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#### Summary:

Triple-negative breast cancer (TNBC) is a particularly aggressive type of breast cancer. TNBC does not have the three receptor types commonly present in breast cancer cells. This means that the most common drugs used to treat breast cancer are not effective. The lack of targeted treatments for TNBC makes the disease much more likely to spread and recur. There is an urgent need to develop new, effective therapies for this type of breast cancer. Previous research has shown that TNBC tumors have a high level of a protein normally found on nerve cells in the brain called NMDA receptors. Some patients, including patients with breast cancer, naturally develop antibodies that target NMDA receptors. In these patients, these anti-NMDA receptor antibodies can kill cancer cells. However, in some patients, the antibodies can cause inflammation in the brain, known as encephalitis. Symptoms of encephalitis can include changes in mood, hallucinations, memory loss and seizures.

The goal of Dr. Kleeman's project is to create a safe and effective treatment for TNBC by finding antibodies that can target NMDA receptors on cancer cells without causing damage to the nervous system. The project involves several steps. First, Dr. Kleeman will make a mouse model of TNBC with NMDA receptors on the surface of cancer cells. Then, he will use this mouse model to find antibodies that can bind to NMDA receptors. Cryogenic electron microscopy (cryo-EM) is a type of electron microscopy that can be used to obtain images of proteins. Dr. Kleeman will use cryo-EM to study how the mouse antibodies bind to NMDA receptors. The idea is to find antibodies that bind to NMDA receptors without causing changes to the NMDA receptor structure that could result in encephalitis. Finally, he will use the new antibodies to treat mice with TNBC and to determine if they should potentially be tested in patients with TNBC. Overall, Dr. Kleeman's project hopes to show that anti-NMDA receptor antibodies can be used as a new treatment for the 40,000 patients diagnosed with TNBC in the USA every year.

#### Biography:

Dr. Kleeman received his undergraduate degree from the University of Cambridge, UK and his MD from the University of Oxford, UK. Subsequently, he completed a two-year internal medicine internship in the National Health Service, UK. He started his PhD studies at Cold Spring Harbor Laboratory, NY in August 2020, in the laboratories of Dr. Tobias Janowitz and Dr. Hiro Furukawa. His research is focused on the study of immune responses against NMDA receptors and their application to the treatment of triple-negative breast cancer.