**UKE Paper of the Month November 2016**

Science 21 Oct 2016:Vol. 354, Issue 6310, pp. 358-362

**A pathogenic role for T cell–derived IL-22BP in inflammatory bowel disease**

Penelope Pelczar, Mario Witkowski,Laura Garcia Perez, Jan Kempski, Anna G. Hammel, Leonie Brockmann, Dörte Kleinschmidt, Sandra Wende, Cathleen Haueis, Tanja Bedke, Marco Witkowski, Susanne Krasemann, Stefan Steurer, Carmen J. Booth, Philipp Busch, Alexandra König, Ursula Rauch, Daniel Benten, Jakob R. Izbicki, Thomas Rösch, Ansgar W. Lohse, Till Strowig, Nicola Gagliani, Richard A. Flavell, Samuel Huber

**ABSTRACT:**
Intestinal inflammation can impair mucosal healing, thereby establishing a vicious cycle leading to chronic inflammatory bowel disease (IBD). However, the signaling networks driving chronic inflammation remain unclear. Here we report that $CD4^+$ T cells isolated from patients with IBD produce high levels of interleukin-22 binding protein (IL-22BP), the endogenous inhibitor of the tissue-protective cytokine IL-22. Using mouse models, we demonstrate that IBD development requires T cell–derived IL-22BP. Lastly, intestinal $CD4^+$ T cells isolated from IBD patients responsive to treatment with antibodies against tumor necrosis factor–α (anti–TNF-α), the most effective known IBD therapy, exhibited reduced amounts of IL-22BP expression but still expressed IL-22. Our findings suggest that anti–TNF-α therapy may act at least in part by suppressing IL-22BP and point toward a more specific potential therapy for IBD.

**STATEMENT:**
*"We identified in a translational interdisciplinary approach a new mechanism of IBD pathogenesis. TNF-α antibodies are currently one of the most effective therapies of IBD, but what determines response to anti-TNF-α therapy in IBD remained elusive. Our data suggest that anti-TNF-α therapy may block IL-22BP expression by intestinal T cells, thus allowing IL-22-induced mucosal healing. Our data imply that targeting IL-22BP directly might allow for a more effective and specific therapy of IBD without invoking the undesirable and potentially dangerous side effects of anti-TNF-α antibodies such as susceptibility to infections. Furthermore IL-22BP might serve as a biomarker to predict response to anti-TNFalpha therapy."*

**BACKGROUND:**
This work was performed at the I. Department of Medicine in the group of Samuel Huber who holds a professorship at UKE since 2013. This work was mainly performed by Dr. Penelope Pelczar, Dr. Mario Wittkowski and Laura Garcia Perez. It was part of the PhD thesis of Laura Garcia Perez within the DFG research training group "SFB841".