

## EULAR Synovitis Study Group (ESSG)

**Chairs: Dr. Andrew Filer and Dr. Aurélie Najm**

Due to the development of minimally invasive synovial biopsy techniques, research on synovial tissue is strongly accelerating, and numerous groups all over the world are getting familiar with biopsy procedures and analytical techniques. Clinical applications have never been so close; in this perspective, crossing the bridge between research projects and care is the ultimate goal that spirits the work performed by the teams involved in the EULAR Synovitis Study Group (ESSG).

Early diagnosis, prediction of disease severity and prediction of response to therapy are still unmet needs in Rheumatology. In order to deliver clinically meaningful answers to these questions, synovial tissue research needs to reach important milestones that we place in priority on the ESSG agenda:

- **Standardisation.** Heterogeneous distribution of the inflammatory processes inside the synovium was one of the first hurdles faced by research groups in the past. It resulted in the definition of minimal numbers of samples (containing lining and sublining) to be obtained from a biopsy procedure in order to get a representative picture of synovial inflammation. Beyond these definitions, additional consensus statements need to be developed on minimal requirements regarding sampling procedures, preservation and storage of the samples and other pre-analytical steps.
- **Education.** There is a high demand from young rheumatologists in being trained in the available synovial biopsy procedures. It is the wish of ESSG to organize regular training sessions, in close collaboration with the EULAR School of Rheumatology, in order to provide access to adequate information and experience in the field to our trainees. The first synovial biopsy course endorsed by EULAR has taken place in Brussel in September 2018 and will be conducted regularly.
- **Exchange of information.** In view of the work-intensive collaborative projects developed inside ESSG, we intend to improve access to experimental data through a dedicated secure platform.
- **Research.** Many high-quality research projects are presented at our meetings, and endorsed by ESSG. We want to put the emphasis on large-scale prospective multicentric research initiatives, which have the ambition to provide final answers to clinically relevant questions.

ESSG is an inclusive community of scientists and physician-scientists dedicated to high-quality research in the field of synovitis with the goal of implementing the systematic assessment of synovial tissue as a clinical tool. Increased interest in synovial biopsies is a world-wide trend, and ESSG wishes to promote collaborative initiatives with non-European scientists in the field. Preliminary contacts with ACR scientists taken by our previous chair, C. Pitzalis, D. Veale, J. Fonseca and B. Lauwerys showed common interests in developing pre-analytical standards and collaborative research projects, and ESSG is willing to promote the creation of a formal ACR/EULAR synovitis study group.

## RESEARCH PROJECTS

### R4-RA – Principal Investigator: Costantino Pitzalis

This is the first prospective multicentric trial using synovial biopsies to stratify patients in treatment groups. The main aim of this project is to test the hypothesis that the presence or absence of specific synovial cellular and molecular signatures (B cells and B cell-associated signatures), assessed following a synovial tissue biopsy, will enrich for response/non-response to the B cell depleting anti-CD20 monoclonal antibody

(mAb) Rituximab. In addition, we will examine if clinical response is associated with inhibition of B cell-linked pathways within the synovium and dependent on local B cell lineage depletion and whether survival of auto reactive B cells within "protected" synovial niches are responsible for B-cell joint re-population and disease resistance-relapse. See : <http://www.r4ra-nihr.whri.qmul.ac.uk/>

**Value of synovial tissue histological markers for prediction of response to treatment in rheumatoid arthritis. Principal Investigators: Aurélie Najm, Douglas Veale**

This multicentric project aims to study synovial tissue histological biomarkers value to guide treatment choices and predict responses in synovial tissue biopsies performed in rheumatoid patients naïve of biologics and whom response to treatment at 6 months is known.

These results will allow to define a consensual set of histological items to be further used for prediction of response to treatment in RA.

**Standardization of synovial tissue handling procedure – Principal Investigators: Rogier Thurlings, Stefano Alivernini**

We currently perform a collaborative research project on the standardization of synovial tissue handling procedures. Our focus is the possibility to cryopreserve synovial tissue to retain cell viability. A specific protocol has been developed and tested at the Radboud university Medical Center Nijmegen, the Netherlands. The reproducibility and validity of this procedure is tested at the Catholic University of the Sacred Heart, Rome, Italy. The results of these procedures will be shared with the synovitis study group partners in a shared electronic research environment. The aim is to have this serve as a basis for future collaborative synovial tissue research projects.

**Prediction of response to TNF inhibitors in rheumatoid arthritis based on gene expression profiling in the synovium – Principal investigator: Patrick Durez**

This project is a prospective multicentric study in which synovial tissue is obtained from patients with rheumatoid arthritis prior to initiation of TNF blocking therapy. The underlying hypothesis is that high expression of TNF-dependent transcripts is associated with poorer response to TNF blocking agents at 3 months. The study is performed in association with DNALytics, a spin-off company of the Université catholique de Louvain, and intends to recruits 110 patients in 2017-2018.

**Safety of Ultrasound guided biopsy procedures – principle Investigator Andrew Filer**

This is a large scale, multicentre retrospective service evaluation gathering data on adverse events associated with ultrasound guided biopsy, endeavoring to obtain data from as large a number of groups as possible in order to reflect the real world experience of biopsy procedures.