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A PROTEOMIC SIGNATURE OF FATIGUE IN PRIMARY SJÖGREN'S SYNDROME

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Background: Fatigue is a frequent and often disabling phenomenon in patients with chronic inflammatory and immunological diseases, neurodegenerative diseases, and cancer. The underlying biological mechanisms of fatigue are largely unknown and hypotheses are conflicting. It is important to uncover the pathophysiology and identify signalling pathways that generate and regulate this substantial phenomenon.

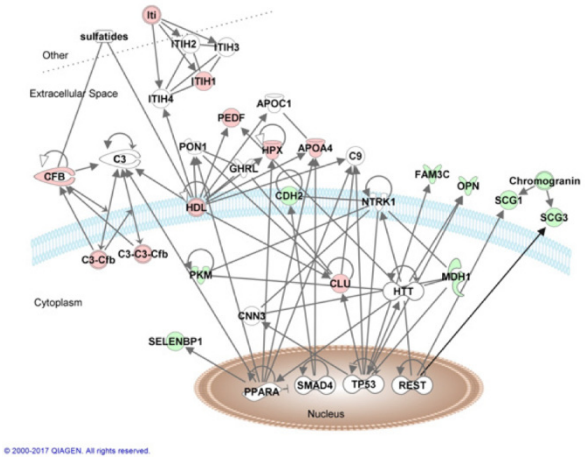
Objectives: Based on the hypothesis that fatigue originates from cerebral processes, we investigated whether relevant proteins and/or signaling pathways for fatigue could be revealed in the cerebrospinal fluid (CSF) of patients with primary Sjögren's syndrome.

Methods: Label-free shotgun mass spectrometry was performed to analyze the CSF proteome of 20 patients with primary Sjögren's syndrome. Fatigue was measured with the fatigue Visual Analogue Scale (fVAS).

Results: After depletion of high-abundance proteins, more than 800 proteins were identified and quantitated. Multivariate analyses showed that patients with low and high fatigue could be separated based on their CSF protein profiles, and 15 proteins were selected as top discriminatory proteins. Among these were apolipoprotein A4, hemopexin, pigment epithelium derived factor, secretogranin-1, secretogranin-3, selenium-binding protein 1, and complement factor B.

The figure shows the top network from Ingenuity Pathway Analysis (IPA) with 14 of the differentially expressed proteins (red = upregulated, green = downregulated) and proteins that are directly associated to them (white molecules).

Image/graph:



Conclusions: Most of the discriminatory proteins have important roles in regulation of innate immunity, cellular stress defense, and/or functions in the central nervous system. Some have been associated with severe depression and loss of appetite, which are important features of chronic fatigue. These proteins and their interacting protein networks may therefore have central roles in the generation and regulation of fatigue, and the findings add new, relevant, and important evidence to the concept of fatigue as a biological phenomenon signaled through specific molecular pathways.

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Disclosure of Interest: None declared