ME-CFS24-004 - The impact of mast cell activation on epithelial and endothelial barrier dysregulation in post-infectious ME/CFS

Zusammenfassung

Malgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) is a debilitating disease, with women being 2-3 times more often affected. Viral infections are considered the main triggers for ME/CFS, but the precise pathomechanisms remain unclear. The COVID-19 pandemic has provided new insights into post-infectious ME/CFS and a significant number of Post-COVID Syndrome (PCS) patients develop ME/CFS.

Mast cells, activated by viral triggers, release various inflammatory mediators, which contribute to inflammation and tissue damage by disrupting epithelial and endothelial barriers. Thus, mast cell activation (MCA) may trigger symptoms associated with the disease, such as cognitive impairment, pain and brain fog. Of interest, recent studies have shown that mast cells exhibit a stronger response and release of mediators upon activation in women. Unpublished data of our own research group show that post-infectious ME/CFS patients suffer from symptoms indicating MCA and respond to the treatment of MCA.

We suggest virally triggered mast cells to play a crucial role in the development of post-infectious ME/CFS. We hypothesize that MCA drives ME/CFS pathology via epithelial and endothelial barrier disruption. Our study will evaluate: (1) immune-related mast cell mediators and cell junction protein changes in post-infectious ME/CFS patients, (2) the proximety of viral fragments to activated mast cells in intestinal tissues, and (3) mast cell phenotype alterations in these patients. Utilizing patient-derived samples, we will conduct in vitro co-culture models, examine MCA markers, and perform single-cell RNA sequencing to elucidate mast cell transcriptomic signatures.

The project DegranulateME aims to provide insights into the pathogenesis of post-infectious ME/CFS, emphasizing the role of MCA in barrier integrity and inflammation. These insights are crucial for developing causative treatment approaches to restore barrier function and manage symptoms in post-infectious ME/CFS.

Wissenschaftliche Disziplinen:
Immunology (60%) | Metabolomics (30%) | Genetics (10%)

Keywords:
mast cell activationepithelial barrier dysregulationendothelial barrier dysregulationviral persistanceviral reactivation

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Weiterführende Links zu den beteiligten Personen und zum Projekt finden Sie unter
https://www.wwtf.at/funding/programmes/ei/ME-CFS24-004/