

# Investigation of the roles of tertiary lymphoid structures and their potential as therapeutic target in kidney diseases

Takahisa Yoshikawa<sup>1)</sup>, Keisuke Taniguchi<sup>1)</sup>, Yuki Sato<sup>1)</sup>, Motoko Yanagita<sup>1)2)</sup>

1) *Department of Nephrology, Graduate School of Medicine, Kyoto University*

2) *Institute for the Advanced Study of Human Biology (WPI-ASHBi), Kyoto University*

---

## **Abstract**

Tertiary lymphoid structures (TLSs) are ectopic lymphoid aggregates formed in non-lymphoid organs under chronic inflammatory conditions, such as autoimmune diseases, infections, and cancers. We demonstrated that TLSs develop in aged injured kidneys in both mice and humans, where their number and maturation stages are associated with poor renal function, suggesting TLSs as novel markers of kidney injury (*JCI Insight* 2016, *Kidney Int* 2020). TLSs have been identified in various kidney diseases, including transplanted kidneys, IgA nephropathy, and lupus nephritis, and are linked to disease severity and poor renal outcomes, highlighting their clinical significance. For instance, mature TLS formation in non-rejected transplanted kidneys predicts poor renal outcomes (*J Am Soc Nephrol* 2022). In terms of their pathogenicity, TLSs can exacerbate inflammation and kidney injury by inhibiting proximal tubule repair through excessive cytokine production and promoting proinflammatory phenotypes in the damaged tubules (*J Am Soc Nephrol* 2023). Immunosuppressant treatments can reduce TLS formation and mitigate kidney injury, indicating TLSs as potential therapeutic targets (*Kidney Int* 2020). Additionally, we demonstrated that senescence-associated T cells and age-associated B cells accumulate within TLSs and interact via CD153-CD30 signaling, promoting TLS expansion and aggravating kidney injury (*J Clin Invest* 2022). Therefore, we are currently working on development of therapeutic approaches targeting CD153-CD30 signaling to improve outcomes in kidney diseases with TLS formation.