

Regulation of Nutrient Transporter Expression During T Cell Activation

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The activation of resting T cells is a highly energetically demanding process. T cells more than double in size, and they are transformed from quiescent cells into rapidly dividing and biosynthetically active blasts. These changes require dramatic alterations in cellular metabolism to accommodate increased biosynthetic and energetic needs. We have previously shown that T cell activation leads to upregulation of glucose transport and glycolysis, and that this is dependent on signals from both TCR and CD28, including PI3K signaling. However, it is likely that multiple nutrient utilization pathways are affected during T cell activation. The cell membrane serves as a barrier for nutrient uptake, requiring the expression of nutrient-specific transporters on the cell surface. We have examined the expression of the glucose transporter GLUT1, the amino acid transporter-associated heavy chain 4F2 (CD98), and the transferrin receptor (CD71) during T cell activation. Expression of all three transporters is increased by anti-CD3/anti-CD28 stimulation, although to differing extents and following different kinetics. Studies using specific inhibitors indicate multiple signaling pathways (including mTOR, PI3K, ERK, and p38 MAPK) contribute to transporter upregulation, with each pathway partially responsible for the increased expression.