

Dr. Anna Podolanczuk

In this application for a 5-year K23 Career Development Award, I propose mentored research and career development leading toward a career as an independent clinical and translational investigator in interstitial lung disease. The goal of this research project is to identify the role of high-density lipoprotein in idiopathic pulmonary fibrosis (IPF), a fatal lung disease that affects 1 out of 200 older adults and has a median survival of 3-5 years from diagnosis. Currently there is no medical therapy that improves symptoms or reverses fibrosis in IPF patients. This proposal builds upon my preliminary data showing that high levels of high density cholesterol (HDL-C) are associated with a reduction in lung injury, inflammation and fibrosis (subclinical ILD) on CT in community-dwelling adults enrolled in the NHLBI-funded Multi-Ethnic Study of Atherosclerosis. These data are consistent with animal model data showing that treatment with apolipoprotein A-I (ApoA-I; the main component of HDL) attenuates lung fibrosis. Under the mentorship of Dr. David Lederer, I am therefore proposing to examine the associations of HDL and its main components (ApoA-I, ApoA-II, and paroxonase-1) with clinical outcomes and serum biomarkers of lung injury, inflammation and remodeling in adults with clinically-diagnosed IPF enrolled in Dr. Lederer's FAR-ILD study (Families At-Risk for ILD; R01 HL103676-06, scored 5th percentile Dec 2016). I will also explore the structure (using quantitative proteomics in Dr. Emily Chen's lab) and function (using a macrophage efflux assay in Dr. Alan Tall's lab) of HDL particles in adults with IPF as well as in two comparator groups: first-degree family members with subclinical ILD enrolled in the FAR-ILD study, and healthy controls. With guidance from my mentors, I have crafted a 5-year career development plan that includes training in lipoprotein biology (co-mentor: Dr. Tall), quantitative proteomics (co-mentor: Dr. Chen), clinical epidemiology (Dr. Lederer), and biostatistics (Dr. RoyChoudhury). In the last two years of the award I will apply for R01 funding and transition to independence. The proposed activities will prepare me to conduct patient-oriented and translational research to discover novel risk factors for IPF and other ILDs. I will also be prepared to design and conduct clinical trials targeting novel pathways (including those uncovered in this K23 proposal) to prevent and treat ILD.