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Impaired Th17 response of patients with chronic mucocutaneous candidasis

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Chronic mucocutaneous candidiasis (CMC) constitutes a selective inability to clear infection with the yeast *Candida albicans* resulting in persistent debilitating inflammation of skin, nails, and mucous membranes. To date the underlying defect is unknown. In order to characterise cellular immunity in CMC patients, we analysed chemotaxis and myeloperoxidase (MPO) release of neutrophils and T cell proliferation and cytokine production to *Candida albicans*. Only recently, Th17 cells have been reported to be involved in clearing Candida infections – this is why we focussed on characterizing Th17 in CMC-patients.

Patients with chronic mucocutaneous candidiasis (CMC, $n = 4$) and healthy controls and immunecompetent patient with current candida infections, of same sex and similar age ($n = 14$) were enrolled into the study. Neutrophil chemotaxis was assessed by transwell migration assay, MPO release by ELISA. T cell proliferation capacity was investigated by thymidine incorporation and cytokine secretion into supernatants by ELISA. In order to characterise the mechanisms of T cellular immune response to Candida, we analysed *in vitro* T cell IL-17 secretion in response to Candida antigen.

Neither neutrophil migration nor MPO release differed between CMC patients and healthy controls. Three out of four patients (75%) showed a higher relative lymphocyte stimulation index (SI Candida/SI PHA) than controls. However, Candida-specific IFN-gamma production was significantly reduced in CMC patients. Notably, Candida-specific T cell IL-10 production was markedly higher in CMC patients. Importantly, T cells from CMC patients produced significantly lower amounts of Th17-associated cytokines IL17 and IL22. Immunecompetent patients with Candida infections showed a much higher secretion of IL-17 than both CMC patients and matched controls. Production of IL-17 in CMC patients was also diminished after mitogen stimulation. IL-17 secretion was limited to CD4+ T cells throughout. The Th17 differentiating cytokines IL6 and IL1beta were comparable in all three groups.

The inability to clear the yeast *Candida albicans* in our CMC patients does not seem to be due to an impaired neutrophil function nor due to a reduced antigen specific proliferation of lymphocytes. In fact, our patients proliferated stronger to Candida antigen relative to PHA than healthy controls. However, the impaired IL17 cytokine production could play an important role in the pathogenesis of chronic mucocutaneous candida infections.

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