

# **Defective TLR9-driven STAT3 activation in B cells of patients with CVID**

Borzutzky, Arturo; Rauter, Ingrid; Fried, Ari; Rachid, Rima; McDonald, Douglas R.; Hammarstrom, Lennart; Grimbacher, Bodo; Abraham, Roshini S.; Geha, Raif S.

## **Abstract**

B cell activation by Toll-like receptor 9 (TLR9) ligands is dependent on STAT3 and is important for optimal antibody responses to microbial antigens. B cells from patients with common variable immune deficiency (CVID) have impaired proliferation and differentiation in response to the TLR9 ligand CpG, despite normal levels of TLR9 expression. We demonstrate that CpG-driven STAT3 phosphorylation, but not activation of NF $\kappa$ B and p38, is selectively impaired in B cells from CVID patients. These results suggest that defective STAT3 activation contributes to the defective TLR9 and antibody response of B cells in CVID.

## **Keywords**

B cells; Common variable immunodeficiency; STAT3 Transcription factor; Toll-like Receptor 9.