Background

Rheumatoid arthritis (RA) is an autoimmune disorder that targets joint tissues for destruction. Despite affecting more than 200,000 people each year in the US, its pathogenesis is relatively unknown.

Previous research at Pope Lab has identified regulatory T cells (Tregs), known for suppressing autoimmunity, as a potential mediator in RA development:

• Both the number and percentage of Tregs decreased significantly in older HUPO mice, a knockout model that mimic the symptoms of human RA\(^1\)
• Adoptive transfer of Tregs reduced severity of inflammation at week 3\(^1\)
• IL-2, which maintain Tregs survival, was found to be significantly lowered in ex-vivo spleen culture\(^1\)

Objective

The goal is to determine whether an exogenous delivery of IL-2 immune complex (IL-2C) could stimulate Treg differentiation, inhibiting autoreactive T-cells and reducing arthritis

• IL-2 was bound by its monoclonal antibody for higher biological activity

Methods

HUPO mice with mild inflammation were selected and sorted into two groups with matching characteristics; repeated for control mice

• Received either PBS or IL-2C injection three consecutive days each week
• Assessed for inflammation, deformity and grip strength weekly
• Half of the mice was collected after 3 weeks and the remaining at 6 weeks for flow cytometry and ankle histology

Scoring Data

Figure 1: inflammation score of HUPO mice over 6 weeks

Progression of RA-like signs in HUPO mice

Figure 2: Change in inflammation score of HUPO mice over 6 weeks

Change in inflammation of HUPO mice after treatment

Flow Cytometry Analysis

Figure 3: T Cell counting at week 3

Figure 4: T Cell counting at week 6

Conclusion & Next Step

Studying inflammation was useful because it is most indicative of RA progression. The scoring data show that the difference in change in inflammation at week 6 was significant between IL-2C and PBS treated HUPO mice.

In addition, the %Treg in CD4+ cells increased significantly in IL-2C treated HUPO mice at week 6, but not at week 3. This suggested that IL-2C required time to exert its effect on Tregs.

The overall result was promising as it highlighted the potential benefit of increased Tregs in controlling autoimmune diseases such as RA. In the future, it is necessary to optimize injection schedule for longer treatment and to select mice before the onset of arthritis.

References


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