

P057 Evidence of a PI3-K independent role for PKB/Akt in T lymphocyte chemotaxis

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Chemokine directed migration of T lymphocytes is critical for the adaptive immune response. The phosphoinositide 3-kinase (PI3-K) signalling pathway is pivotally involved in directional cell migration of neutrophils and monocytes. However, data suggests that PI3-K is a dispensable signal in T lymphocyte migration. Protein kinase B (PKB)/Akt is a major proximal downstream component of the PI3-K –dependent signalling cascade, however due to poor selectivity of inhibitors the role of PKB has been difficult to explore pharmacologically. In 2005, a new class of PH domain-dependant inhibitors were described that show greater than 50-fold selectivity for Akt 1/2 over other closely related AGC family kinases. This inhibitor, Akti-1/2 (Calbiochem), was used to determine whether PKB/Akt was also dispensable in T lymphocyte signalling. Addition of the Akt inhibitor abrogated chemotaxis in primary and CEM cell-line models of PI3-K independent chemotaxis (IC₅₀ 9.15 μ M and 7.3 μ M respectively). Further pharmacological analysis using Ro-32-0432, which preferentially inhibits conventional and novel PKC isoforms, has revealed a potential role for protein kinase C in the phosphorylation of PKB/Akt. In summary, our data indicates a potential PI3-K independent role for PKB/Akt in T lymphocyte chemotaxis.