Erasmus MC
University Medical Center Rotterdam

Department of Immunology

Immunology Seminar Thursday, May 9, 2019, 16:00 hrs.
Library Dept. Immunology, 12th floor room Na-1202k

"Are you always what you eat? The links between T cell metabolism and function"

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Regulation of $CD8^+$ T cell fate and function is strongly linked to metabolic reprogramming. The flexibility of T cell metabolism is crucial for activation, differentiation, survival and function in vivo. Glycolytic engagement after T cell activation is dependent on CD28-mediated signalling and increased glucose import, mediated by the upregulation of glucose transporters. During acute glucose restriction (AGR) or differentiation, $CD8^+$ T cells are dependent on CD28 costimulation-dependent mitochondrial remodelling for survival and prolonged function. During AGR, the enhanced mitochondrial capacity is accompanied by upregulation of the facilitative glucose transporter GLUT1, contributing to enhanced glucose transport capacity. In concert with this, AGR $CD8^+$ T cells display altered subcellular redox balance, which is rapidly reverted upon glucose re-exposure. The enhanced transporter expression and altered redox balance facilitate augmented glucose import and altered carbon allocation after extracellular glucose is replenished. This metabolic network supports metabolic remodelling during transient substrate limitation. By coculturing metabolically conditioned antigen-specific $CD8^+$ T cells with tumour spheroids, we observed enhanced effector cytokine production in a model of substrate competition in the tumour microenvironment. We believe that metabolic conditioning can be utilized to enhance therapeutic efficiency of T cell products for adoptive cellular therapy.

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