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Identification of Tofacitinib, Filgotinib and Ruxolitinib on experimental Sjögren's syndrome model in mice

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Background

Sjögren's syndrome, which is affected hundreds of millions of people worldwide, is a chronic autoimmune disorder characterized by leukocytic infiltration into the exocrine glands, such as the salivary and lacrimal glands. However, the pathological mechanism remains to be elucidated, and urgent need for the novel treatment should still meet. Over the past decades, an extensive progress has been made in establishment of Sjögren's syndrome model in mice, which offers us an invaluable tool to understand SjS pathogenesis and makes it possible to develop the novel drug and treatment.

In this study, we identified the potential effect of Tofacitinib, Filgotinib and Ruxolitinib on the experimental Sjögren's syndrome model in C57/B6L mice from both In-life study and *ex-vivo* study at the endpoint. Our data suggest that Tofacitinib, Filgotinib and Ruxolitinib, three JAK inhibtors exhibits the effect on reducing the severity of Sjögren's syndrome in mice, reduces autoantibodies producion and promotes the saliva secretion in mice, which also provides the direction of novel JAK inhibitor on treatment for Sjögren's syndrome.

Methods

Induction of ESS in mice

The ESS model was induced in C57/B6L mice with SG protein immunization. In general, SG protein was prepared by homogenized for bilateral SG of 8-week-old C57BL/6 mice. The SG protein concentration of the supernatant was measured by BCA, added to the same volume of Freund's complete adjuvant and emulsified to 4 mg/mL. On day 0, the emulsion was subcutaneously injected into the back of the 8-week-old mice, and this operation was repeated on day 7. On the 14th day, an equal volume of Freund's incomplete adjuvant was mixed with SG to form an emulsion of the same concentration to boost immunity and injected in the same way.

Results

After three weeks of JAKs treatment, mice in Tofacitinib, Filgotinib and Ruxolitinib were markedly increased saliva flow when compared with those in vehicle group.

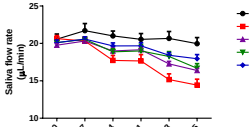

Figure 1 The effect of three JAK inhibitors on Saliva flow rate

Compared with vehicle group, mice in Tofacitinib, Filgotinib and Ruxolitinib group showed a less release of antibody against the dsDNA and M3R into blood.

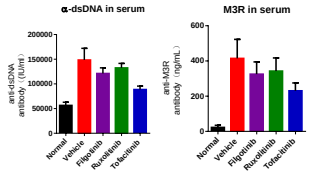

Figure 2 The effect of three JAK inhibitors on reducing the autoantibody against dsDNA and M3R in serum

Compared with vehicle group, mice in Tofacitinib, Filgotinib and Ruxolitinib group exhibited a less ANA autoantibody in both saliva and serum.

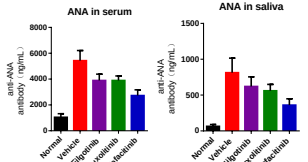

Figure 3 The effect of three JAK inhibitors on reducing the autoantibody against ANA in both saliva and serum

Furtherly, Tofacitinib, Filgotinib and Ruxolitinib reduced the percentage of Th1/Th17 cells in the spleen of ESS mice.

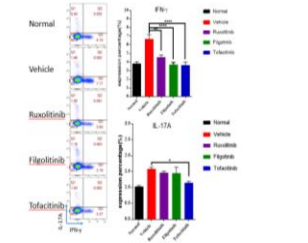

Figure 4 The effect of three JAK inhibitors on reducing the presense of Th1/Th17 cell in spleen

In addition, Tofacitinib, Filgotinib and Ruxolitinib also reduced the percentage of circulted Th1/Th17 cells in the blood of ESS mice.

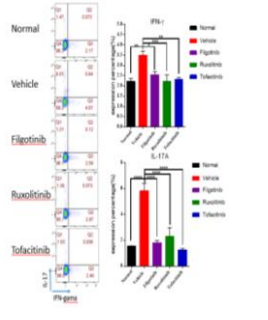

Figure 5 The effect of three JAK inhibitors on reducing the presense of Th1/Th17 cell in blood

Summary

In the present study, we found that JAKs inhigtors (Tofacitinib, Filgotinib and Ruxolitinib) improved the saliva flow of ESS mice, and inhibited the release of autoantibodies including those against for dsDNA, M3R and ANA. In addition, Tofacitinib, Filgotinib and Ruxolitinib reduced the presense of Th1/Th17 cells in both spleen and blood of ESS mice. In all, the JAKs inhibitor potentially improve the syndrome of ESS mice.