weeks later. STP938 was administered to mice developing signs of arthritis from Day 28 to 45 orally daily b.i.d.

**Results:** STP938 inhibited the in vitro proliferation of HEK-293 cells as well as Jurkat and human PBMCs. STP938 demonstrated a significant and dose-dependent inhibition of KLH-specific T and B cell responses in vivo. STP938 significantly reduced the disease severity in the CIA model in a dose-dependent manner as determined by clinical and histopathological readouts.

**Conclusion:** Our preliminary in vitro and in vivo results indicate that inhibition of CTPS1 specifically blocks proliferation of cells derived from the lymphocyte lineage and reduces cell-driven inflammatory response. These data highlight the therapeutic potential of STP938 in treating patients with autoimmune diseases such as rheumatoid arthritis.

**REFERENCES:**


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**OP0036**

**IL-6 ACTIVATES YES-ASSOCIATED PROTEIN (YAP) IN FIBROBLASTS AND INDUCES YAP-SNAIL COMPLEX FORMATION TO DRIVE SYNOVIAL LINING PATHOLOGY IN INFAMMATORY ARTHRITIS**

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**Background:** In rheumatoid arthritis (RA), the fibroblast-like synoviocytes (FLS) in synovial lining become invasive and cause joint destruction. The molecular mechanisms underlying this process have been incompletely understood.

**Methods:** In the present study, we evaluated the intestinal permeability in RA patients by analyzing tight junctions in colonic biopsies and serum markers.

**Results:** Patients with rheumatoid arthritis (RA) have an altered gut microbiota (dysbiosis) characterized by a lack of main bacterial taxa that regulate tight junctions. These changes result in increased intestinal permeability, which can lead to an increased intestinal permeability, responsible for the passage of antigens and inflammatory molecules, and can therefore promote systemic inflammation. Gut microbiota tends to normalize with disease control (2), suggesting that systemic inflammation may directly influence the composition of microbiota and the gut barrier. It was shown in many inflammatory diseases that intestinal permeability is impaired, but to date there is very little data in RA.

**Objectives:** To evaluate the intestinal permeability in RA patients by analyzing tight junctions in colonic biopsies and serum markers.

**Methods:** Colonic biopsies from 20 RA patients who underwent colonoscopy for screening with normal histology were compared with those from 20 age and sex-matched controls. ZO-1, occludin and claudin 2 junction proteins were evaluated by immunohistochemistry. The staining intensity was assessed by two blinded independent readers. The serum concentrations of LPS-binding protein (LBP), CD14s and zonulin were evaluated by ELISA in 25 patients naive of DMARDs, 41 patients before and after introduction of a DMARDs and 21 controls. Elevation of zonulin in serum indicates an increase in intestinal permeability while LBP and CD14s indicate bacterial translocation.

**Results:** ZO-1 expression was significantly lower in biopsies from patients with RA than controls (mean score ± SD of 1.6 ± 0.56 vs 2.0 ± 0.43; p = 0.01). Age, sex, disease duration and immunological status did not significantly influence the expression of colonic junction proteins. LBP and CD14s were higher in serum from RA patients as compared with those from 20 age and sex-matched controls. IL-6 and IL-1β expression was significantly higher in serum from RA patients as compared with those from 20 age and sex-matched controls. IL-6 and IL-1β expression was significantly higher in serum from RA patients as compared with those from 20 age and sex-matched controls.

**Conclusion:** Our preliminary results indicate that inhibition of YAP could reduce joint destruction in RA.

**REFERENCES:**


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