Anders Bengtsson, professor at the Department of Rheumatology, and his research team is studying systemic lupus erythematosus (SLE) in a number of unique projects. These projects include a study on an incipient cohort of SLE patients, a study which have been ongoing for almost 40 years, as well as translational research to help understand the pathophysiology of the disease. The ultimate goal with the research is to study the biological events in SLE and determine the connection between the changes and disease progression.

One of Anders Bengtsson’s longest going projects is a study on an incipient cohort of SLE patients, a project which started 1981. The project involves regular and continuous examination of patients with SLE to detect biological and clinical changes which can be associated with the disease. The project is unique since close to 100% of new cases of SLE are detected, provided that the patient, at some point, has sought care and has a medical record. The data acquired in the study to identify new SLE cases come from different clinical (immunology, diagnostics, pathological) and primary care registries to detect patients in an early stage of SLE which have yet to receive a diagnosis. Today, the cohort includes roughly 300 patients in southern Sweden, and important data on long term prognosis have been the result of the project.

The cohort study is also connected to a large biobank with samples from different time points of disease. These samples are used in a translational research project with an aim to determine what factors could be contributing to the increased risk of cardiovascular disorders, such as stroke, in SLE patients. One group of proteins which is currently under investigation is the type 1 interferons.

“Type 1 interferons are normally highly expressed during virus infections. However, patients with SLE also display elevated levels of type 1 interferons”, says Anders Bengtsson.

The research suggests that the increased expression of type 1 interferons is causing disruptions in the innate immune system, which in turn contribute to the increased risk of cardiovascular disorders. Platelets have been shown to express a type 1 interferon gene profile in SLE patients as they dissociate from the megakaryocytes. They also appear smaller compared to platelets from healthy donors, an observation which raises some questions.

“The small platelets in SLE patients have us wonder whether they are apoptotic already as they are released from the megakaryocytes”, says Anders Bengtsson.

Patients with SLE usually have poor processing of apoptotic cells; a hallmark of SLE. If the platelets in SLE patients are already apoptotic as they enter the blood stream they too would also be poorly processed. An increase in the number of circulating, poorly-processed, platelets could be a contributing factor to an increased risk of cardiovascular disorders in SLE patients.

In addition to the platelets, neutrophils and neutrophil extracellular traps (NET) are also suspected to add to the problem. However, instead of focusing on NETs themselves, Anders Bengtsson and his research team are focusing more on mechanisms neutrophils use to generate NETs. They have found that some SLE patients display a lower production rate of reactive oxygen species (ROS), which are important for initiating NET production. The ROS production also decreased relative to the disease progression in these patients.
So, what could be the cause to this decrease? One possible explanation Anders Bengtsson is investigating is a mutation in the human neutrophil cytosolic factor 1 (NCF-1) gene. It has been implied in animal studies that mutations in the animal NCF-1 gene disrupts the host’s ability to produce ROS. The same mutation was also found in a number of SLE patients, and these patients displayed a similar impairment in ROS production.

Despite mutations in human NCF-1, there is still an active NET production in SLE patients with the phenotype. It is not determined if neutrophils use an alternate pathway to generate NETs, or if the NET composition is different from NETs generated with ROS.

“The significance of NETs in SLE is still debatable. They could just as well be the result of a bystander effect”, says Anders Bengtsson.

Having previously changed the clinical approach to monitoring disease progression in SLE patients, Anders Bengtsson is now hoping to contribute to yet another improvement by trying to identify the underlying causes to increased risk of cardiovascular disorders in SLE patients. Anders Bengtsson is positive that with the development of future technologies in proteomics and genomics it will not only be possible to push the research on SLE further, but maybe even preventing the disease from progressing.

“If we can stop the disease progression we would prevent the irreversible tissue damage and avoid the use of treatments such as cortisone which cause adverse effects”, says Anders Bengtsson.

- Joakim Hising