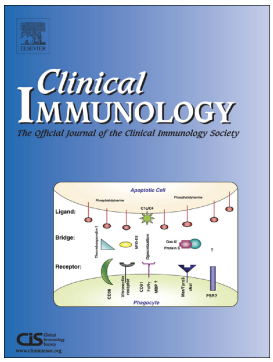
CVID enteropathy is characterized by exceeding low mucosal iga levels and interferon-driven inflammation possibly related to the presence of a pathobiont



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PII: S1521-6616(18)30294-8
DOI: doi:10.1016/j.clim.2018.09.008
Reference: YCLIM 8102

To appear in: *Clinical Immunology*

Received date: 25 April 2018
Revised date: 2 August 2018
Accepted date: 16 September 2018

Please cite this article as: Natalia Shulzhenko, Xiaoxi Dong, Dariia Vyshenska, Renee L. Greer, Manoj Gurung, Stephany Vasquez-Perez, Ekaterina Peremyslova, Stanislav Sosnovtsev, Martha Quezado, Michael Yao, Kim Montgomery-Recht, Warren Strober, Ivan J. Fuss, Andrey Morgun , CVID enteropathy is characterized by exceeding low mucosal iga levels and interferon-driven inflammation possibly related to the presence of a pathobiont. Yclim (2018), doi:10.1016/j.clim.2018.09.008

CVID Enteropathy is Characterized by Exceeding Low Mucosal IgA Levels and Interferon-Driven Inflammation Possibly Related to the Presence of a Pathobiont

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Abstract

Common variable immunodeficiency (CVID), the most common symptomatic primary antibody deficiency, is accompanied in some patients by a duodenal inflammation and malabsorption syndrome known as CVID enteropathy (E-CVID). The goal of this study was to investigate the immunological abnormalities in CVID patients that lead to enteropathy as well as the contribution of intestinal microbiota to this process. We found that, in contrast to noE-CVID patients (without enteropathy), E-CVID patients have exceedingly low levels of IgA in duodenal tissues. In addition, using transkingdom network analysis of the duodenal microbiome, we identified *Acinetobacter baumannii* as a candidate pathobiont in E-CVID. Finally, we found that E-CVID patients exhibit a pronounced activation of immune genes and down-regulation of epithelial lipid metabolism genes. We conclude that in the virtual absence of mucosal IgA, pathobionts such as *A. baumannii,* may induce inflammation that re-directs intestinal molecular pathways from lipid metabolism to immune processes responsible for enteropathy.