The UGrasp project

Long-term vision of UGrasp

The application of systems medicine to multiple clinically overlapping but molecularly distinct diseases will lead to an unprecedented possibility to start treatment of these patients on a molecular taxonomy rather than using a clinical diagnosis, in other words, initiating true personalized medicine.

At a glance

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Project description

Within the UGrasp initiative we focus on the concealed causative multi-domain inflammatory pathways that are accountable for diseases in several clinically distinct and archetypical forms of chronic inflammation (Scleroderma, Uveitis, Sjogren’s disease, SLE, Psoriatic Arthritis) that collectively form a major European health burden. To this end, we will use a Systems Medicine approach that combines in depth phenotyping of the peripheral immune-compartment of patients and mathematical modelling of the derived high-throughput data to reveal the preparatory epigenetic mechanisms that drive chronic inflammatory diseases. The systems medicine approach is very well suited for monitoring early clinical trials and the knowledge derived from this strategy will be pivotal to achieve precision medicine in the near future.

In the last decade, experimental and clinical evidence has revealed unequivocal evidence for a complex and dynamic interaction of multiple layers of the immune system in the pathophysiology of chronic inflammatory diseases that comprises altered gene expression in multiple cell subsets, various cytokines and circulating regulatory molecules (e.g. microRNAs) and delineate the need for better understanding of the underlying causative molecular pathways. This highly justifies an integrated and State-of-the-Art approach for which we propose to employ Systems Medicine taking into account multiple layers (epigenome, methylome, transcriptome, metabolome, etc.) from a group of clinical well-defined patients. Systems Medicine is an interdisciplinary approach that systematically describes the complex interactions between all parts of the human biological system. To this aim, data are collected from all the components of a biological system analyzed and integrated in order to generate a mathematical model that describes or predicts the response of the system to individual perturbations. To delineate these networks acquisition of high throughput analyses of distinct layers (e.g. mRNA, microRNA, methylation status, proteome) and various cellular subsets (e.g. T cells, dendritic cells, B cells, NK cells) that constitute the network is obligatory.

The Laboratory of Translational Immunology (LTI) invests in translational research topics exploiting state-of-the art scientific technology and is in close proximity to the large outbound patient departments of the University Medical Center Utrecht (The Netherlands) that has the largest combination of several unique forms of chronic inflammatory disease (including Sjogrens Syndrome (pSS), Systemic sclerosis (SSc), Systemic Lupus erythematosus (SLE), Psoriatic arthritis (PsA), seronegative spondylarthropathies (SpA), rheumatoid arthritis, psoriasis, uveitis and age-generated macula degeneration), fibrotic conditions as well as infectious conditions, in the world. The expertise in translational research, intervention, treatment and systems medicine makes it a perfect opportunity to collaborate with leading pharma partners in novel therapeutic
intervention and biomarker studies. The key advantage of the UGrasp project is the possibility to investigate if the underlying pathways are shared with molecularly/clinically similar immune disorders or other related systemic autoimmune diseases within the same institute. The ultimate goal thereby is to start treating patients on the basis of molecular taxonomy rather that clinical diagnoses true which more effective therapy will be given to patients and eventually, health care costs will be significantly lowered.

**Conclusions**

Very recently, by employing a systems medicine approach we revealed important molecular pathways that lead to some paradigm shifting results in scleroderma [1]. This validated the use of this approach in the field of immunology on the basis of which we can now start to unravel the molecular pathways of other chronic inflammatory diseases.

**Selected readings/references**