Singapore Immunology Network

A*STAR

SIgN SEMINAR

hosted by Dr Ng Lai Guan

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Macrophage clearance function requires glutaminase-dependent metabolism

Macrophage plasticity and adaptability to local environmental cues rely on a rapid metabolic rewiring. Glutaminase (GLS) converts glutamine to glutamate to fuel anabolic processes and support redox and epigenetic reactions. Here, we identify a key role for GLS in macrophage effector functions. Though GLS deficiency diminished alternative macrophage polarization, loss of GLS1 also reduced macrophage efferocytosis. This was neither associated with canonical glutamate dehydrogenase (GLUD1)-dependent conversion of glutamate into α-ketoglutarate in the mitochondria to fuel the tricarboxylic acid cycle or epigenetic modifications or classical mTor-dependent metabolic reprogramming. Gls1 deficient macrophages rather refocused cellular metabolism to a high redox state and a low transamination-dependent mitochondrial efficiency. Targeted deletion of GLS1, but not Glud1, in myeloid cells resulted in failure of apoptotic cell uptake and subsequent macrophage infiltration in the vessel wall leading to necrotic core formation within atherosclerotic plaque. Our findings position glutaminase-dependent metabolic reprogramming as a critical process that enables continued clearance of ACs by macrophages to avoid the pathologic consequences of defective efferocytosis in vivo.

10 September 2019 (Tuesday)
11:00am – 12:00pm
SIgN Seminar Room, Immunos Level 4

Seminar is open for all to attend.

Registration is not required.

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