John M. Potter

Technical Writing HQ – Capstone Project

Medical Writing

Half the Puzzle? The SP140 gene appears to be implicated in both Crohn's Disease and Multiple Sclerosis

Although widely different diseases, patients with Crohn's Disease and Multiple Sclerosis appear to be contending with similar immune system dysfunctionality. Medical researchers now believe a common gene may be partly responsible for this dysfunction.

SP140 and Crohn's Disease

Last year, Crohn's Disease researchers who began examining patterns of gene co-expression found a network of 41 genes that were co-expressed across the terminal ileum and colon in Crohn's Disease and Ulcerative Colitis patients. They discovered that these gene co-expressions highlight possible novel interactions between a subset of risk genes such as SP140 and PTPRC (Inflammatory Bowel Diseases, 2016).

They also discovered that the SP140 gene suppresses innate immunity within a subset of Crohn's Disease patients.

Because the SP140 gene is an epigenetic "reader," it recognizes changes which occur within gene-regulating DNA proteins. Moreover, the gene is crucial for ensuring that infection-fighting macrophages work correctly.

Genetic profiling reveals that a subset of Crohn's Disease patients exhibit SP140s that produce defective SP140 messenger RNA splicing and diminished SP140 protein levels. As a result, antibody-producing B Cells that contain such SP140s struggle to produce additional SP140s.

Because these B Cells lack adequate SP140s, researchers believe proper macrophage activation may be compromised. Moreover, these SP140-deficient individuals display suppressed innate immune gene signatures, a genetic anomaly that sets them apart from other Crohn's Disease patients.

SP140 and Multiple Sclerosis

Medical researchers believe a diminished SP140 gene presence plays a role in the pathogenesis of Multiple Sclerosis (MS) as well.

In MS patients, the SP140 protein exhibits several gene variants that exist in a strong, non-random association with each other. These variant genes fail to express the full-length RNA isoform (ScienceDirect, 2021) of protein SP140, producing an isoform lacking exon 7, which is a segment of DNA coding for SP140.

Unfortunately, "the ultimate effect of the exon-skipping seems to be the reduction of the SP140 protein" (Human Molecular Genetics, 2015).

These findings suggest that the failure to create normal SP140s hobbles the immune system of MS patients. Like Crohn's Disease patients, MS patient's innate immunity may be limited by an inability to activate macrophages properly.

The Other Half of the Puzzle

A genetic immune anomaly is typically inconsequential until a pathogen learns how to exploit it. Medical researchers are reviewing whether a bacterium called Mycobacterium avium subspecies paratuberculosis (MAP) has taken that route.

Medical researchers recognize MAP as a multi-host mycobacterial pathogen that can initiate and maintain systemic infection and chronic inflammation in cattle. The livestock industry refers to this malady as Johne's Disease.

Several researchers suspect that MAP causes similar symptoms in humans, most notably Crohn's Disease.

The bacterium is not only ubiquitous and resilient, it can shed its cell wall and incorporate itself into infection-fighting macrophages. Researchers believe these infection-fighting macrophages could theoretically become a target of the immune system. If so, this hypothesis would explain why Crohn's Disease symptoms appear autoimmune in nature.

Given the SP140 gene's significance in fighting infection, it's not surprising to learn that a pathogenic bacterium such as MAP might be implicated in both diseases.