

**P050** Analysis of the Role of PI3K Isoforms in CXCR4- and CXCR3-Mediated T Lymphocyte Chemotaxis.

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Previous work in transformed cell lines and PI3K mutant mice, have revealed that different phosphoinositide 3-kinase (PI3K) isoforms can make varying contributions to T lymphocyte chemotaxis. We assessed the effect of broad spectrum inhibitors (LY294002 and Wortmannin) and siRNAs directed against specific PI3K isoforms in freshly isolated and cultured human T lymphocytes (with and without IL-2) on chemotaxis.

We show that CXCR4-mediated chemotaxis of freshly isolated human T lymphocytes is significantly inhibited by LY294002 and Wortmannin. However, following culture with or without IL-2, T lymphocytes, become insensitive to these PI3K inhibitors. This pattern of PI3K inhibitor resistance also extends to CXCR3-mediated chemotaxis.

This data was supported by delivery of PI3K isoform specific siRNA into T lymphocytes via the Amaxa Nucleofector™ device. We show that a 60 % reduction of individual PI3K isoforms has no significant effect on CXCR4-mediated chemotaxis. Yet, despite the lack of effect on the chemotactic response we demonstrate that the cytokine profile elicited by CD3/CD28 activation indicates a surprising increase in IL-8 production.