GeNeuro: Pioneering a Promising New Tack in MS Research

GeNeuro is an emerging Swiss biotech company that has identified a completely novel therapeutic target in MS and is developing an innovative approach to treating the disease. Its scientists are using samples from the ACP Repository to help test responses to the specific target antigen,\(^1\) while intending to bring a new drug to market. Their drug is aimed at blocking a suspected source of the inflammatory and neurodegenerative components of the disease, rather than targeting the immune response of the body, as most current treatments do. By neutralizing the suspected source – known as the multiple sclerosis retrovirus (MSRV)-Env protein -- rather than by targeting the patient's immune system, the drug that GeNeuro is developing could prove to be both safe and effective, and potentially able to slow or even halt the progression of the disease in all its forms.

The innovators at GeNeuro are not new to the game. In fact, their approach is the result of 25 years of research before they created the company in Geneva, Switzerland in 2006. Through research, they discovered and gained an understanding of the MSRV-Env protein, which they now regard as a possible cause of the inflammation and neurodegeneration that characterizes the disease. So what is the MSRV-Env protein, how does it function and how might GeNeuro’s drug candidate stop it in its tracks?

Let’s begin by understanding what a retrovirus is. Most people are familiar with the human immunodeficiency virus (HIV), which causes AIDS. HIV is a retrovirus, a type of virus that incorporates itself into the genetic material of the person it infects. It’s also exogenous, meaning that it originates outside of the person rather than being part of the person's original genome. Once the retrovirus enters a cell, it integrates itself into the person’s genome. The HIV virus is subsequently copied by the cell’s genetic processes, and these copies go on to infect and destroy other cells within the body’s immune system, lowering the ability of the immune system to fight disease.

\(^1\) An antigen is any substance that causes an immune system to produce antibodies against it.
Many types of retroviruses have become incorporated into the human genome over time and are known as human endogenous retroviruses (HERVs). These are the result of “ancient” exogenous retroviruses that integrated themselves into the genomes of humans and our primate ancestors over the millennia of evolution. Most have since accumulated mutations that have rendered them unable to produce infectious, exogenous viruses. Until recently, many scientists considered HERVs a type of ancestral “junk” DNA and thought they served no function. However, in recent years we have come to understand that in some people with a particular genetic makeup, these ancestral genetic insertions in the human genome can be activated by external environmental factors, such as viruses.

In the 1990’s, an endogenous retrovirus was discovered in the cells of an MS patient. It became known as the MS retrovirus or MSRV. Years of research and numerous scientific studies by GeNeuro and academic groups, established an association between a specific protein (Env) that is made by MSRV, and MS. We now know that there is an extremely high prevalence of MSRV-Env in the blood and brain lesions of many MS patients when compared to controls. Moreover, its presence correlates with the clinical progression, severity and prognosis of the disease, as reported by several independent laboratories.

The presence of MSRV-Env in people with MS may be an important cause of the inflammation and neurodegeneration that characterizes the disease. In all likelihood, it exists in a dormant state until the host (the human being) is exposed to an external threat such as Epstein-Barr or other Herpes viruses. That exposure activates MSRV-Env synthesis, which in turn triggers a response from the host’s innate immune system via a receptor on the immune cells that is called the toll-like receptor-4 (TLR-4). As you may recall from previous articles we’ve published, the small proteins which regulate the body’s immune system, known as cytokines, send signals that lead to inflammation and myelin damage, while simultaneously decreasing the body’s capacity to repair damaged myelin.

GeNeuro has used samples from the ACP Repository to validate their previous data on the frequency of MSRV-Env and to investigate its presence in people with different forms of MS and in different geographic locations. A future project will use ACP samples to help GeNeuro validate a bioassay to be used on clinical samples to determine MSRV-Env levels in response to their drug.

Given almost any substance, it is possible to make monoclonal antibodies (organic substances to fight disease that are created in laboratories by cloning single cells) that detect the substance, bind to it and neutralize it. They are designed and produced through genetic

---

2 Receptors are cell surface molecules that receive chemical-signals from outside a cell.
3 A bioassay is a type of scientific experiment that involves the use of live animal, plant, tissue or cell to determine the biological activity of a substance, such as a drug. Bioassays are typically conducted to measure the effects of a drug on a living organism and are essential in the development of new drugs.
engineering, and hence their creation has become an important tool in biochemistry, molecular biology, and medicine. GeNeuro has strong expertise in the development of monoclonal antibodies. The company has generated a humanized monoclonal antibody, GNbAC1, that targets the MSRV-Env protein. As described previously, it acts in the early stages of the inflammatory process, representing a potentially new and well-tolerated treatment for MS, without targeting the immune system itself. With a good safety profile and a new mechanism of action, the treatment may have a therapeutic effect on both relapsing-remitting and progressive forms of MS. GNbAC1 is currently in Phase IIb clinical development and we look forward to keeping you posted on its progress in the pages of this newsletter.