Monocyte biomarkers define sargramostim treatment outcomes for Parkinson’s disease

Mai M. Abdelmoaty\textsuperscript{1}, Jatin Machhi\textsuperscript{1}, Pravin Yeapuri\textsuperscript{1}, Farah Shahjin\textsuperscript{1}, Vikas Kumar\textsuperscript{2}, Katherine E. Olson\textsuperscript{1}, R. Lee Mosley\textsuperscript{1}, and Howard E. Gendelman\textsuperscript{1}

\textsuperscript{1}Department of Pharmacology and Experimental Neuroscience, College of Medicine, University of Nebraska Medical Center, NE 68198, USA
\textsuperscript{2}Mass Spectrometry and Proteomics Core, University of Nebraska Medical Center, Omaha, NE 68198, USA

Abstract

Dysregulation of innate and adaptive immunity heralds both the development and progression of Parkinson’s disease (PD). Deficits in innate immunity in PD are defined by impairments in monocyte activation, function, and pro-inflammatory secretory factors. Each influences disease pathobiology. To define monocyte biomarkers associated with immune transformative therapy for PD, changes in gene and protein expression were evaluated before and during treatment with recombinant human granulocyte-macrophage colony-stimulating factor (GM-CSF, sargramostim, Leukine\textsuperscript{®}). Monocytes were recovered after leukapheresis and isolation by centrifugal elutriation, before and 2 and 6 months after initiation of treatment. Transcriptome and proteome biomarkers were scored against clinical motor functions. Pathway enrichments from single cell-RNA sequencing and proteomic analyses from sargramostim-treated PD patients demonstrate a neuroprotective signature, including, but not limited to, antioxidant, anti-inflammatory, and autophagy genes and proteins (LRRK2, HMOX1, TLR2, TLR8, RELA, ATG7, and GABARAPL2). This monocyte profile provides a novel strategy to track clinical immune-based interventions.

Sponsored by: Partner Therapeutics and the University of Nebraska Foundation, which includes community donations from the Carol Swarts, M.D. Emerging Neuroscience Research Laboratory, the Margaret R. Larson Professorship, the Eisenberg Parkinson's Research Fund, and the Frances and Louie Blumkin and Harriet Singer Research Foundations.

Presenter name and contact information:
Mai Mostafa, PhD
Department of Pharmacology and Experimental Neuroscience
College of Medicine, University of Nebraska Medical Center, DRC 3020, Omaha, NE 68198-5800
Phone: 402-559-2547
Email: mai.mostafa@unmc.edu