of Malassezia induced inflammation. The exposure of human antigen-presenting cells (APCs) to different clinical isolates of Malassezia strains resulted in secretion of significant amounts of proinflammatory cytokine IL-1β. When APCs were pre-treated with Z-VAD, a pan-caspase inhibitor, the release of IL-1β upon stimulation with Malassezia was abrogated. This suggests that Malassezia-induced IL-1β secretion is dependent on inflammasome activation. To elucidate which type of inflammasome is activated, we generated cells deficient for NLRP3 or NLRP1. IL-1β release was absent in cells lacking NLRP3, whereas NLRP1-deficiency did not affect IL-1β secretion upon Malassezia exposure. Our findings indicate that Malassezia is a potent inducer of inflammatory response which is mediated through the NLRP3-inflammasome

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Lisztt-study: lichen planus mucosae at uzs, efficacy of oral alitretinoin

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Background: Lichen planus (LP) is a relatively common immunological disorder of the stratified squamous epithelium that affects one to two percent of the general adult population. The oral mucosa is involved in up to eighty percent of patients (twenty-five percent mucosal involvement only). Conventional oral retinoids (Acitretin, Etretinat, Isotretinoin and Tretinoin) are listed as evidence based treatment recommendations for LP. In comparison, Alitretinoin has shown to have additional anti-inflammatory effects and less mucocutaneous side effects, which could favorably impact this disease and thereby support patient compliance as well. Alitretinoin was not yet systematically investigated in mucosal lichen planus.

Methods: This is a single center, prospective, open label, single arm pilot study investigating the efficacy and safety of oral Alitretinoin in twenty patients suffering from severe oral mucosal lichen planus (MLP). Patients are treated with Alitretinoin thirty milligrams once daily for twenty-four weeks with a follow up of another twenty-four weeks. The primary objective is to determine the efficacy of Alitretinoin in reducing signs and symptoms of severe MLP with respect to the proportion of responders based on the ‘scoring system for mucosal disease severity’ as well as +/- (indifferent) and – (negative). Control stainings were performed at plaque psoriasis samples.

IL-33 was expressed in 86.1% of psoriasis-like pustular reactions (PPR) but only in 55.6% of dermatitis-like reactions (DLR) (p = 0.009, Fisher exact test). IL-1β was expressed in both PPR and in DLR in 63.9% (not significant = n.s.). IL-1β release was absent in cells lacking NLRP3, whereas NLRP1-deficiency did not affect IL-1β secretion upon Malassezia exposure. Our findings indicate that Malassezia is a potent inducer of inflammatory response which is mediated through the NLRP3-inflammasome

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Interleukin 33 is differentially expressed in psoriasis-like drug reactions to TNF-α antagonists

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Since their introduction TNF-α antagonists play a major role in the treatment of autoimmune disorders like psoriasis, rheumatoid arthritis, ankylosing spondylitis, Crohn's disease and others. Probably due to their immunologic nature, these drugs sometimes produce puzzling cutaneous side effects that are the subject of this investigation. For instance, although TNF-α antagonists are used to treat psoriasis, they can produce paradoxical skin inflammation in a small fraction of patients that can clinically resemble psoriasis, dermatitis and other conditions.

Of 21 patients (13 female, av. 48 years), 47% had a reaction either to infliximab and adalimumab or both (1 patient) and 6% had a reaction to etanercept. Clinical features as well immunohistochemistry for TNF-α, INF-α, IL-1β, IL-22, IL-6, IL-17, CD123, IL33, MXA, IL-8 and IL-36αa were performed. In each patient two histologic samples were taken and were evaluated by a grading system from + to ++++ (weak, medium, strong and highly active signal) as well as +/- (indifferent) and – (negative). Control stainings were performed at plaque psoriasis samples.

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Results: Four of a total of nine so far included patients have finished twenty-four weeks of treatment with Alitretinoin. In all four patients a reduction in disease severity measured by the Escudier score was apparent. Four of the remaining five patients have a decreased Escudier score under treatment at the actual follow up visits. One patient discontinued treatment after twelve weeks because of treatment failure. The following adverse events were observed: headache and mucosal dryness (eyes, mouth).

Conclusions: The clinical data suggest Alitretinoin to be effective in patients with chronic MLP. The study is ongoing. Please contact Dr. Kunz if you supervise patients with extensive MLP.