THE KOREAN SOCIETY OF NEPHROLOGY
APCN & KSN 2024
June 13(Thu) - 16(Sun), 2024 Coex, Seoul, Korea
APSN
Promoting Sustainable Kidney Health: The Asia-Pacific and Beyond

Submission No. : CKD2-0003
Session Title : Chronic Kidney Disease 2
Session Topic : Translational Research and Nover Therapeutic Targets in CKD
Date & Time, Place : June 14 (Fri) / 10:30-12:00 / Room 3 (GBR 104-105)

Tertiary lymphoid structures: A Novel Kidney Inflammation Marker and Therapeutic Target

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It is well known that aged kidneys are poorly repaired after injury compared to young kidneys; however, the mechanism underlying this is unknown. We have previously found that the formation of tertiary lymphoid structures (TLSs) in damaged aged kidneys results in prolonged inflammation and maladaptive repair. TLS is an inflammatory microenvironment formed in non-lymphoid organs during chronic inflammation, in which T and B cells are activated and proliferate. We found that TLSs form in approximately half of the cases in the aged human kidney, mature through three stages, and that more advanced stages of TLSs form when inflammation and damage in the kidney are prominent. Furthermore, we analyzed protocol biopsies of transplanted kidneys and found that TLSs could be identified in approximately half of the patients one month after transplantation and that stage II TLSs were identified in approximately 20% of patients one year after transplantation, with the same group having a worse renal prognosis after five years. Recently, we reported that CD153-CD30 signaling between senescence-associated T cells and age-associated B cells is essential for the expansion of TLSs and that blockade of this signaling leads to the suppression of TLS formation and improvement of kidney function. Furthermore, we found that TLSs induce inflammatory characteristics to proximal tubules and fibroblasts, causing their failed repair, which, in turn, support the migration and survival of hematopoietic cells, contributing to the expansion of TLSs. This may help explain the pathogenic nature of TLSs. TLS is not only a prognostic indicator but may also be a promising therapeutic target for kidney diseases.

Keywords: tertiary lymphoid tissue, tertiary lymphoid structure, inflammation, maladaptive repair