J Clin Cell Immunol 2017, 8:3(Suppl)
DOI: 10.4172/2155-9899-C1-037

Investigation of a T cell subset that constitutively signals via STAT1 activation and is unresponsive to JAK1 inhibition: A potential mechanism of T cell subset autoimmune activation

Christopher Gaunt[1, 2]
[1]University of Cambridge, UK
[2]GlaxoSmithKline, UK

Introduction: JAK-STAT (Janus kinase-signal transducer and activator of transcription) is a conserved cell signalling pathway responsible for transduction of signal induced by receptors for a diverse range of interferons, cytokines and growth factors. Polymorphisms of JAKs and STATs are functionally and clinically relevant to a variety of human diseases, particularly cancer and immune-related, but also common multigenic diseases.

Statement of the Problem: A population of CD4+ T cells demonstrating constitutive STAT1 phosphorylation were identified both in systemic lupus erythmatosus (SLE) patients and healthy volunteers. STAT1 phosphorylation in these cells is both independent of IL-6 stimulation and resistant to JAK1 inhibition. These cells may represent a novel paradigm of JAK-independent STAT activation, giving rise to a pathogenic population that is aberrantly regulated during activation in autoimmune disorders. The aim of this preliminary research was to confirm the existence of this population and begin characterisation of an extracellular phenotype in the hope of identifying population-specific markers.

Methods: The expression of various surface (CD3, CD4, CD25, CD127, CD45RA, CD197, CXCR3 and CCR6) and intracellular (pSTAT1, pSTAT5, FOXP3) markers in whole blood or isolated lymphocytes from 106 healthy volunteers were analysed by flow cytometry.

Results: The constitutively signalling population was demonstrated to persist for up to 48 h in un-stimulated samples and in the presence of a selective JAK1 inhibitor. The population demonstrated a CD25 low/intermediate and CD127+ phenotype, with FOXP3 expression in some cells. The population was shown to be CD45RA-, indicative of a T-memory cell phenotype. Chemokine receptor analysis demonstrated the population to be CXCR3- and CCR6+, indicative of a Th17-like phenotype.

Conclusion: The constitutive STAT1 signalling population may represent a terminally activated group of CD4+ cells that can no longer regulate STAT activation through potential loss of regulatory mechanisms (SOCS) or constitutive kinase activation, that may be driving autoimmune disease.

cmg65@cam.ac.uk