Using artificial intelligence to quantify cellular senescence in renal biopsies and predict outcome after kidney transplantation

Summary for layperson

Aging is a complex biological process, closely linked to cellular senescence, a persistent state of cell-cycle arrest limiting the proliferative life span of cells. Senescent cells accumulate during age or in response to cellular stress, and produce inflammatory cytokines contributing to age-related diseases such as cancer, osteoarthritis, atherosclerosis, neurodegenerative disorders and chronic kidney disease. In fact, experimental and clinical studies indicate that cellular senescence is a critical element in different renal pathologies. According to the senescence theory of aging, the “biological (or molecular) age” of an individuum can be estimated by measuring the total burden of senescent cells. As a result of pathological processes triggering cellular senescence, the biological age does not always correlate with the chronological age and might differ among organs in the same individuum. Therefore, the ability to selectively measure the biological age of a tissue would have many scientific and clinical implications. The application of machine learning on large “omics” datasets provides novel opportunities to investigate complex, multifactorial problems, such as the biology of aging.

The aim of this study is to take advantage of the power of artificial intelligence to translate the current knowledge on cellular senescence into clinical nephrology through the identification of a transcriptional profile to quantify cellular senescence in renal biopsies. We will apply computational algorithms on RNAseq datasets of well-characterized experimental models, in which senescence is triggered in cell lines *in vitro,* and cohorts of human renal biopsies from healthy people to generate a transcriptional signature to quantify senescence specifically suited for the human kidney. The aim is to obtain a reliable indicator of renal age, which can be applied to improve diagnostics and prognosis estimation. As a first clinical application, we will use this newly developed indicator of renal senescence to predict renal outcome after kidney transplantation.

This study will take advantage of novel computational technologies to translate the increasingly recognized role for cellular senescence in kidney pathophysiology into clinical praxis. In the context of transplantation, a simple score to predict long-term outcome would help in the clinical management of kidney transplant recipients and – if the predictive value would be confirmed at time point of surgery – to optimize renal allograft allocation. The same approach can be applied to any renal pathology and not only in the kidney. Therefore, if successful, this study might pave the way for similar studies in a variety of clinical conditions.