Title: **Unveiling heterogenous clinical phenotypes from bulk transcriptomics data in Dermatitis Herpetiformis**

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Abstract
Dermatitis herpetiformis (DH) is an autoimmune skin condition manifesting as itchy blisters in the extremities of the body that is thought to develop from untreated celiac disease (CeD) with both forms being gluten induced. The rash in DH resolves slowly after gluten-free diet (GFD). Although the gluten-induced transcriptomic changes of the small intestine are well studied in CeD, corresponding studies have not been conducted in DH. Despite DH manifesting as a rash, it is thought that the immune response responsible for the skin symptoms originates from the gut.
To understand the relation of skin symptoms to intestinal symptoms, we have studied the transcriptomic landscape of DH patients during gluten challenge. RNA sequencing was applied to duodenal biopsies of DH patients on GFD and after a gluten challenge, as well as to DH peripheral blood mononuclear cells (PBMCs). In addition, we aimed to find transcriptomic differences between patients with different clinical outcomes.
PBMCs showed very little change during gluten challenge, with the only gene induced on day 6 being CXCR2. Intestinal biopsies on the other hand show clear inflammatory changes, similar to the gluten-induced inflammation known from CeD. Surprisingly, regardless of intestinal lesion status at the end of the gluten challenge, transcriptomic signature was similar to across patients. Especially CCL11,mmunoglobulins, and HLA-DPB1 are highly expressed post-challenge.
Our findings indicate that the gluten induced inflammation in DH gut is similar to CeD, and although differences between clinical outcomes are present, more patients would need to be examined to reach any robust conclusions.