

## ***Asymmetric T Lymphocyte Division Initiating Adaptive Immunity***

Steven L. Reiner

*Abramson Family Cancer Research Institute and Department of Medicine, University of Pennsylvania, Philadelphia, PA 19104, USA*

A hallmark of the adaptive immune response is heterogeneity of cell fate among antigen-experienced T lymphocytes. Whether diversity could emanate from the progeny of a single naïve T cell has not been resolved. We found that the first division of a T cell responding to a pathogen *in vivo* is characterized by unequal partitioning of proteins with established roles in signaling, cell fate specification, and asymmetric cell division. The polarity signature of the dividing T cell, together with mutations that disrupt polarity, suggest that asymmetric partitioning is aligned perpendicular to the mitotic spindle owing to a sustained interaction between the T cell and its antigen-presenting cell prior to division. Additionally, the first daughter T cells from the immune response display phenotypic and functional indicators of being differentially fated as the precursors of the effector and memory lineages. These results reveal an unappreciated mechanism for mobile somatic cells to apportion diverse cell fates during division and provide a plausible mechanism for a single T cell undergoing clonal selection to achieve both terminal differentiation and self-renewal.

These studies were supported by the NIH and the Abramson Family.

### **Citations:**

Chang, J.T., V.R. Palanivel, I. Kinjyo, F. Schambach, A.M. Intlekofer, A. Banerjee, S.A. Longworth, K.E. Vinup, P. Mrass, J. Oliaro, N. Killeen, J.S. Orange, S.M. Russell, W. Weninger, and S.L. Reiner. 2007. Asymmetric T lymphocyte division in the initiation of adaptive immune responses. *Science* 315:1687-1691.

Intlekofer, A.M., N. Takemoto, C. Kao, A. Banerjee, F. Schambach, J.K. Northrop, H. Shen, E.J. Wherry, and S.L. Reiner. 2007. Requirement for T-bet in the aberrant differentiation of unhelped memory CD8+ T cells. *J Exp Med* 204:2015-2021.

Reiner, S.L. 2007. Development in motion: helper T cells at work. *Cell* 129:33-36.

Reiner, S.L., F. Sallusto, and A. Lanzavecchia. 2007. Division of labor with a workforce of one: challenges in specifying effector and memory T cell fate. *Science* 317:622-625.