Blood immune cells and psoriasis

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Thesis title: In depth analyses of peripheral blood immune cell populations in patients with psoriasis - Effect of biological treatment and alternative medicine

Psoriasis is a chronic immune-mediated disease of the skin with systemic inflammation and accompanied comorbidities. Although the disease severity may vary over time, most patients with psoriasis suffer from mild to moderate disease. In many cases, local treatment will be sufficient to control the symptoms, but at the cost of several side effects. ω-3 poly-unsaturated fatty acids (PUFA) have shown promising results in clinical trials with mild-to-moderate psoriasis. Up to one-third of patients with psoriasis are affected with psoriatic arthritis (PsA). Targeted treatment with biologic therapies has transformed the management of both diseases. However, despite the success of therapy for some patients the existence of patients whose symptoms do not improve with applied treatment, highlight the needs for predictive biomarkers of response and more targeted treatment approach that should improve patient care and deliver substantial economic savings.

The general aim of this dissertation was to explore the systemic immune response through clinical and biological investigation and to identify disease-specific immune profiles and indicators in patients with psoriasis of different disease severity, treated with alternative medicine and biological treatment. In study I, we explored the impact of phospholipid bound

docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) contained in herring roe oil (HRO) on circulating immune cell activity and plasma cytokine levels in non-severe plaque psoriasis. The plasma concentrations of cytokines were measured by Luminex technology and circulatory immune cell activity was analyzed by multicolor flow cytometry. In study II, we employed flow cytometry to perform in-depth phenotyping of peripheral blood mononuclear cells (PBMCs) and examine their respective activity through the expression of cell surface markers in healthy controls and patients with moderate to severe plaque psoriasis/PsA on stable anti-tumor necrosis factor (TNF) treatment. In study III, we performed immune analyzes of dendritic cell (DC) populations in patients with moderate to severe plaque psoriasis/PsA, before and during therapy with the anti-TNF drugs infliximab (IFX), etanercept, the anti-IL-17A secukinumab, and the anti-IL12/IL-23 ustekinumab, to identify immune cell populations/subsets relative to clinical response. In all studies, clinical and standard laboratory parameters were incorporated in the analyses.

In study I, positive clinical outcome of ω-3 PUFAs in patients with psoriasis was possibly related to the decreased levels of CCL2 and increased levels of IFN-γ over time. Additionally, reduced activity due to lower expression of CD38 on CD4+ and CD8+ T cells, and CD56bright NK cells supported the beneficial effect of HRO supplementation. In study II, patients with psoriasis or/and PsA on stable biological treatment with infliximab (IFX) still retain imprint from the disease and have phenotypic peculiarity. The increase in active intermediate CD14+CD16+ monocytes reflected the preserved ongoing systemic inflammation. However, the beneficial effect of IFX treatment was reflected in reduced cytotoxicity of NK cells in both patient groups and CD8+ T cells in patients with PsA. In study III, explored frequencies of DC populations and their subsets differed in patients compared to controls as well as patients with psoriasis compared to PsA, but mostly did not change upon treatment. However, the persisting low levels of pDC in peripheral blood in patients with PsA might relate to the presence of arthritis and should be further investigated. Sustained reduction of CD5+ DC2 subset in secukinumab-treated patients could probably be related to the presence of PsA and lower treatment rensponsiveness.

Further studies of cytokines and peripheral blood mononuclear cells may be of great importance in the further stratification of patients for appropriate therapeutic interventions. More personalized treatment can improve quality of life and change the course of comorbidities.

Papers:

1. Petrovic A, Bueide I, Tveit KS, et al. Herring roe oil in treatment of psoriasis - influence on immune cells and cytokine network. Front Immunol. 2023 Sep 8;14:1128986. doi: 10.3389/fimmu.2023.1128986. PMID: 37744329; PMCID: PMC10515196.

2. Petrovic A, Samuelsen VM, Davies R, et al. Immune cell activity during anti-TNF treatment in patients with psoriasis and psoriatic arthritis. Clin Exp Immunol. 2024 Nov 12;218(3):329-340. doi: 10.1093/cei/uxae070. PMID: 39121030; PMCID: PMC11557139.
3. Petrovic A, Bergen LLT, Solberg SM, Biological treatment in severe psoriasis: Influence on peripheral blood dendritic cells. Scand J Immunol. 2023 Dec;98(6):e13321. doi: 10.1111/sji.13321. Epub 2023 Aug 13. PMID: 38441394.