

## INITIATION OF AUTOIMMUNE DIABETES GOVERNED BY BETA CELL DEATH

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Autoimmune diabetes begins with the activation of naïve, potentially diabetogenic T cells, a developmentally regulated process that occurs in the pancreatic lymph node (PLN). To uncover factors that control beta-cell specific T cell priming, we examined two probable contenders: the antigen presenting cell and the target cell. *In vivo* studies ruled out alterations in the development or function of PLN dendritic cells (DCs) as determinants of diabetes initiation. Beta cell death, on the other hand, exerted control on the timing and extent of T cell priming. By blocking the death-signaling pathway in beta cells, we established that beta cell turnover is required for optimum priming of naïve, autoreactive CD4<sup>+</sup> T cells. We propose that beta cell death provokes diabetogenic T cell priming by intensifying antigen capture and presentation by DCs. Autoimmunity may be provoked by the death of parenchymal cells during tissue remodeling.