

# TL1A Expression is Upregulated in Rheumatic Diseases and Anti-TL1A Antibody Reduces Disease Symptoms and Pathological Changes in Rat Collagen-Induced Arthritis

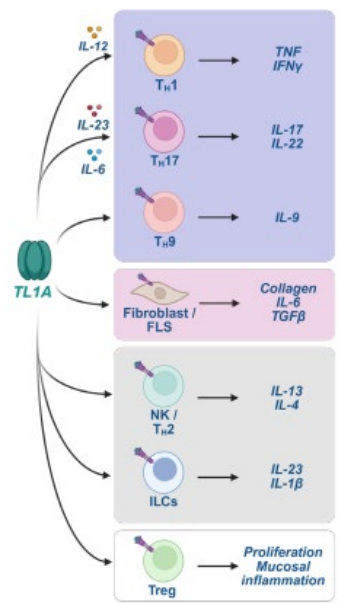
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## Background

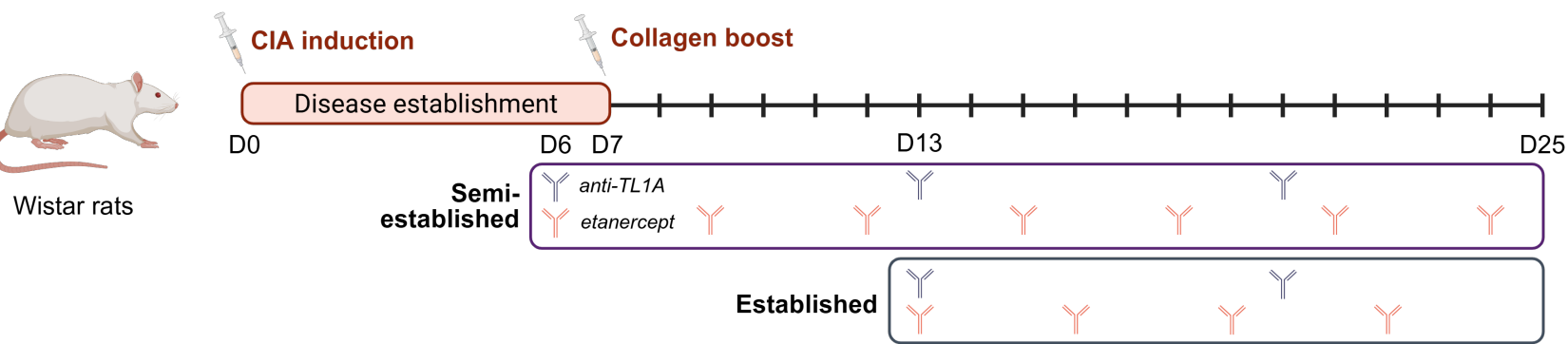


- TL1A is a cytokine that activates T cell subtypes and fibroblast-like synoviocytes.
- Variants in the TL1A gene are associated with rheumatoid arthritis (RA), psoriatic arthritis (PsA), and axial spondyloarthritis (axSpA), and TL1A expression is increased in each<sup>1-4</sup>.
- TL1A inhibition has shown promising results in Phase 2 studies of patients with **Crohn's disease (CD)** and **ulcerative colitis (UC)** and is under investigation in additional immune-mediated conditions.

## Methods

- Gene expression data from published RA, axSpA, and PsA studies deposited in NCBI GEO were merged and queried to assess TL1A expression in healthy controls (HC) and in those with rheumatic diseases.
- Anti-TL1A and etanercept (anti-TNF) antibodies were studied in the rat collagen-induced arthritis (CIA) model. Female Wistar rats were injected with a bovine type II collagen emulsion on days 0 and 7. Anti-TL1A antibody was injected (IV) once weekly. Etanercept was injected (IP) every 3 days. Treatment began on day 6 for the semi-established model and on day 13 for the established model. The study concluded on day 25 (Figure 1).

Figure 1: Rat CIA model schematic



- Body weight, hind paw volume and arthritis scores were measured twice per week. At study conclusion, X-ray images of the hind paws were taken and scored. Decalcified hind paw sections were scored by a blinded pathologist.

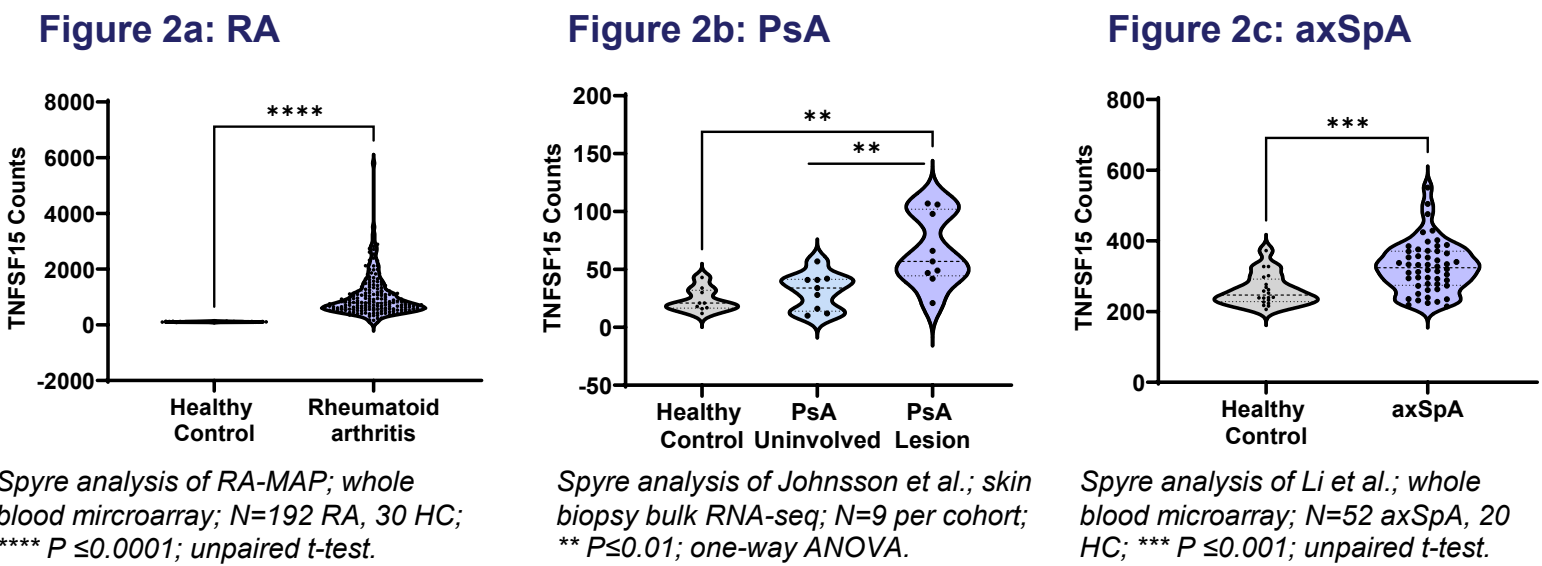
## References

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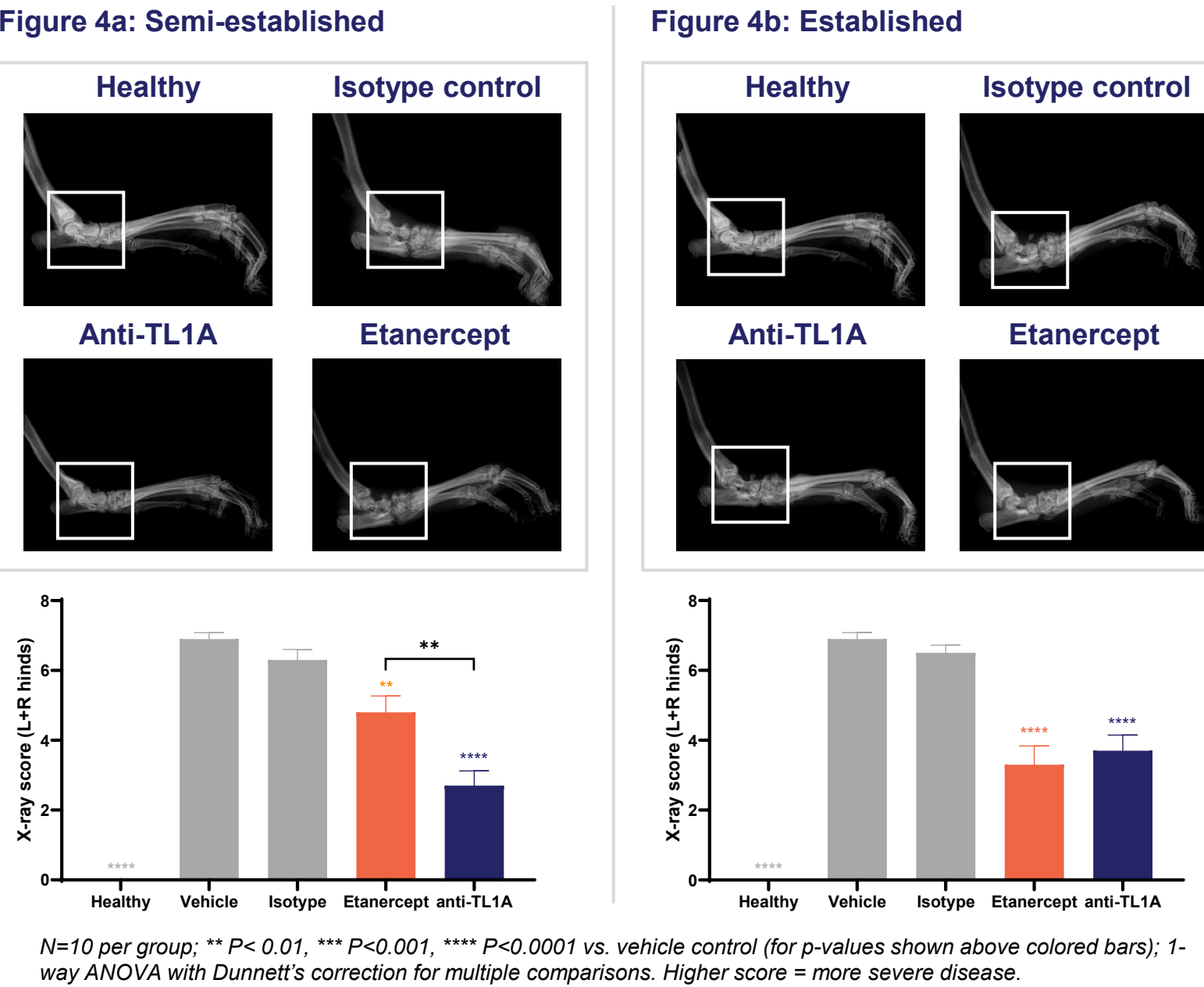
**Disclosures:** All authors own equity in Spyre Therapeutics, Inc..

## Results

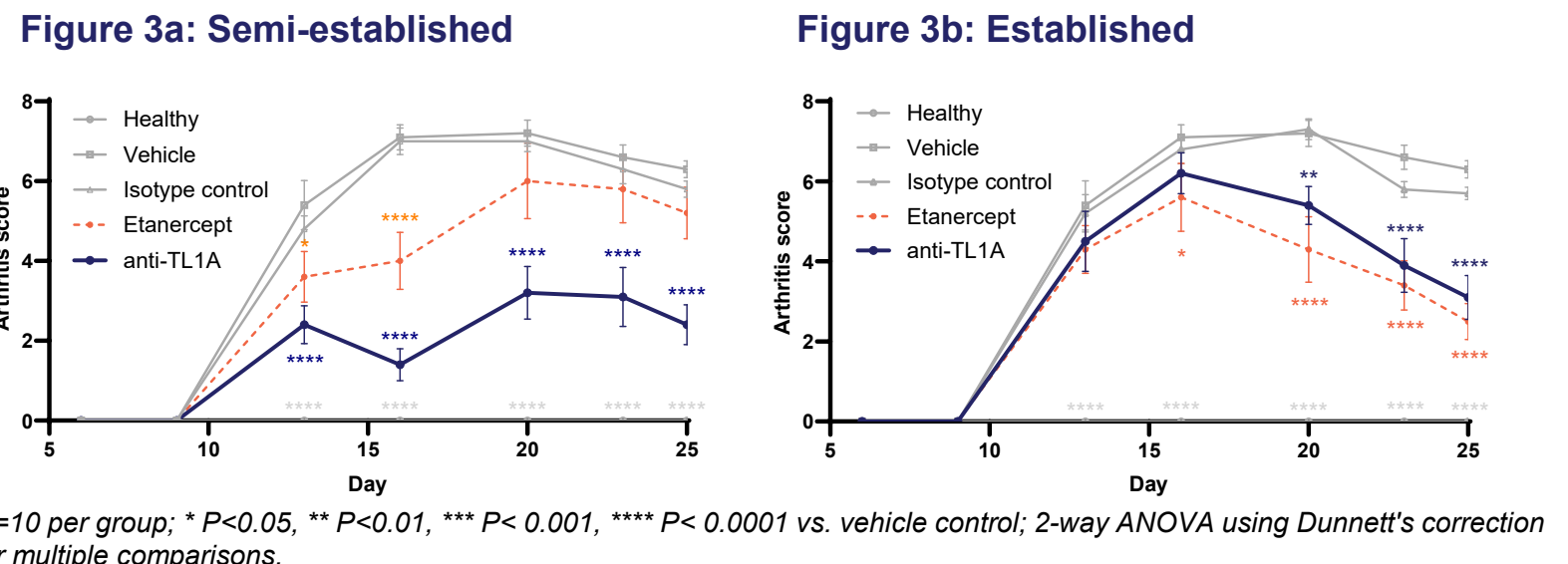
### TL1A is upregulated in RA, PsA, and axSpA relative to healthy controls



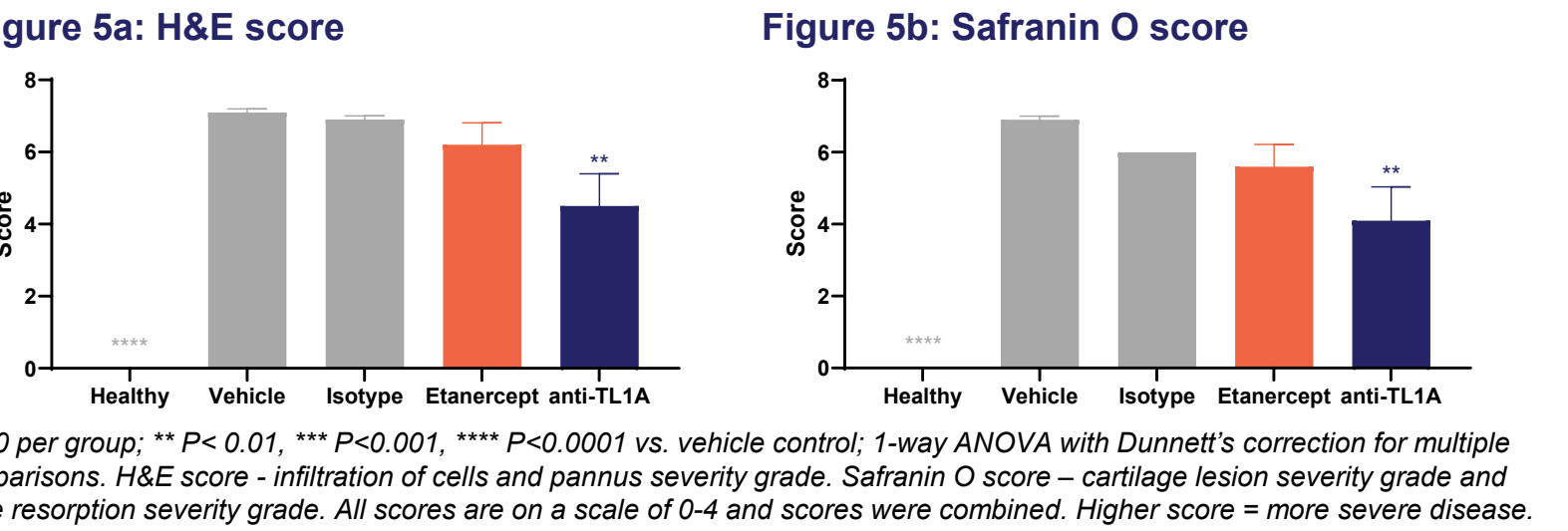
### Anti-TL1A antibody meets or exceeds the efficacy of etanercept when assessing x-ray scores in rat CIA models



### Anti-TL1A antibody meets or exceeds the efficacy of etanercept when assessing disease activity scores in rat CIA models



### Anti-TL1A antibody exceeds the efficacy of etanercept when assessing histology in the semi-established rat CIA model



## Conclusions

- TL1A gene expression is increased** in the blood of **RA** and **axSpA** patients and in skin lesions of **PsA** patients compared to healthy controls, based on analysis of gene expression data from published studies<sup>5-7</sup>.
- Anti-TL1A antibody treatment reduced disease symptoms and pathology scores** in the rat CIA model, with superior efficacy relative to etanercept when initiated prior to full symptom onset.
- These data support **clinical testing of the anti-TL1A antibody SPY072** in the ongoing **SKYWAY-RD Phase 2 basket study** in which SPY072 is being evaluated for the treatment of **RA, PsA, and axSpA** (NCT07148414).