LIÈGE université
Interface Entreprises
Research & Innovation

Research & Innovation in the field of Osteoarthritis

Technology offers & Competencies at the University of Liège

March 2021

The University of Liège (ULiège) is a Belgian research university, hosting more than 3,500 researchers, scientists and technicians, and offering many advanced skills in science and technology, humanities and social sciences, and life sciences.

Research in the field of life sciences, and particularly in the sector of human health, at ULiège is encompassing several topics of major interest such as immunology, oncology, virology, hematology, cancerology, cardiovascular diseases, neurosciences and chronic inflammation. ULiège has notably built up a strong expertise in the inflammatory joint diseases, as osteoarthritis.

This brochure aims to inform you on some technology offers available at the University of Liège in the field of osteoarthritis and chronic inflammation.

ULiège is actively looking for companies ready to take part in their next development stages through specific research and/or commercial agreements.

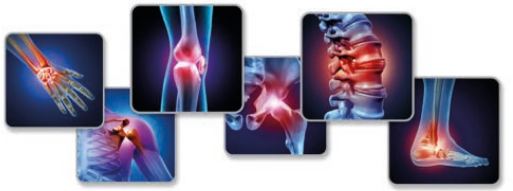
ULiège-Interface Entreprises, the Knowledge Transfer Office of the University, plays a central role in bringing scientists and companies together on projects, in supporting the maturation process of technologies based on results from research, in licensing and in accompanying the creation of spin-off companies. By developing partnerships with the appropriate companies, ULiège-Interface Entreprises is committed to operate a successful collaboration and technology transfer. We are convinced that ULiège's opportunities represent valuable assets for economic growth and innovation solutions, especially in the field of human health.

We look forward to exploring with you any strategic partnership to help you to grow your business.

Dr Ir Michel Morant
General Manager of ULiège-Interface Entreprises
University of Liège

Technology Offers

Osteomodulin:
a new biomarker for diagnosing Osteoarthritis



KEY ACHIEVEMENTS

- Identification on a new circulating biomarker based on a proteomic approach
- *In vitro* results

KEY COMPETITIVE ADVANTAGES

- Could be used in non-invasive test (blood-based)
- Could be complementary of others biomarkers for OA

UPCOMING CHALLENGES

- Validation in animal model and in large cohort of patients
- Development of a reliable immunoassay to measure Osteomodulin

INTELLECTUAL PROPERTY

- Granted Patent in EU and JP and patent application in US "Osteomodulin and osteomodulin fragments as biomarkers of osteoarthritis and use thereof" EP3433618 B1 (validated in BE, CH, DE, DK, ES, FR, GB, IE, IT, LU, PT, SE, TR)
- JP6817315 B2
- US2019011459 A1

PARTNERSHIP SOUGHT

Licensing of patent portfolio

Osteoarthritis (OA) is a progressive disorder characterized by destruction of articular cartilage and by subchondral bone and synovial changes. Currently, the diagnosis of osteoarthritis is based on clinical and radiological changes which occur late during disease progression. There is a need for **a simple, rapid and effective method** for the diagnosis of osteoarthritis and other ageing-related diseases but also to monitor the efficacy of treatments, or to determine the prognosis for a patient diagnosed with osteoarthritis and other ageing related diseases.

The musculoSKeletal Innovative research Lab (**mSKIL**), from Liège University (ULiège), has discovered that a new biomarker, **Osteomodulin**, is less expressed and less secreted by sclerotic subchondral osteoblasts during osteoarthritis.

Furthermore, they found fragments of Osteomodulin in body fluids, in particular in serum, of OA patients and that **serum** concentrations of the Osteomodulin fragments were **lower** than compared to those of healthy individuals.

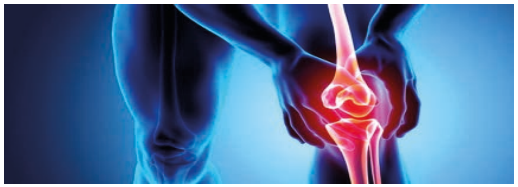
The decrease of Osteomodulin in OA patients could reflect **abnormal bone remodeling** in OA subchondral bone, suggesting that Osteomodulin could be a biomarker of subchondral bone metabolic changes in osteoarthritis.

Osteomodulin could then facilitate the diagnosis of osteoarthritis and inform prognosis, monitoring and therapeutic strategies for the disease.

Sanchez and al, Plos One, 2018, 13 (3): e0194591

Contact:
ULiège Interface Entreprises
Isabelle RENARD, TTO
i.renard@uliege.be

Measuring Fibulin-3 biomarker in biological fluids: a new method for diagnosing Osteoarthritis



KEY ACHIEVEMENTS

- Prototype immunoassay (ELISA) available
- *In vitro* and *in vivo* results
- Used in human studies

KEY COMPETITIVE ADVANTAGES

- Non-invasive test (blood or urine based)
- Simple and rapid method
- Early diagnosis and disease management

UPCOMING CHALLENGES

- Verification and Validation studies
- Transfer Process
- Regulatory certification for Diagnostic tool

INTELLECTUAL PROPERTY

- Granted Patent in EU and USA "Biomarker for osteoarthritis and/or other ageing-related diseases and use thereof"
- EP2286240 B1 (validated in AT, BE, CH, DE, DK, ES, FR, GB, IE, IT, LU, PT, SE, TR)
- US8771968 B1
- US9052313 B1

PARTNERSHIP SOUGHT

Licensing of patent portfolio

Osteoarthritis (OA) is a progressive disorder characterized by destruction of articular cartilage and by subchondral bone and synovial changes. Currently, the diagnosis of osteoarthritis is based on clinical and radiological changes which occur late during disease progression. There is a need for a **simple, rapid and effective** method for the diagnosis of osteoarthritis and other ageing-related diseases but also to monitor the efficacy of treatments, or to determine the prognosis for a patient diagnosed with osteoarthritis and other ageing related diseases.

The musculoSKeletal Innovative research Lab (**mSKIL**), from Liège University (ULiège), has discovered and validated a new method for diagnosing osteoarthritis based on the concentration of **Fibulin-3 fragments** biomarker in biological samples (whole blood, serum, plasma, urine,…).

The determination of Fibulin-3 fragments concentration may be determine by any suitable assay such as an enzyme assay, an immunoassay, mass spectrometry, HPLC, …

In particular, an immunoassay (ELISA) has been developed and tested in vitro and in vivo but also in human studies. Fibulin-3 fragments were **increased** in serum and urine of OA patients compared to healthy controls. The immunoassay demonstrated **good analytical performances** with respect to precision, recovery, linearity and specificity.

Moreover, it has been shown that Fibulin-3 concentration is **associated** with the **incidence of clinical knee OA** among middle-age overweight and obese women. Therewith, it meets the criteria of a **prognostic biomarker** according to the BIPED biomarker classification for OA.

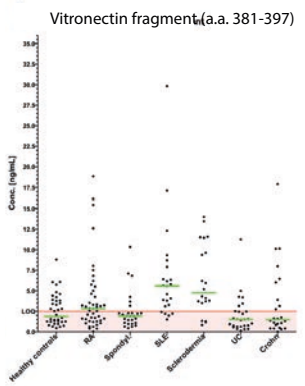
Fibulin-3 can then be a reliable biochemical marker that can facilitate the diagnosis of OA and inform prognosis, monitoring and therapeutic strategies for the disease.

Henrotin and al, Arthris Rheum, 2012, 64 (7): 2260-7
Runhaar and al, Osteoarthritis Cartilage, 2016, 24 (4): 672-8
De Visser and al, Cartilage, 2019, 10 (3): 329-334

Contact:
ULiège Interface Entreprises
Isabelle RENARD, TTO
i.renard@uliege.be

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

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



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) treaments
- 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

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

INTELLECTUAL PROPERTY

- EP3109640B1
- EP3479120B1
- WO2018/007173 (US pending)

Contact:
ULiège Interface Entreprises
Annick HOUBRECHTS, TTO
a.houbrechts@uliege.be

Research Teams

MusculoSKeletal Innovative research Lab (mSKIL),

http://www.mskil.uliege.be/index.html

The musculoSKeletal Innovative research Lab (mSKIL), previously known as the Bone and Cartilage Research Unit, has joint the CIRM (Center for Interdisciplinary Research On Medicines) in 2019. The lab is highly specialized in the pre-clinical and clinical investigation of drugs, food supplements and medical devices used in the treatment of MusculoSKeletal (MSK) disorders and rheumatic diseases, particularly in osteoarthritis, sarcopenia and intervertebral disk degeneration.

mSKIL has developed innovative in vitro and in vivo models for studying MSK and rheumatic diseases. The lab has developed in vitro models and technologies for studying cytokines network, oxidative stress, senescence, cartilage repair and degradation, bone remodeling, synovial inflammation and skeletal muscle cells metabolism. It has an extensive expertise in co-culture systems and in the culture of chondrocytes in hypoxic conditions and under mechanical strains (Flexercell system). The lab has developed an original culture model of osteoarthritic subchondral bone osteoblasts allowing the comparison of the sclerotic and nonsclerotic osteoblast responses to biochemical or mechanical stimuli. mSKIL has also in vivo models for studying pain, inflammation, osteoarthritis, and intervertebral disk degeneration.

mSKIL has all devices in the lab to perform cell cultures, ELISA, western-blot, real time PCR and histological analysis. It also has a gait analysis system, CatWalk from Noldus, and a configurable mechanical tester, Mach-1 from Biomomentum.

Furthermore, the lab has a great expertise in the diagnosis and follow-up of osteoarthritic patients, mainly by the measurements of cartilage and bone turnover markers in serum, urine and synovial fluid. The team has conceptualized, developed and validated new biomarkers for evaluating oxidative-related cartilage degradation in serum, urine and synovial fluid. They actively collaborate to the transfer of these technologies in the industry.

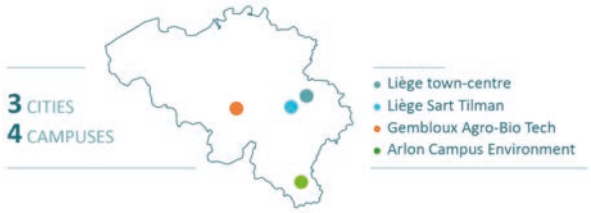
The Laboratory of Rheumatology, GIGA

https://www.gigarheumatology.uliege.be/

The Laboratory of Rheumatology belongs to the Thematic Research Unit of GIGA-I3 (Infection-Immunology-Inflammation) located in the University Hospital of Liège.

The Lab works on the physiopathology of osteoarthritis (OA), using multiple approaches. First, it uses in vitro and ex vivo models based on primary cells and tissue (i.e. cartilage and synovial membrane) coming from patients undergoing surgical joints resection. Second, since 2002, biological fluids and tissues provided from OA and non-OA patients have been collected with the help of clinicians and orthopaedic surgeons. Such biobanking allowed the team to perform several translational proteomics researches by mass spectrometry. Finally, two OA mice models generated by destabilization of the medial meniscus (DMM) or collagenase injection in joints (CIOA), were also implemented in the laboratory. Thanks to all these complementary approaches, the Laboratory of Rheumatology investigated signaling pathways integrated within four topics developed below: (i) chondrocyte dedifferentiation and fibrosis, (ii) human synovial fibroblast survival depends on autophagy (iii) senescence-therapeutic intervention in OA and (iv) proteomic studies for biomarkers discovery.

By investigating signaling pathways involved in the intra-articular cell plasticity, autophagy and senescence but also in synovial inflammation and fibrosis, the lab aims to develop new therapeutic strategies.



Established in Liège, Gembloux and Arlon, the University of Liège is ideally placed at the heart of Europe. In Belgium, ULiège is the only complete public university of the Wallonia-Brussels Federation.

Its excellence is underpinned by two centuries of teaching and University research, in tandem with an intellectual tradition that has placed Liège firmly on the map since the Middle Ages.

A core priority of the University of Liège is openness to society and the world at large. Every year, the university develops collaboration projects with hundreds of international institutions.

The University of Liège has consolidated its local presence through the diversity of its various campuses. It is actively developing quality management in addition to a responsible environmental and energy policy.

LIÈGE université
Interface Entreprises
Research & Innovation

Université de Liège
Interface Entreprises
LIEGE science park
Avenue Pré-Ailly, 4
4031 Liège
Belgium

+32 4 349 85 11
interface@uliege.be

www.uliege.be
www.recherche.uliege.be
www.entreprises.uliege.be