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"Ex vivo induction and expansion of Human Natural Killer T cells by CD1d1-Ig coated artificial antigen presenting cells"

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Background: Natural killer T (NKT) cells comprise a specialized subset of T lymphocytes that express cell surface markers characteristic of NK cells. The ability of these cells to produce cytokines, activate cells of both the innate and adaptive immune responses, and recognize antigen in the context of CD1d molecules strongly suggest that NKT cells play a pivotal role in maintaining immune homeostasis. Moreover, many studies examining patients with autoimmune disease or cancer have shown that there is a reduction in both NKT cell number and function. Thus, these data suggest that rather than direct *in vivo* NKT cell modulation, *ex vivo* expanded effector NKT cells would be an excellent therapeutic modality. To date, immunotherapy utilizing the NKT/CD1d system has been limited by the use of autologous DC in the presence or absence of a synthetic glycolipid, α-galactocylceramide. However, the quantity and quality of autologous DCs can vary substantially based on the underlying disease and the patient's pre-treatment regimen. Consequently, our lab has developed a novel technique for generating artificial antigen presenting cells (aAPC), which can facilitate the growth of primary T cells.

Design: We have utilized this unique system to generate CD1d expressing aAPC. aAPC were made by coupling CD1d-Ig and anti-CD28 Abs to magnetic beads. In this system, CD1d-Ig was used to provide the cognate antigen specific signal through the TCR and anti-CD28 Abs provided the costimulatory signal. To expand the NKT cell population, T cells were isolated from peripheral blood mononuclear cells (PBMC), and then co-cultured with lipid-pulsed aAPC.

Results and Conclusion: Our data demonstrate that these CD1d-based aAPC can effectively propagate canonical ($V\alpha14^+$) and noncanonical ($V\alpha14^-$) NKT cells. Further studies will be performed to characterize the phenotype and function of aAPC-expanded NKT cells. Collectively, these studies will enhance our knowledge of NKT cell biology and could potentially be used as a novel adoptive immunotherapeutic strategy.