

## **Discovery of a pancreatic lipase in cytotoxic T lymphocytes.**

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Anti-viral and anti-tumor immunity is dependent upon lymphocyte-mediated killing of pathogenic cells. The cytotoxic granules of CD8<sup>+</sup> T and natural killer lymphocytes are extremely potent effectors of cellular apoptosis. We examined whether some of the unknown granule proteins could augment the deadly processes mediated by the cytotoxic proteins perforin and granzymes. Lipases, having phospholipids as their natural substrate, may increase membrane permeability and/or mediate damage directly. The gene encoding a digestive pancreatic lipase, pancreatic lipase related protein 2 (PLRP2), is expressed in IL-4 stimulated splenocytes which have differentiated into cytotoxic T cells and is also constitutively expressed in the cytotoxic T cell line CT.4R (Grusby M, Glimcher L, Cell 1990). Yet after the discovery of this gene, investigators were unable to detect the presence of this protein in lymphocytes though PLRP2 was readily detectable in pancreatic granules. Our lab has now detected the presence of the PLRP2 protein within the granule extract of the CT.4R cell line using polyclonal antibodies to a PLRP2 peptide. Using conA-stimulated T cells from mouse splenocytes and grown in IL-4, a combination of IL-2 and IL-4, our lab was able to detect the gene expression of PLRP2 on days 3, 7 and 14, with increases in expression at each time point. In addition, we have observed a reduction in killing of the PLRP2 KO mice cytotoxic T cells compared to wild type using <sup>51</sup>Cr release assays while the granzyme B levels were similar. These observations raise the possibility that PLRP2 is a functional component of the cytotoxic granules and that it may be secreted upon stimulation to either promote death or clearance of infected cells. Supported in part by NIH R01CA38942 and T3209563.