Dear Friends,

Continuing our trend of reporting on exciting current MS research, this month we introduce you to one of our most active partners, Swiss biotech company GeNeuron, that is using samples from the ACP Repository to test new theories about causes and treatments for both relapsing and progressive forms of the disease.

Then, we present the second in our new series of monthly articles by MS researcher, Farren Briggs, who teaches and conducts research in his lab at Case Western Reserve University. This month’s article, *Vitamin D - Food for Body and Mind?*, looks at recent studies and published articles to draw learnings about the impact of vitamin D on people with MS.

Finally, we want to thank pharmaceutical company, Biogen, for renewing their support of this newsletter for another year. Thanks, Biogen!

**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 antigen¹, 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.

¹ An antigen is any substance that causes an immune system to produce antibodies against it.
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.

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,

2 Receptors are cell surface molecules that receive chemical-signals from outside a cell.
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 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.

**Vitamin D – food for body and mind?**

By Farren Briggs PhD, ScM

A quick search of PubMed (a US government-funded free resource that catalogues over 26 million citations including most, if not all, scientific, biomedical and health publications) for publications including “vitamin D” and “multiple sclerosis” results in 754 scientific articles and reviews between 2010 and 2016. That’s an average of 2.4 new publications per week! And so far 2017 is on track with 45 publications as of April 23rd. Thus, there is always something to read on vitamin D, for those of us invested in MS. But this month, two publications caught my attention – one on the body, the other on the mind.

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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.

Dr. Susanne Hempel and her team published a comprehensive systematic review of randomized controlled trials (RCTs) investigating the impact of modifiable factors (including smoking, exercise, and diet) on MS progression in *Multiple Sclerosis Journal*. The goal of a systematic review is to average the results of previous studies, acknowledging the differences and similarities of the individual studies. In this systematic review of English-language publications, six RCTs investigating vitamin D supplementation and change in the Expanded Disability Status Scale (EDSS) were considered. EDSS is a scale commonly used to summarize total disability in people with MS. It is based on a neurological examination, and multiple functional systems are assessed. Based on the examination, a score from zero to ten is assigned (with zero representing a “normal” neurological exam). However this scale heavily favors walking ability – thus, most interpret EDSS values as a measure of physical disability as opposed to a measure of the person’s overall well-being. Of the six RCTs, five studies randomized people with MS to receive a high dose of vitamin D supplementation versus a placebo and one study compared a high dose to a low dose of vitamin D supplementation. Thus, an average for the five more similar RCTs was generated. There appears to be a slight trend for better EDSS outcomes over the time intervals of the studies, which ranged from six months to two years. On average, persons with MS who were randomized to receive vitamin D supplementation had a 0.22 lower EDSS score compared to those who were assigned a placebo. Thus, the therapeutic potential of vitamin D supplementation for improving EDSS scores appears modest.

In *Scientific Reports*, Dr. Hala Darwish and her team, published on the impact of vitamin D supplementation on cognition. The study compared the cognitive performance in two groups: 39 persons with MS who were vitamin D deficient to 44 persons with MS who had sufficient levels of vitamin D in their serum. At the beginning of the study, all participants complete a slew of cognitive tests covering short and long term memory, language, learning, attention, recognition and mental flexibility - and the deficient group performed significantly lower than the sufficient group at baseline. The study was only three months long, and during that time the vitamin D deficient group was provided a high dose of vitamin D supplementation while the sufficient group received normal care. At the end of the three months, 22 participants had dropped out. However there were still 31 individuals who were in the original deficient group – their serum levels of vitamin D significantly increased after supplementation – and there were 30 individuals in the original sufficient group. Most interestingly, after this short course of vitamin D supplementation, their memory (long term and visuo-spatial) significantly improved. When considering all participants, higher serum levels of vitamin D predicted better performance on the memory tests over this short 3-month period. Dr. Darwish and her team are currently expanding the number of participants in their study and will be following them for at least a year – I am intrigued, and look forward to their next publication.

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7 [https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5379671/](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5379671/)
So what does this all mean? Well, vitamin D seems to do a body and mind good. However, the findings from Dr. Darwish’s study suggest the memory of those deficient in vitamin D may benefit more from vitamin D supplementation.

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