

T CELL CHEMOTAXIS TO LYSOPHOSPHATIDYLCHOLINE VIA G2A RECEPTOR

Caius G. Radu*, Li V. Yang[†], Mireille Riedinger[†], Matthew Au* and Owen N. Witte*[†]

*Department of Microbiology, Immunology and Molecular Genetics, UCLA

[†]Howard Hughes Medical Institute, UCLA

G2A is an immunoregulatory G protein-coupled receptor (GPCR) predominantly expressed in lymphocytes and macrophages. Ectopic overexpression studies have implicated G2A as a receptor for the bioactive lysophospholipid lysophosphatidylcholine (LPC). However, the functional consequences of LPC-G2A interaction at physiological levels of receptor expression and in a cellular context relevant to its immunological role remain largely unknown. Here we show impaired chemotaxis to LPC of a T lymphoid cell line in which G2A expression was chronically downregulated by RNA interference (RNAi) technology. Rescuing this phenotype by reconstitution of the physiological level of receptor expression further supports a functional connection between LPC-G2A interaction and cellular motility. Overexpression of G2A in the T lymphoid cell line significantly enhanced chemotaxis to LPC. It also modified migration towards the LPC related molecule lysophosphatidic acid (LPA), indicating the possibility of cross-talk between G2A and endogenous LPA receptors. The role of G2A in LPC mediated cell migration may be relevant to the autoimmune syndrome associated with genetic inactivation of this GPCR in mice. The experimental system described here can be useful for understanding the structural requirements for LPC recognition by G2A and the signaling pathways regulated by this ligand-receptor pair.