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Research Summary:

Research in our laboratory broadly focuses on understanding lipid signaling and its relevance in brain physiology and pathophysiology. At the cellular level, our main goal is to delineate the lipid-based mechanisms involved in the control of endolysosomal trafficking and autophagy. We elected to focus on these pathways due to their critical importance in maintaining neuronal homeostasis and growing implication in neurodegenerative processes. Accordingly, a major research goal is to determine whether perturbations of lipid signaling along the endolysosomal and autophagic pathways can underlie pathogenic processes primarily in Alzheimer’s disease, but also in other neurodegenerative disorders, such as Parkinson’s and Huntington’s disease. Finally, a growing research focus in our laboratory is in the area of biomarker discovery. Here, our main goal is to identify lipid biomarkers from human biospecimens (e.g., plasma, cerebrospinal fluid) that can be diagnostic for neurodegenerative disorders or predictive of disease onset or severity. Although they are not genetically encoded, lipids are attractive metabolites from the point of view of biomarker discovery because of their great chemical diversity and functional properties. Additionally, changes in lipid levels can inform us of dysregulation of specific molecular pathways because lipid metabolizing enzymes are typically key components of regulatory networks within cells, tissues or organisms. To address these fundamental questions, our lab has historically employed multidisciplinary approaches, which range from cell biological techniques, protein and lipid biochemistry, to mouse genetics and behavioral assessments of genetically-modified mice. Importantly, we have successfully developed novel technologies to interrogate lipid metabolism using state-of-the-art mass spectrometry-based approaches, commonly referred to as "lipidomics". We now routinely profile lipid species from four main classes of lipids (glycerolipids, glycerophospholipids, sterols and sphingolipids), comprising over 500 individual lipid species. My lab routinely collaborates on lipidomics projects with an increasing number of Columbia investigators in various disease areas, including diabetes and obesity.

Selected Publications:


**More about Gilbert Di Paolo, Ph.D.:**