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Amyloidosis: how proteomics can make a difference in clinical practice

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Amyloidoses are a group of diseases caused by accumulation, in various tissues, of amyloid fibrils derived from different misfolded proteins. Because several organs are often affected, symptoms are non-specific, delaying accurate diagnosis and treatment. Correct typing of amyloid deposits is imperative to distinguish the various types of amyloidosis, for which specific therapies are available. Alongside immuno-histochemistry, mass spectrometry (MS)-based methods are considered the gold standard, but they are only routinely used in a few places in the world.

Here we present how we are implementing a proteomic analysis[1] of laser-microdissected amyloid depots via LC-MS/MS using a nano LC coupled with a timsTOF flex instrument. While learning from the experience of other centers, we are testing several alternatives and ideas emerging from other approaches to proteomics to improve sensitivity and decrease analysis time. Exploiting the capacities of the Parallel Accumulation–Serial Fragmentation (PASEF) technology, we generate high-quality data, which are then processed using MaxQuant (Swiss-Prot database for identification) and R for inspecting proteins relevant to the diagnosis. As a preliminary step to validate our method, we have analyzed 16 fat tissue samples of patients with various immunoglobulin light chain (kappa or lambda) amyloidoses and compared our results with the findings of the UK National Amyloidosis Centre in London. We are also testing our method on kidney biopsies. Although proteomics is not (yet) used widely in clinical practice, here is an example where it makes a difference for the patients. Local – and therefore timely and 'cheap' – processing of samples can have a real impact on treatment course, and ultimately on prognosis.

Reference

1. D. Canetti, *et al.*; Clin. Chem. Lab. Med., **58**, 948-957 (2020)