ME-CFS26-004 - Persistent Platelet-Monocyte CrossTalk Underlies Failure to Resolve Inflammation and Symptoms in ME/CFS

Abstract

Growing evidence indicates that ME/CFS involves immune dysregulation, impaired circulation, vascular inflammation, and abnormal coagulation, often following infectious triggers such as SARS-CoV-2 or Epstein-Barr virus. These infections increase extracellular vesicle (EV) release from infected and bystander cells exposed to chronic inflammatory signals. Preliminary data from our group show significantly elevated (CD9/CD41/CD61)? platelet derived EVs (pEVs) in ME/CFS plasma compared with healthy controls, suggesting dysregulated platelet activity. Normally, pEVs interact with intermediate monocytes to support inflammation resolution; however, failures in this process, observed in other chronic inflammatory conditions, may contribute to persistent symptoms and autoimmunity. We therefore hypothesize that sustained monocyte subset skewing together with altered pEV-monocyte interactions drives thrombo-inflammatory activity and prevents full resolution of the post infectious phase, contributing to ME/CFS multisystem symptoms.

This project will quantify monocyte subsets and dissect platelet-monocyte crosstalk using multiparameter and imaging flow cytometry and high-resolution confocal microscopy. We will characterize platelet-monocyte aggregates (PMA), pEV-monocyte subset interactions, and their links to chronic inflammation and microclot (fibrinolysis-resistant fragments) presence. Importantly, during this 6-month project we will build a high-quality collection of live platelets, PBMCs, and platelet-poor plasma to enable extended collaborative work. These samples will support proteomic profiling of pEVs and monocyte derived EVs (mEVs) from isolated subpopulations, allowing deeper mechanistic investigation of sustained platelet-monocyte crosstalk in ME/CFS subsets. Together, this work advances mechanistic understanding of thrombo-inflammatory activity in ME/CFS and creates foundational resources for future biomarker discovery and precision medicine strategies.

Scientific disciplines:
Immunology (75%) | Infectious diseases (15%) | Bioinformatics (10%)

Keywords:
ME/CFS with/without SARS-CoV-2 onsetPlatelet-monocyte crosstalkExtracellular vesiclesThrombo-inflammationFailure of inflammation resolution

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Further links to the persons involved and to the project can be found under
https://www.gmbh.wwtf.at/funding/programmes/ei/ME-CFS26-004/