Treatment of **Rheumatoid Arthritis** in a Collagen-Induced Arthritis **Mouse Model** Using Intra-articular Injection of **AAV**-delivered s**IL-17RA**

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Introduction

Rheumatoid Arthritis (RA) is an autoimmune disorder marked by:

- Chronic inflammation of joint tissues
- **Irreversible joint damage, disability, and increased mortality if left untreated.**[1]

What are **Adeno-associated viruses (AAV)?**

- Non-pathogenic viruses
- Target specific tissues for entry
- Can express packaged transgenes for up to several years.[2]

Central Research Question

Using AAV6, we delivered the **extracellular domain of Interleukin-17 Receptor A (sIL17RA)**, into a late-stage RA mouse model to inhibit **Interleukin 17A (IL17A)**, a key cytokine in RA pathophysiology, to halt disease progression.[3]

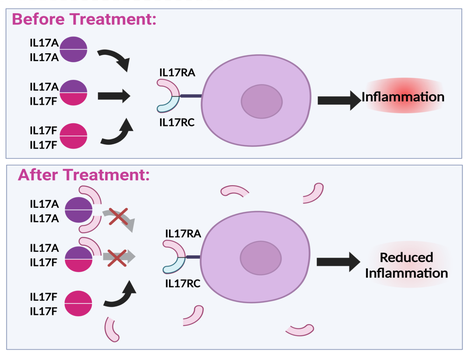

Figure 1. *Anticipated mechanism of sIL17RA treatment. Figure partially adapted from Robert and Miossec.*[4]

Acknowledgements

This research was funded in part by a Summer Undergraduate Research Fellowship from the Office for Undergraduate Research at the University of North Carolina at Chapel Hill. Special thanks to Eric Hastie (Research Advisor). Figures made using Biorender.

Materials and Methods

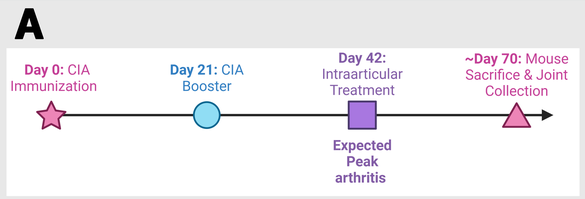

Figure 2A. *Timeline of Mouse Experimentation.*

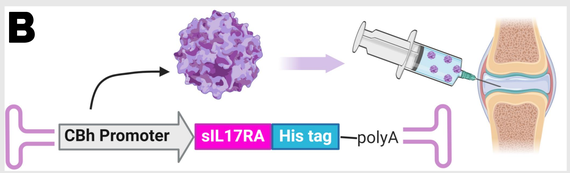

Figure 2B. *pTR-CBh-sIL17RA construct was packaged into AAV6 and injected intraarticularly into CIA mice.*

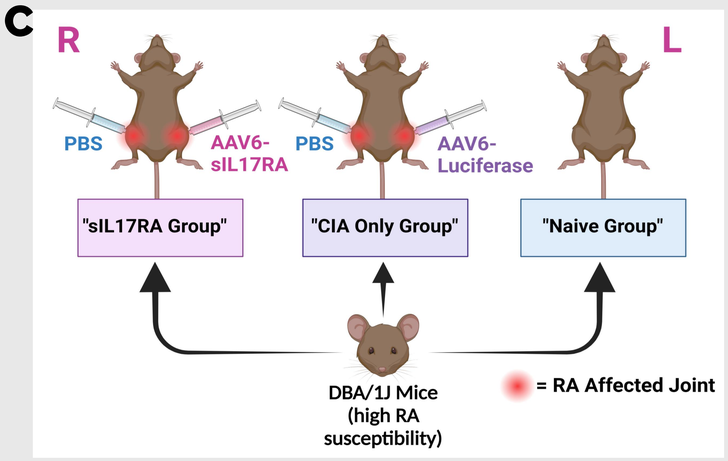

Figure 2C. *Animal Study Design.*

Results

1	2	3	4	5
Positive control supernatant	Positive control cell lysate	Negative control cell lysate	sIL17RA supernatant	sIL17RA cell lysate

Figure 3A. *L: Western blot (WB) of sIL17RA expression produced from pTR-CBh-sIL17RA visualized with anti-His tag antibody. R: WB of GAPDH (loading control).* ***Figure 3B.*** *Lane key for figure 3A.*

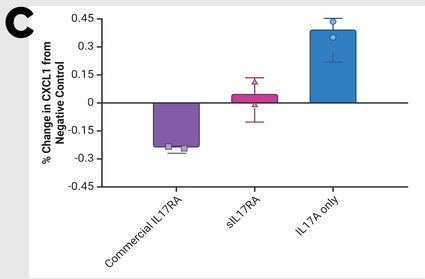

Figure 3C. *Ability of sIL17RA produced from pTR-CBh-IL17RA to inhibit the effect of IL17A in vitro (measured by CXCL1) was compared to that of a commercial IL17RA. Presented is the % changes in CXCL1 conc. from the negative control. One-way ANOVA p<0.05.*

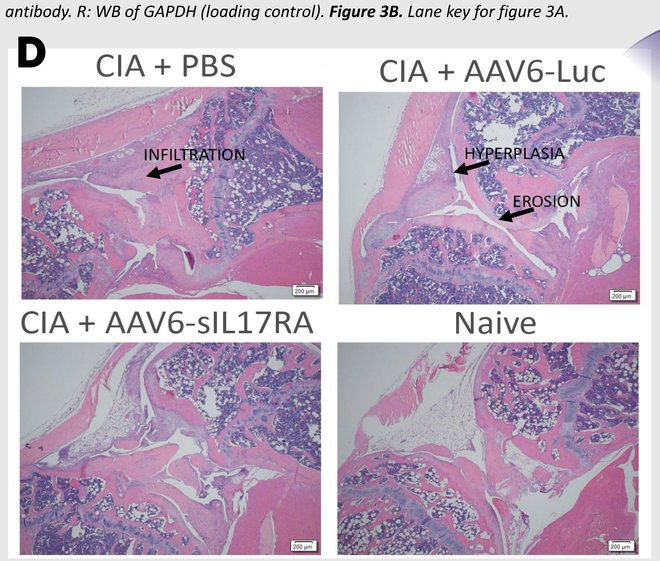

Figure 3D. *Representative images of joints from each treatment group. Examples of the markers used to score arthritis severity are marked above.*

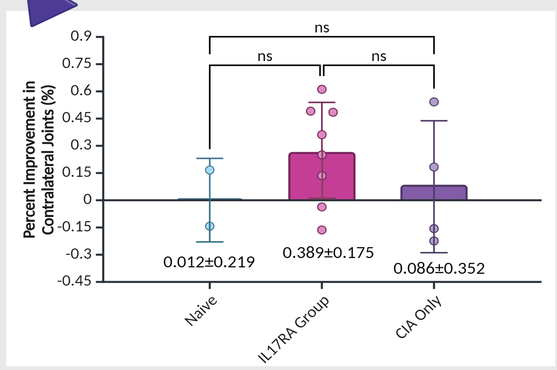

Figure 3E. *Comparison of % improvement between the L and R knee joints. Error bars are 1 SD from the mean. No statistical significance among groups, but AAV6-sIL17RA group trends towards improvement.*

Discussion

- Percent score improvement between the R/L joints of the IL17RA group ***trended towards improvement***
- 2 mice in the IL17RA group may have been ***inadequately injected*** (future experiments include measuring AAV titer in the joint)
- Local sIL17RA ***did not enter systemic circulation*** at appreciable amounts

Conclusions

This study indicated:

- The **potential of sIL17RA** as a therapeutic treatment for RA
- AAV as a promising **local delivery mechanism** for sustained expression of therapeutic agents
- The significance of the cytokine, IL17A, in **late RA pathophysiology**

Future Directions

- sIL17RA **prophylaxis** treatment
- **Systemic injection** (as RA is a systemic disease)
- Utilization **alongside another therapeutic agents** that directly target dysfunctional cells

References

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