Quantitative LC-chip-MS/MS method to discriminate Immune-Mediated Inflammatory Diseases

Immune-mediated inflammatory diseases (IMID) present a group of common and highly disabling chronic conditions that share inflammatory pathways. Disorders belonging to this group include, but are not limited to rheumatoid arthritis, lupus and systemic sclerosis. The prevalence of IMID in Western society is about 5%–7%. As some IMID are often tricky to be distinguished from each other, there is still current need for solid biomarkers that will allow clinicians to precisely address the pathology as soon as possible. Patients with immune-mediated inflammatory disease will also directly benefit from the stratification of therapeutic options.

The Rheumatology Department at CHU/University of Liège (BE) has developed a LC-chip-MS/MS quantitative method that simultaneously quantifies C3f and the vitronectin fragment (amino acids 381-397) in blood. Both peptides were previously shown to be overexpressed in sera from patients suffering from severe osteoarthritis compared to early osteoarthritis and healthy controls (Cobraiville et al., Talanta, 169 (170-180), 2017).

The simultaneous quantification of the two proteomic biomarkers also provides an efficient tool to discriminate lupus and systemic sclerosis from other IMIDs. This achievement is supported by the molecular biology underlying the pathologies:

- high concentration of C3f is associated with an increased cleavage of C3 due to complement activation.
- In lupus, serum hypocomplementemia is known to be a worsening factor predicting clinical flares in lupus;
- vitronectin is a component of extracellular matrix.

KEY ACHIEVEMENTS

- Robust LC-chip-MS/MS method
- Simultaneous quantification of C3f and vitronectin fragment (a.a. 381-397) in blood/serum
- Validation on a large cohort:
  - osteoarthritis cohort (n=284; K&L severity 0-4)
  - IMID cohort (n=259) including rheumatoid arthritis, ankylosing spondylitis, lupus, systemic sclerosis, ulcerative colitis, Crohn’s disease and osteoarthritis patients.
- Ability to discriminate between
  - early (K&L0-2) vs late (K&L3-4) osteoarthritis
  - lupus & systemic sclerosis vs other IMIDs

KEY COMPETITIVE ADVANTAGES

- Quantification of biomarkers from biological fluids
- Measure of multiples analytes in a single sample
- Lowering volume and time analysis
- Possibility to diagnose patients earlier
- Possibility to monitor the efficacy of (new) treatments
- Diagnostic, prognostic and theranostic potential

UPCOMING CHALLENGE

Validation on larger cohorts

PARTNERSHIP SOUGHT

Collaboration to monitor treatment efficacy
License agreement to develop and implement the LC-chip-MS/MS method

INTELLECTUAL PROPERTY

- EP3109640B1 (DE, FR, UK)