Thomas M. Yankee, J Vaccines Vaccin 2012, 3:4
http://dx.doi.org/10.4172/2157-7560.S1.005

OMICS Group Conferences
Accelerating Scientific Discovery

2nd International Conference on
Vaccines and Vaccination

August 20-22, 2012 Hilton Chicago/Northbrook, USA

TCR signaling pathways regulating CD8$^+$ T cell survival during the expansion phase

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Infection with Listeria monocytogenes results in robust expansion of antigen-specific CD8$^+$ T cells. The extent of the expansion is controlled by the fine balance between cell proliferation and cell death, which are controlled by the signals downstream of the T cell receptor (TCR). Ligation of the TCR triggers the assembly of an adaptor protein complex consisting of LAT, Gads, and SLP-76. Gads binds phosphorylated LAT and recruits SLP-76 into the complex. The LAT/Gads/SLP-76 complex recruits PLCγ1, ultimately leading to the mobilization of intracellular calcium. To investigate the function of the LAT/Gads/SLP-76 complex during a CD8$^+$ T cell-mediated immune response, we crossed our Gads$^{-/-}$ mouse line with OT-I mice. OT-I mice express an MHC class I-restricted TCR that binds SIINFEKL, a peptide derived from chicken ovalbumin. Naïve CD8$^+$ T cells from Gads$^{+/+}$ and Gads-/- OT-I mice were adoptively transferred into wild-type mice which were subsequently infected with recombinant strains of L. monocytogenes that express ovalbumin (rLM-ova) or a mutated form of ovalbumin that generates mutated forms of ovalbumin (rLM-APL). We found that the peak of the expansion phase was reduced when the CD8$^+$ T cells lacked Gads or were stimulated with rLM-APL. However, the mechanisms behind the reduced expansion are different. Gads-deficiency resulted in reduced survival while low affinity antigens stimulated less proliferation. We conclude that the signaling pathways regulating survival and proliferation of expanding CD8$^+$ T cells are different and more research needs to be performed to dissect these pathways.

Biography

Dr. Yankee received his Pharm.D. from the University of Illinois at Chicago in 1995. In 1999, he completed his Ph.D. from the Department of Medicinal Chemistry and Molecular Pharmacology at Purdue University in West Lafayette, Indiana. He then joined the laboratory of Dr. Edward Clark at the University of Washington in Seattle, Washington. In 2005, he joined the faculty at the University of Kansas Medical Center in Kansas City, Kansas as an Assistant Professor. Dr. Yankee was promoted to Associate Professor in 2011. Dr. Yankee's primary research interests include the signaling pathways that regulate T cell development and activation

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