Dr. Ali Gharavi

Summary:
Glomerular diseases are responsible for a large fraction of end stage renal disease (ESRD) worldwide. There are four idiopathic disorders that account for the majority of cases: IgA nephopathy (IgAN), focal segmental glomerulosclerosis (FSGS), membranous nephropathy (MN) and minimal change disease (MOD). The major challenges include relative rarity, under-diagnosis, and etiologic heterogeneity of these disorders (resulting in the scarcity of well powered case cohorts), and relapsing-remitting patterns of activity with slow average rates of progression and high variability in prognosis (necessitating long-term follow up of several years to decades). Therapeutic options for these diseases are also resently limited. There has been recent progress in defining critical disease mechanisms for these four disorders, including discoveries of new genetic susceptibility alleles, novel circulating factors, and specific environmental insults inciting the disease. Accordingly, this project aims to develop a longitudinal observational cohort of 650 patients with IgAN, FSGS, MN and MCD (along with 650 ethnically and geographically matched healthy controls). The cohort will be followed at 6-month intervals with prospective collection of clinical data and biological materials, including blood, urine, saliva, and fecal material. These data and biomaterials will facilitate integration of clinical, genetic, biochemical, and immunologic studies to advance the science of glomerular disease. As part of this proposal, we suggest a number of innovative clinical, genetic, and biomarker pilot studies that would become feasible with the establishment of this cohort. In addition to enabling well-powered translational studies, this unique resource will also provide invaluable insights into the natural history of these disorders. The findings from this cohort will also lay basis for new therapeutic clinical trials, and thus will directly impact the care of patients. The proposal brings together an experienced team of investigators with considerable contributions to the field of glomerular disease, including members of the Columbia Glomerular Center, Columbia Renal Pathology Division, Columbia Pediatric Nephrology Division, and the Gaslini Pediatric Institute. Moreover, our proposal has a considerable support from the industry, FDA, and patient advocacy groups.