Rapid Novor, Inc

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Deep dive into immunity: decode with proteogenomics

Immunological investigator, Rapid Novor, is decoding the immune response by sequencing and quantifying the antibody repertoire to provide in-depth profiling to develop personalized medicine and patient-specific treatment options.

Understanding how the immune system responds is a vital step in developing new therapeutics and diagnostics, and towards knowing more about the natural history of disease. Rapid Novor is developing new approaches to decoding the immune response, providing unprecedented insights to researchers.

In the six years since its spinoff from the University of Waterloo in Ontario, Canada, Rapid Novor has helped hundreds of researchers around the world reduce their target product variability, enable the engineering of therapeutic candidates, recover lost cell lines, and secure antibody supply chains with the help of protein sequencing. In July 2020, Rapid Novor received \$5 million in Series A funding to scale its research solutions by building a state-of-the-art facility, while expanding its team and tripling laboratory space.

Home to Canada's largest privately funded mass spectrometry proteomics facility, Rapid Novor is leading the way for immunological investigation. Its newest service, Novorlg, will help researchers to decode the immune response at specific time points by sequencing and quantifying the antibody repertoire.

Meeting the challenge of immune profiling

The conventional approach to profiling the immune response involves the isolation and sequencing of the mRNA of B cell receptors in peripheral blood using next-generation sequencing (NGS). This approach, however, is restricted to circulating B cells. It misses the majority of antibody-producing B cells, which are found in the connective tissue, lymph nodes and spleen. The presence of non-antibody-producing or naïve B cells can also affect the analysis. As a result, NGS profiling does not necessarily represent the humoral immune response and further screening is needed to capture functionally relevant antibodies.

Rapid Novor's core technology, REmAb, uses mass spectrometry to sequence the amino acids in antibodies, without the need to have access to

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Mingjie Xie, CEO Rapid Novor



Fig. 1] The NovorIg platform. The platform combines proteomic and genomic approaches to profiling the immune response.

the cell line, or knowledge of the genomics. This approach can provide a full-coverage sequence in just 36 hours, compared with traditional protein sequencing methods that can take up to 6 months.

Rapid Novor's aim for Novorlg is to create an immunological investigation service that combines proteomics and bioinformatics data with large scale NGS genomics data, analysed by the company's proprietary Big Data algorithms. By taking specific antibody protein sequences and tracking their relative abundance over time in the sample using mass spectrometry, Novorlg will allow the creation of a broader and more accurate immune profile, including time-specific details of the antibody repertoire composition (Fig. 1).

"While the importance of antibodies in immunity is well understood, there is currently no other technology available to directly sequence and profile antibody proteins from blood. Our technology fills this void by making direct decoding of the antibody-mediated immune response a reality," said Mingjie Xie, Rapid Novor's CEO.

Immune profiling: applications and needs

From a clinical perspective, an antibody profile provides an insight into health, and into the progression of disease or response to treatment. For example, in the blood cancer multiple myeloma, the levels of an abnormal antibody, known as the M-protein, indicate disease progression. As multiple myeloma is notorious for having a high relapse rate, continual monitoring of this biomarker is required. Immune profiling can detect increases in the pathological antibodies from blood sooner and with greater sensitivity than other bloodbased methods such as immunofixation, which

could allow treatment to be resumed earlier. This could improve patient outcomes. As the profiling requires only blood samples, it is less invasive than the methods based on bone marrow sampling. Rapid Novor is developing EasyM, a multiple myeloma blood test that will monitor residual disease and can detect relapse six to eight months earlier than existing methods.

Immune profiling is useful in the development of therapeutic antibodies, helping researchers to recognise functional antibodies with therapeutic value more quickly than traditional approaches. A current example of this is the identification of antibodies to SARS-CoV-2, the virus behind the COVID-19 pandemic. By sequencing the antibody proteins directly from the blood of convalescent COVID-19 patients combined with B cell sequencing, Rapid Novor was able to identify potential therapeutic antibodies. Immune profiling can also indicate the immune response to vaccination, and help to guide future vaccine development.

As the Novorlg technology has the adaptability to support diverse research applications and needs, Rapid Novor is working with a number of companies carrying out clinical trials. These clinical trials are benefitting from data-backed insights provided by Rapid Novor for the creation of personalized medicine and establishment of patient-specific treatment options.

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