

Hello,

My name is Arnaud Germain and this video is a preview of our latest results on ME/CFS blood proteomics.

But first of all, what is this disease?

ME/CFS stands both for Myalgic Encephalomyelitis and Chronic Fatigue Syndrome. Myalgic Encephalomyelitis is a complicated name that tries to incorporate the many symptoms ME/CFS patients endure, which include muscle pain as well as the inflammation of the brain and spinal cord.

Although the disease causes many problems, the hallmark symptom of ME/CFS is post-exertional malaise, which means that patients become extremely exhausted for days or weeks from simple tasks such as showering or going out for grocery shopping. For comparison, healthy but sedentary subjects pushing their limits by trying to run an Iron Man triathlon would take a few days to recover from that effort and would feel better for it in the end.

But that is not all, other symptoms include unrefreshing sleep, brain fog, sensitivity to light, gastrointestinal problems, a dysregulated immune response, joint pain and more, resulting in intense exhaustion of ME/CFS patients enduring a combination or all of those crushing symptoms.

In this study, we investigated the abundance of proteins in the blood and obtained data for almost 4,800 proteins. Some of them are very abundant such as hemoglobin, which is the red substance that distributes the oxygen throughout our bodies. The majority of the other proteins are very scarce. Some of these proteins have functions as simple as delivering a message from one part of the body to another. For comparison an order of magnitude of 7 is the difference between the biggest mammal, the blue whale which weighs 180 million grams, and the 2 grams of the smallest mammal, the bumblebee bat. The same order of magnitude difference exists between the most and least abundant blood proteins.

For this pilot study we enrolled 40 women, equally divided between ME/CFS patients and controls.

When we performed a pathway analysis, we found evidence for a disrupted ephrin-Eph signaling pathway, which involves proteins that can recognize each other and allow the transfer of messages from one cell to the next.

Cell to cell communication is crucial to body homeostasis and exists in living organisms since the beginning of time to sense environmental cues, and is even more crucial and complex for multicellular organisms such as humans where the activity of the 40 trillion cells that compose us need to be coordinated.

The ephrin-Eph signaling pathway is no exception and is present throughout the tree of life. During our life, it is central for our development, our physiology and disease regulation. For example, the first stages of development require controlled organ formation, regulated brain and nervous system growth, the establishment of our immune system, supervised vascular system expansion and managed bone formation.

Later, this same pathway is crucial for cell to cell signaling, coordinated immune response, the plasticity of the brain, cell migration, regulated insulin secretion to control blood sugar content as well as properly maintaining stem cell pools throughout our body.

Failures in this pathway have been linked to tumor growth and neurological disorders.

Our study suggests that the ephrin-Eph pathway is imbalanced. If this is true, we can readily appreciate how, in ME/CFS patients an imbalanced ephrin-Eph signaling pathway would lead to a wide array of symptoms affecting all aspects of the body's physiology, including muscles, brain, the immune system, the digestive system and more.

Our results also bring hope for the development of diagnostics, potentially using ratio values from proteins functioning in recognized biological functions. For instance, in our cohort, the ratio of ephrin A5 and the cystic fibrosis transmembrane conductor regulator protein (CFTR) can discriminate controls from patients, with high confidence, shown in red, close to 100% accuracy. Both proteins have proven roles in sugar sensing by the brain.

Please take time to browse our open access manuscript for additional details. Also, feel free to reach out to our team with comments and offers to collaborate in helping the ME/CFS community better understand this perplexing disease that is silently destroying millions of lives throughout the world.