Circulating Extracellular Vesicles and Physical Stress in ME/CFS

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Primary CNF Tools Used: Malvern NS300 NanoSight

Abstract:

Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) is a disabling illness affecting approximately two million Americans, with symptoms including extreme fatigue, pain, unrefreshing sleep, orthostatic intolerance, and cognitive difficulties. There is evidence for abnormal immune cell function and cytokine signaling. Some of the abnormalities in immune response may be due to altered cell-to-cell communication by extracellular vesicles released by immune cells and other cell types in the body. We are measuring number and size of vesicles per volume of plasma in order to detect any differences between ME/CFS patients and controls. Furthermore, we are using this information in order to normalize measures of protein and miRNA cargo between individual samples.

Summary of Research:

The Nanoparticle Tracking Analysis (NTA) instrument Malvern NS300 NanoSight was used for the sizing and quantification of extracellular vesicles (EVs) isolated from plasma samples from subject with ME/CFS and healthy individuals. Samples were obtained from individuals recruited at Ithaca College, New York City, and California within an NIH U54 project. Other samples were directly sent to us from Jackson Laboratory as a collaborative project funded by the NIH. We have measured size and numbers to inform Jackson Laboratory for experiments in which the EVs are mixed with cultured cells to observe effects on their function.

We studied an initial set of 70 samples, shown in Fig.1.

A manuscript is currently in preparation that will describe data concerning size, concentration, and cargo in EVs from these samples. There was no difference in the average size or total concentration of EVs between samples from ME/CFS patients vs. controls. A significant increase in the concentration of the 30-130 nm class of EV (exosome type) was observed in the ME/CFS samples in comparison to healthy controls (Figure 1C).

Conclusions and Future Steps:

We are periodically receiving additional samples from Ithaca College, Weill Cornell Medicine, and Los Angeles, where subjects are performing two successive cardiopulmonary exercise tests. We are measuring size and numbers of EVs in plasma before and after such tests, and analysis of cargo in the EVs is underway.

The rationale behind this study is that it is known that EVs increase in blood following exercise by healthy people, and ME/CFS patients are known to have an abnormal response to exercise.

References:

[1] Giloteaux L., A. O'Neal, S.M. Levine, J. Jesus Castro-Marrero, and M.R Hanson. Cytokine profiling of plasma extracellular vesicles in individuals with Myalgic /Chronic Fatigue Syndrome. Oral presentation by L. Giloteaux at the meeting "Accelerating Research on ME/CFS," held at the NIH, Bethesda, MD on April 4-5, 2019.

[2] Giloteaux, L., J. Castro-Marrero., A. O'Neal, J. Grenier, S. Levine, and M.R. Hanson. Cytokine and miRNA profiling of plasma extracellular vesicles in individuals with Myalgic Encephalomyelitis/Chronic Fatigue Syndrome. Poster presentation by L. Giloteaux at the International Society of Extracellular Vesicles (ISEV) 2019 conference held in Kyoto, Japan, April 23rd-28th.

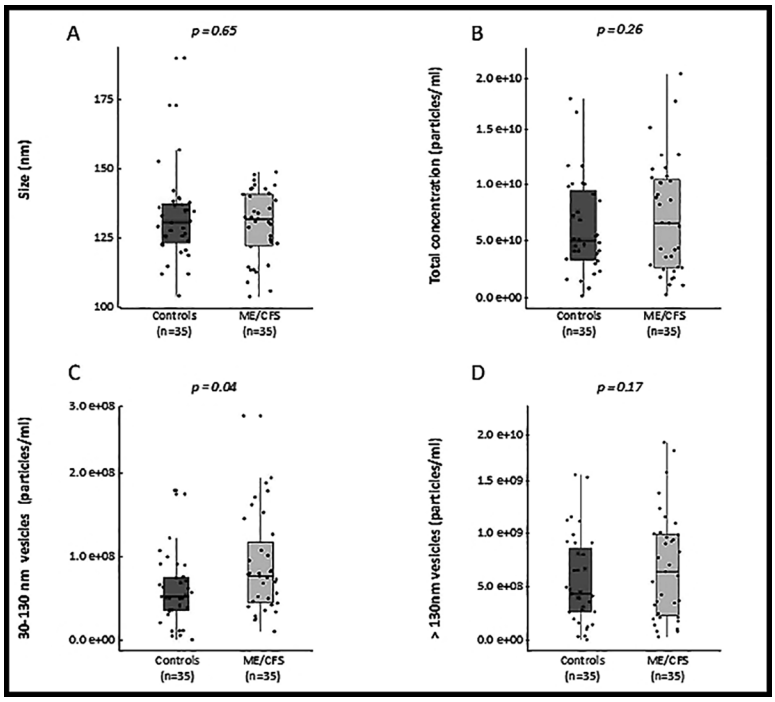

Figure 1: Characterization of EVs by Nanoparticle Tracking Analysis. Size in nanometers (A), total concentration of particles per ml of plasma (B), and the range of concentrations of 30-130 nm vesicles (C) and > 130 nm vesicles (D).