Nov. 15<sup>(Wed)</sup>~18<sup>(Sat)</sup>, 2023 Conrad Seoul, Korea

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Session: KST-TST Joint Symposium

Date & Time, Place: November 18 (Sat), 11:00-12:30, Room 3F-1

Session Title: Hot topics in kidney transplantation

## Glutamine Deprivation Prevents Graft Rejections through the Metabolic-Epigenetic Axis

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T cell fate and function is closely related to nutrient uptake and utilization. Here we demonstrate that glutamine deprivation switch Th17 cells to Treg cells in a time and dose dependent manner accompanied with low  $\alpha$ -ketoglutarate-mediated HIF1 $\alpha$  destabilization. Furthermore, the epigenetic regulation on IL-17 $\alpha$  and FOXP3 promoter was altered through H3K4Me3 and H3K9Me3 modification modulated by KDM4C. Concurrently, hypomethylation of the FOXP3 promoter occurred under glutamine-free conditions lead to attenuated intracellular glutathione levels and elevated levels of reactive oxygen species from fatty acid  $\beta$ -oxidation. Experimental autoimmune encephalomyelitis and skin transplant model show glutamine deprivation ameliorates Th17 cells induced autoimmune response and enhances suppression function of Treg cells. Together, these findings highlight the critical role of glutamine in T cell immunity through a metabolic-epigenetic axis.