Towards an IgA Nephropathy Atlas

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Abstract (Number: WCN24-AB-1863)

Introduction: IgA Nephropathy (IgAN) is the most common form of primary glomerulonephritis worldwide. Recently, there have been advances made in the understanding of IgAN pathophysiology and new therapeutic options have emerged. We now have the first FDA- and EMA-approved therapies for IgAN, with many more novel agents in advanced trials. These unprecedented developments reinforce the need to improve individual disease risk stratification and expand and refine the criteria to choose the best treatment for each patient.

Methods: To achieve these goals, we need to improve our understanding of IgAN pathophysiology and its heterogeneity across patients. This requires a multi-organ systematic approach, profiling all involved organs using different omics technologies, capturing the spatial context, understanding the role of the microbiome, and defining tissue changes during the entirety of the natural history of the disease – an IgAN Atlas. The establishment and interrogation of such a comprehensive IgAN Atlas will require advanced computational and artificial intelligence approaches.

Results: To advance towards this goal, we have established a global team of scientists, clinicians, and patients with the aim of building an IgAN Atlas to accelerate research and ultimately enhance clinical practice. The IgAN Atlas is an open and collaborative initiative and we welcome contributions of any kind from anyone interested in improving our understanding of IgAN pathogenesis and the care we deliver to people living with IgAN.

Conclusion: Here, we describe our research network, an overview of our aims and approach, and illustrate the progress we have made to date in integrating global multi-omics studies in IgAN in several of our ongoing pilot projects.

Ongoing experiments

Kidney tissue

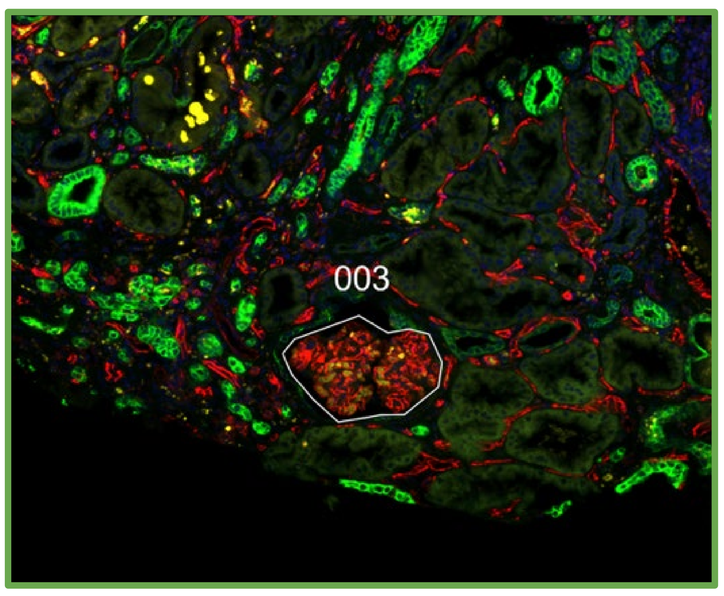


Figure 1. Immune stains of endothelial cells (CD31 - red), macrophages (CD68 - yellow) and tubular cells (PanCK - green) on kidney biopsies from an IgA Nephropathy patient.

Blood, plasma and urine

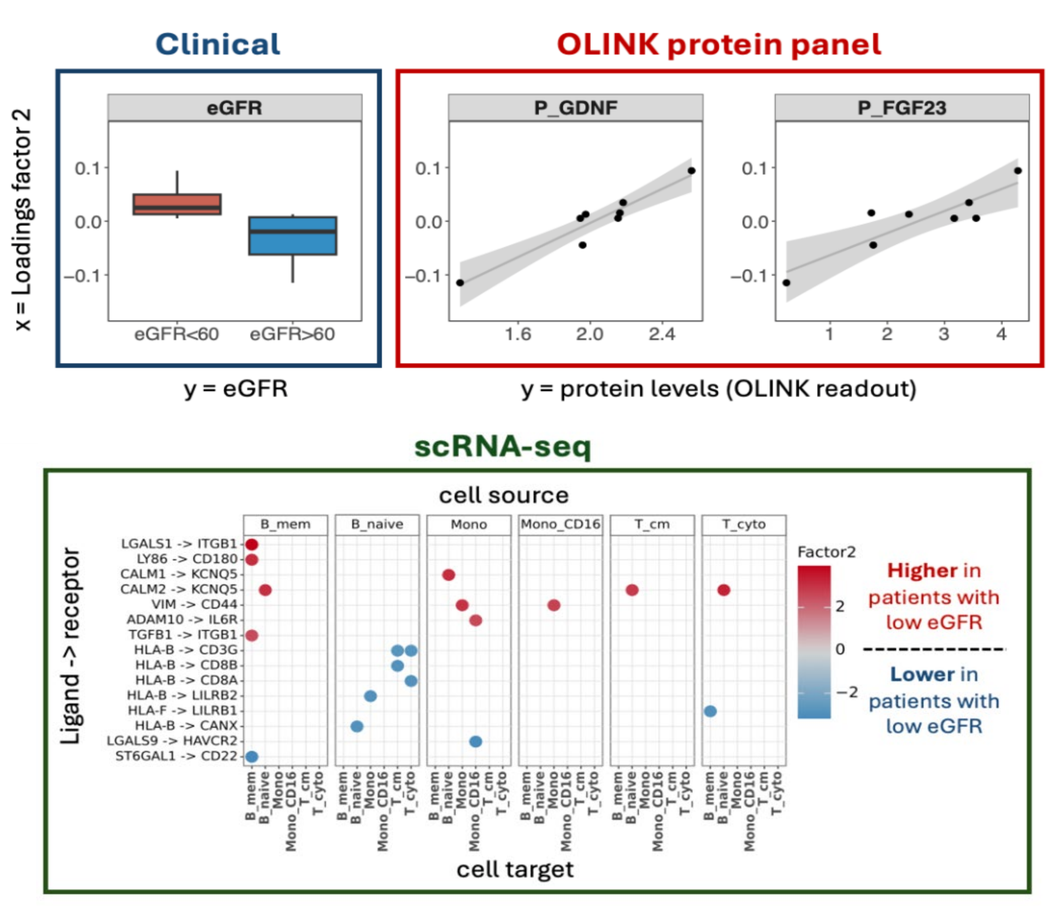
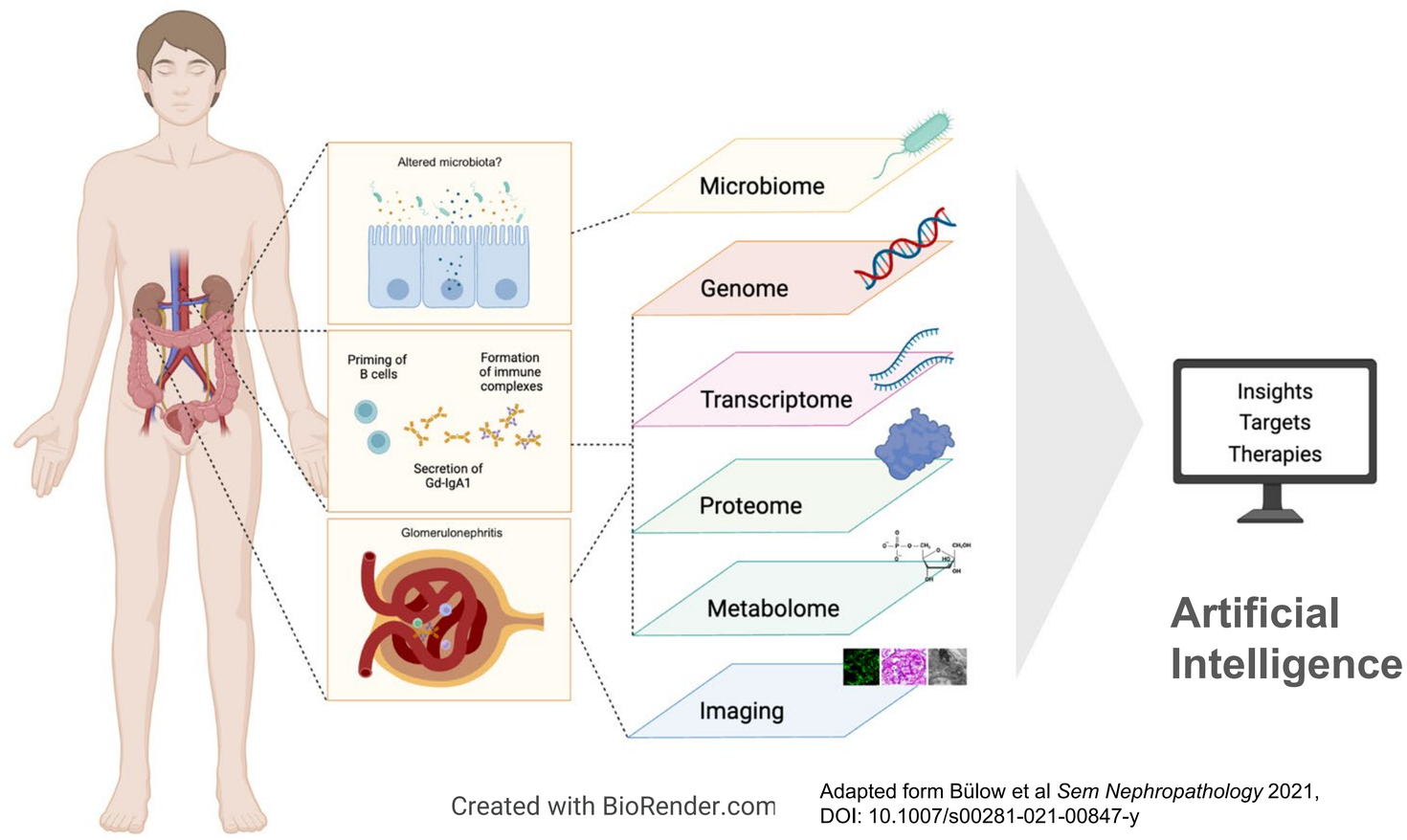


Figure 2. Multicellular gene signature is associated with renal function, serum proteins measured (OLINK technology), and single-cell-RNAseq of Peripheral Blood Mononuclear Cells (PBMCs).

Design



Adapted form Bülow et al *Sem Nephropathology* 2021, DOI: 10.1007/s00281-021-00847-y

Available samples/datasets

Partners	Transcriptomic data (number of samples)	Blood and urine (number of samples)
University of Gothenburg	RNAseq (kidney). IgAN: 69. Controls: 52	IgAN: 80. Controls: 80
Karolinska Institutet	RNAseq (kidney). IgAN: 71. Controls: 11	IgAN: 190. Controls: >200
University of Bari	RNAseq (fecal microbiome). IgAN: 20. Controls: 40	IgAN: 150. Controls: 150
Radboudumc	RNAseq (PBMC). IgAN: 41	IgAN: 41
University of Leicester	Spatial transcriptomics (kidney). IgAN: 53	IgAN: >100. Controls: >100
University of Oxford	snRNAseq (kidney). IgAN: 4. Controls: 4 Spatial transcriptomics. IgAN: 11. Controls: 11	
University of Michigan	RNAseq (kidney). IgAN: 76. Controls: 52 RNAseq (WBCs). IgAN: 612	IgAN: >700
Total	**IgAN: 957. Controls: 170**	**IgAN: 1261. Controls: 530**

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