



Shaping Tomorrow's Nephrology: Insight-Driven Kidney Care

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Effects of Immunosuppressive Therapy on Cellular Aging in Kidney Transplant Recipients: An Integrative Approach

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Objectives : Long-term immunosuppressive therapy remains indispensable for maintaining graft function in kidney transplant recipients (KTRs). However, accumulating evidence suggests that sustained exposure to these agents may promote cellular aging and contribute to chronic allograft injury and systemic complications. While cellular senescence and the senescence-associated secretory phenotype (SASP) have emerged as key processes in aging biology, their roles in the context of immunosuppression-particularly at the level of specific cell types and tissue microenvironments-have not been clearly defined.

Methods : We tried to perform an integrative analysis combining publicly available datasets with prospectively collected clinical samples. A reference framework was established by integrating genetic regulatory data from GTEx, transcriptomic profiles from GEO, and curated senescence-related gene sets from CellAge. In parallel, tissue, urine, and peripheral blood samples were collected from KTRs undergoing protocol biopsies at one-year post-transplantation across different age groups. These data were analyzed to capture both systemic and tissue-level molecular alterations associated with immunosuppressive exposure.

Results : This integrative approach is expected to identify key senescence-associated genes and pathways modulated by immunosuppressive therapy, including differential activation of cellular senescence programs and SASP components across renal cell types. By linking gene expression patterns with genetic regulatory variants, we tried to uncover inter-individual variability in aging responses.

Conclusions : This study provides a framework for examining how immunosuppressive therapy shapes aging-related processes in transplanted kidneys. Defining key molecular drivers of this response may support the development of more refined immunosuppressive strategies that limit aging-related injury while preserving graft function, ultimately contributing to improved long-term outcomes in KTRs.