IDENTIFY BIOMARKERS

Project ALS Commitment: $1.3M

Investigators: Estela Area-Gomez/Columbia University; Ed Boyden/Massachusetts Institute of Technology; Robin Chan/Columbia University; Gilbert di Paolo/Denali Therapeutics; Neil Shneider/Columbia University; Industry Partners

Background: Even as our understanding of ALS advances, the disease remains a "diagnosis of exclusion," meaning that people who may have ALS normally undergo months—even years—of doctor appointments, invasive testing, and concurrent stress before they are officially diagnosed. This also means that most people with ALS have experienced progressively more serious effects of the disease, and are often ineligible for clinical trials, by the time their ALS diagnosis is confirmed. Earlier, more accurate detection of ALS, using a biomarker—a unique change to a person's physiology in ALS—that could be identified through a simple blood test, would reduce this enormous burden on people with the disease and increase the window during which they might be treated effectively.

Recently, Project ALS researchers at Columbia University recognized that lipid levels change in a unique, consistent way in the blood of ALS patients; this "lipid signature," if verified, could constitute the first diagnostic biomarker in ALS. Based on these initial results, Project ALS put together a team of scientists to understand—with an eye toward biomarkers and therapeutic targets—the role of lipids in ALS.

Finally, Project ALS is recruiting experts in nanotechnology and other new imaging techniques to visualize ALS in greater detail than ever before. By closely examining proteins, RNA, lipids, cell nuclei, and molecules, we can identify where, and how, the ALS disease process begins.

Summary of Progress: The initial study that indicated a distinct lipid signature was performed on blood samples from a small cohort of ALS patients at Columbia. Di Paolo and Shneider have collected blood and plasma samples from a larger, more diverse group of patients—both those with the sporadic form of ALS, and those with common familial forms (SOD1, TDP-43, and C9orf72), and are working to confirm earlier results in a wider group of people.

In tandem, researchers in Area-Gomez's lab are working to understand how lipids change in ALS—and where we might intervene to stop these changes. Her team's initial results indicate that a "subcompartment" in our cells called the mitochondria-associated ER membrane (MAM)—which has already been implicated in Alzheimer's

disease—changes significantly in ALS. As the Project ALS lipids team validates exciting initial results to decode a distinct lipid signature and understand why specific lipid subtypes change, we aim to uncover both a diagnostic biomarker to diagnose ALS and a therapeutic target that may slow or stop the disease.

Relevant publications:
Lipids in Alzheimer's disease
Lipids' role in autophagy
The MAM in Alzheimer's disease

Contact us for additional relevant publications or research updates.