

Dr. Krzysztof Kiryluk

Krzysztof Kiryluk, Assistant Professor at Columbia University, is a clinical nephrologist with a formal training in biostatistics. His long-term goal is to develop an independent career conducting translational research in the genetics of IgA nephropathy and other forms of kidney disease. The purpose of this proposal is to foster his scientific development, laboratory skills, and build on his expertise in statistical genetics.

IgA nephropathy (IgAN) is the most common cause of primary glomerulonephritis worldwide. Most IgAN patients exhibit a characteristic under-glycosylation of the IgA1 molecule. An increased serum level of galactose-deficient IgA1 (Gd-IgA1) is emerging as a useful biomarker of IgAN. Gd-IgA1 promotes formation and mesangial deposition of IgA1-containing immune complexes, but the reason why IgAN patients have high Gd-IgA1 is currently not known. Recently, a reliable lectin-based ELISA assay for detection of high levels of serum Gd-IgA1 has been developed. Krzysztof has utilized this assay to demonstrate that Gd-IgA1 levels are elevated in a large proportion of patients with IgAN and their family members as compared to unrelated controls. Moreover, Krzysztof conducted a whole-genome linkage scan for Gd-IgA1 in a large pedigree with familial IgAN and identified a major susceptibility locus on chromosome 10p14-15 (LOD=4.4). Based on these results, he hypothesizes that Gd-IgA1 level is, in part, genetically determined. He proposes to identify gene(s) responsible for high Gd-IgA1 levels by integration of linkage and gene expression data from this and other families with IgAN. In addition, he proposes to perform the first GWAS for Gd-IgA1 to identify possible contributions from common genetic variants to this phenotype. He will follow his findings by differential expression studies in IgA1-producing cells and in vitro functional studies of gene(s) contributing to abnormal glycosylation of IgA1.

The proposed studies will be conducted in the laboratory of Dr. Gharavi (primary mentor), with Dr. Terwilliger (co-mentor) providing him with additional expertise in genetic analysis. Considering the inter-disciplinary nature of this project, Krzysztof has established a network of collaborators from different departments at Columbia University and outside institutions. Krzysztof's training plan builds on his strong background in applied biostatistics and statistical genetics. He will also obtain a "hands-on" training in laboratory methods. In the long term, Krzysztof hopes to build a highly productive independent laboratory to continue his scientific investigations in the field of complex disease genetics.
