Precision Diagnostics in Membranous Nephropathy by Mass Spectrometry-Based Antigen Identification

Membranous nephropathy is an autoimmune kidney disease and the most common cause of nephrotic syndrome in adults. In this condition, the immune system mistakenly attacks proteins in the kidney filters, which can lead to impaired kidney function.

In recent years, several different target proteins (called antigens) responsible for this disease have been identified. Determining the specific antigen is important because it provides information about the underlying cause of the disease and can influence treatment decisions. Some forms of membranous nephropathy may be associated with cancer, medications, or other diseases and may therefore require specific treatment approaches. Currently, the available diagnostic methods, immunohistochemistry and immunofluorescence, in Switzerland can identify only two of the at least 13 known target antigens in blood or kidney tissue.

The aim of this project is to validate a new diagnostic method based on mass spectrometry for the diagnosis of membranous nephropathy in Switzerland. This technique is already used internationally, particularly in the United States, to identify disease-causing antigens in patients with membranous nephropathy. Mass spectrometry allows detailed analysis of kidney biopsy samples and can identify thousands of proteins in a single measurement, providing much more comprehensive information than current methods.

Our research group has already successfully established this technology for the diagnosis of amyloidosis. This project will investigate whether the same approach can be reliably applied to membranous nephropathy. In the long term, the goal is to make this diagnostic method available in Switzerland, enabling more precise diagnoses and individually tailored treatments.

For this pilot project, existing kidney biopsy samples stored in the archives of the Institute of Pathology at the University Hospital Basel will be used. Initially, the method will be tested and validated using ten representative tissue samples. A precise laser-based technique will be used to isolate the affected kidney filters from the biopsy samples, which will then be analysed by advanced mass spectrometry to identify the disease-causing antigens. Since only existing archived tissue samples are used, no additional procedures or burden will be required for patients.

Mass spectrometry is already an established diagnostic technology in clinical chemistry and medical microbiology in Switzerland. However, it has not yet been implemented routinely in diagnostic pathology. This project will provide the scientific foundation for introducing this technology into histopathology. With its ability to provide extensive and precise information about disease-related proteins at relatively low analytical cost, mass spectrometry has the potential to significantly improve kidney disease diagnostics and become a cost-effective tool for routine clinical use in Switzerland. Furthermore, this method may provide direct benefits for individual patients, as identifying the responsible antigen can have immediate diagnostic and therapeutic consequences. Depending on the identified antigen, unnecessary intensive immunosuppressive treatment, which can be associated with significant risks and side effects, may be avoided.