on yeast, so we can somewhat mimic a natural cell in the body. By using a high throughput platform, we can quickly and comprehensively identify all the potential targets that a T cell receptor recognizes. Then we can hone in on particular targets that would be relevant for developing therapies.

Why is it important to identify all potential targets of a T cell receptor?

While T cell receptors can recognize targets very sensitively and specifically, they can also recognize multiple targets. Several years ago, there was a famous clinical trial where people engineered a T cell receptor to be more potent. While doing this, they inadvertently introduced an off target cross reactivity where the receptor recognized another target derived from a heart protein in the patients. Both patients ended up dying of cardiac failure. Such off-target reactivities cannot be detected with conventional methods. With our platform, we can comprehensively predict both T cell receptor specificity and off target cross reactivity. Because neoantigens are only expressed in tumors, cross-reactivity is limited in those targets. This information enables us to engineer more potent and more specific T cell receptors, which is a huge advantage from a safety perspective. As with any high potency therapy in oncology, safety is the number one priority, but also knowing that information well ahead of going into the clinic can save patient lives as well as significant amounts of time and research dollars.

How does this platform help with therapy development?

We're in an era of personalized medicine where targets can be very specific to a single patient. A good case study of this is with neoantigens. When therapies are developed against neoantigens they become extremely personalized, but also significantly more expensive to generate. Whereas, our fundamental hypothesis is that we can find shared immune responses from several patient populations against the same target. This approach allows us to develop a cell therapy that can be beneficial for multiple patients.

What's next?

Our goal is to deliver safe and effective therapies for patients. We've set up collaborations with academics and other partners to get these very precious samples from patients that respond to therapy. Being able to look at these samples and identify targets opens the door for developing T cell receptor therapies to treat not only these patients, who often have very debilitating diseases, but also other patient populations. Ultimately, I hope we can be in the clinic, helping patients who, at the moment, have very limited options for treatment.

GenScript
Make Research Easy

SPRINGER NATURE