

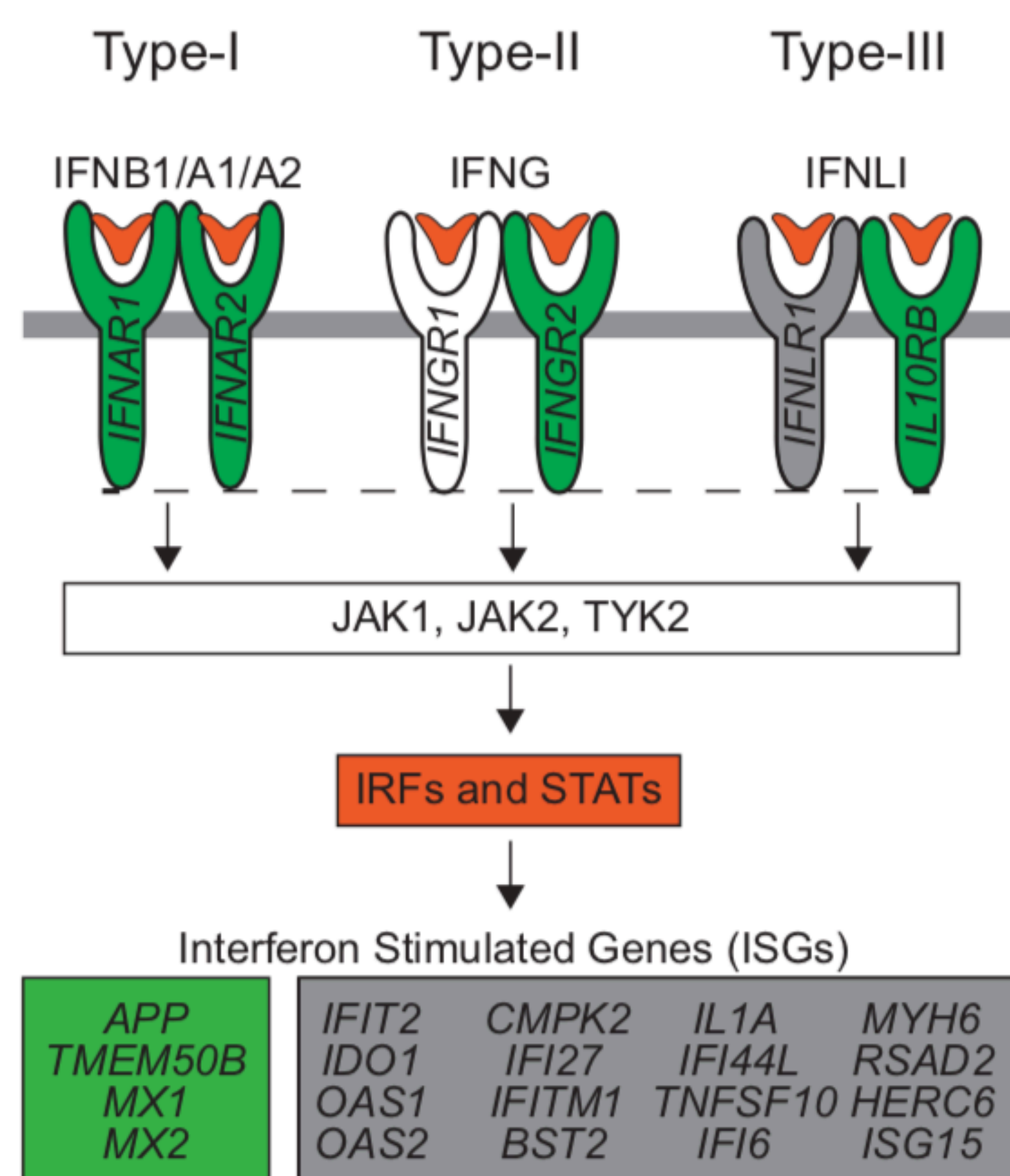
JAK Inhibition for treatment of psoriatic arthritis in Down syndrome

Andrew T. Pham, BS¹; Angela L. Rachubinski, PhD^{1,2}; Belinda Enriquez-Estrada, MS¹;
Kayleigh Worek, MS¹; Melissa Griffith, MD³; Joaquin M. Espinosa, PhD^{1,4}

¹Linda Crnic Institute for Down Syndrome; ²Department of Pediatrics; ³Department of Rheumatology; ⁴Department of Pharmacology

Background

- People with Down syndrome (DS) are predisposed to autoimmune conditions including inflammatory arthropathies¹
- Trisomy 21 (T21) hyperactivates interferon (IFN) and downstream Janus kinase (JAK) signaling²
- Dysregulated innate and adaptive immunity cause psoriatic arthritis (PsA): ↑ production of Type I IFN, TNF alpha, IL-17, IL-12, IL-22, IL-23³
- First-line treatments for PsA are IL-17 and IL-23 inhibitors that have not been studied in DS⁴
- Tofacitinib is also FDA-approved to treat PsA (as a second-line agent) and targets JAK signaling⁴



101 Total IFN-related DEGs

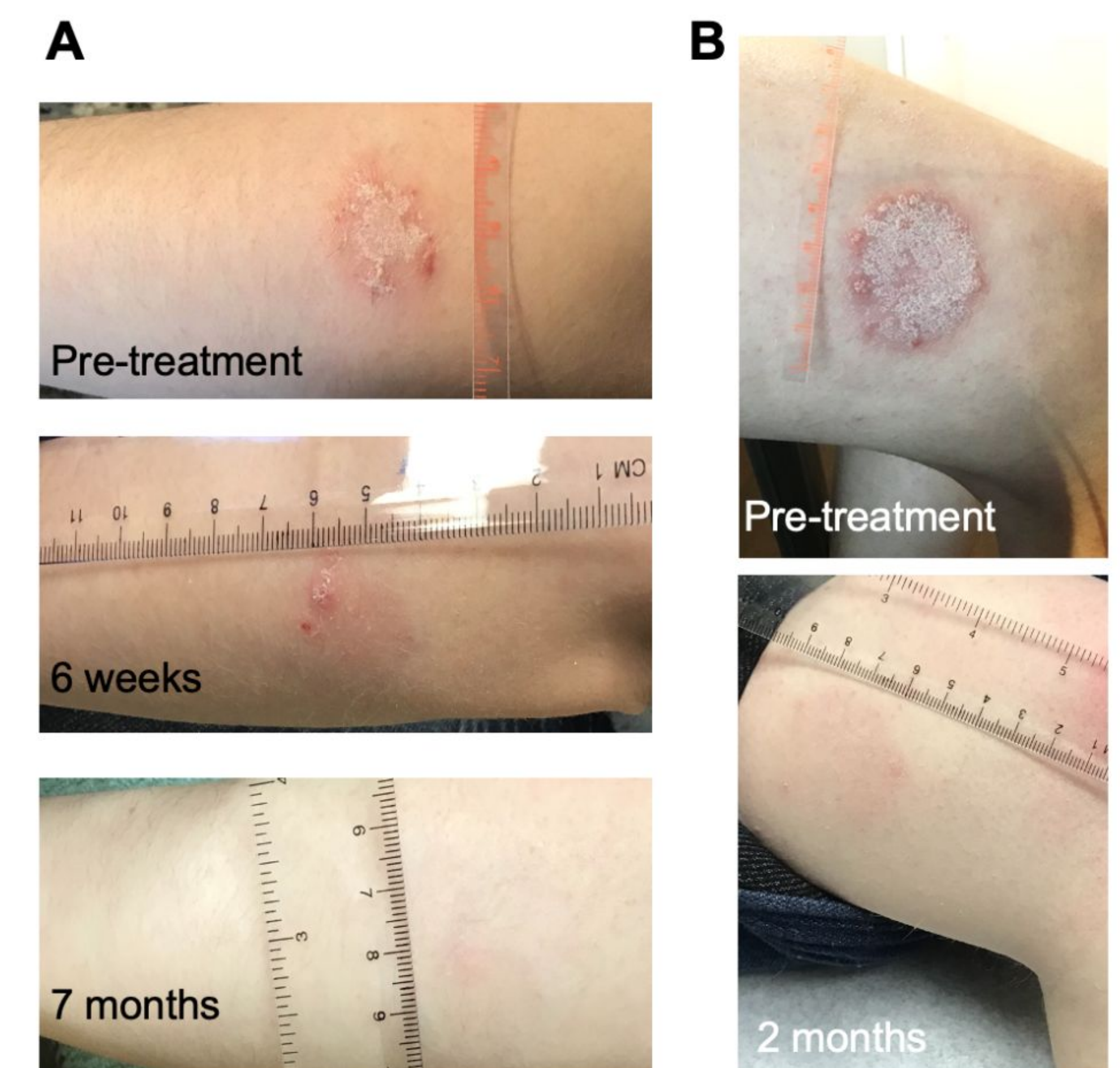
Upstream Regulators T21 vs D21 DEG chr21 Encoded DEG

Case Report

27yo female with DS, psoriasis, hypothyroidism, and celiac disease who presents with persistent left shoulder pain

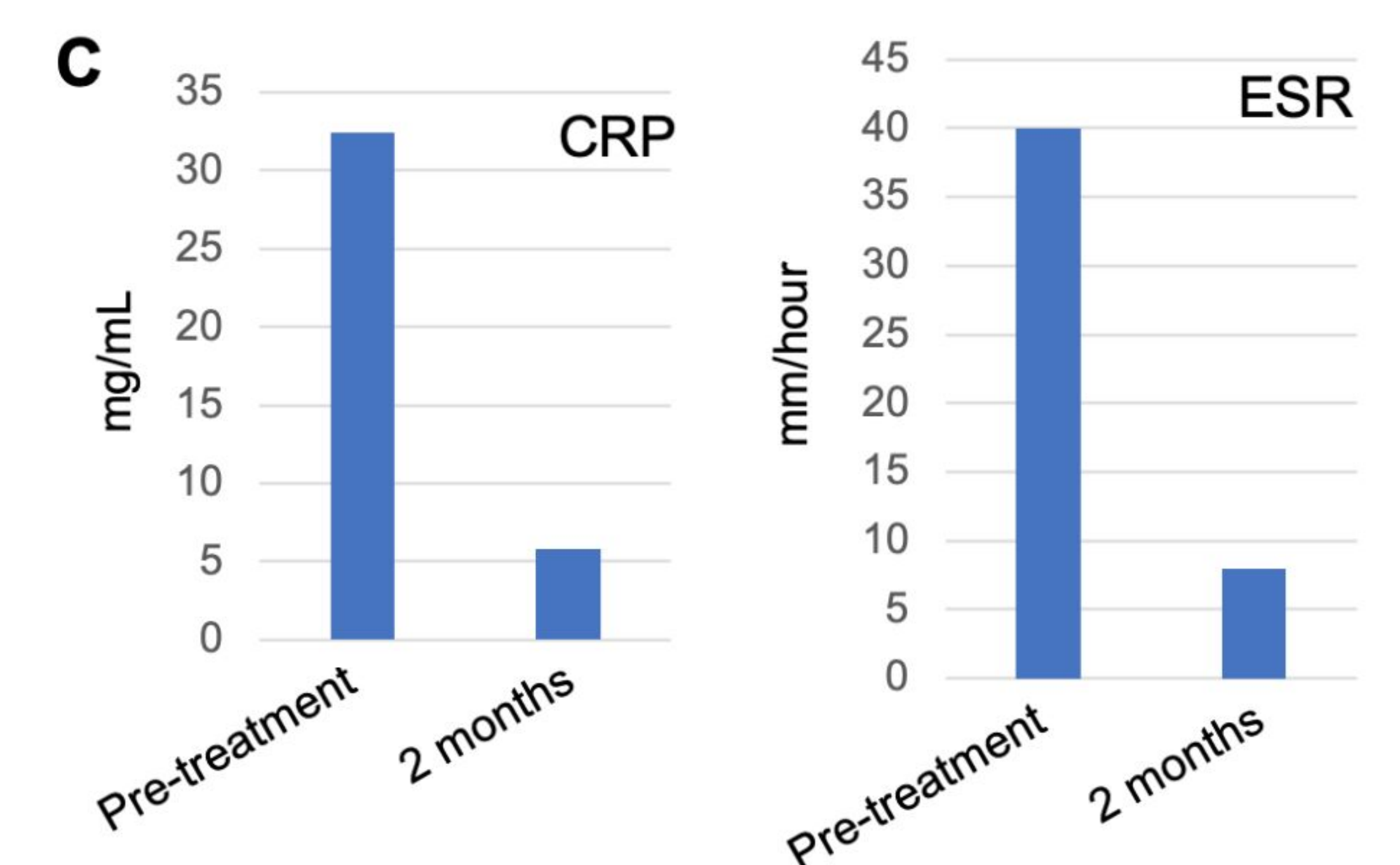
Initial Rheumatology Visit

- Over 4 months, joint pain subsequently involved left hand, elbow, shoulder, and knee, causing her to be homebound
- Pain persisted despite exercise, ibuprofen, heat therapy
- Physical exam notable for dactylitis on 3rd and 4th digits on left hand and psoriasis
- Labs showed elevated inflammatory markers
- Patient started on 5mg Tofacitinib oral twice daily



Post-Treatment

- Within 1 month: regained ability to walk long distances and participated in moderate intensity exercise
- Within 2 months: complete resolution of arthritic symptoms without adverse reactions



(A) Resolution of psoriasis on L arm over treatment course, (B) Resolution of L leg psoriasis over treatment course, (C) Normalization of inflammatory markers 2 months post-treatment

Methods

- Informed consent obtained in accordance with Declaration of Helsinki and specific consent obtained for case report
- Approved under Colorado Multiple Institutional Review Board (COMIRB #15-2170)

Acknowledgements

- CU School of Medicine Research Track
- Families and individual participants who have made the Human Trisome Project possible
- Espinosa Lab

Discussion

- ❖ Response to tofacitinib therapy highlights increased IFN and JAK signaling as contributing factors to autoimmunity in DS
- ❖ Participant's response to tofacitinib encourages further study of whether JAK inhibitors are preferable pharmacotherapy for patients with DS and inflammatory joint diseases

References

1. Bull MJ, Committee on G. Health supervision for children with Down syndrome. Pediatrics. 2011. PubMed PMID: 21788214.
2. Sullivan KD et al. Trisomy 21 consistently activates the interferon response. Elife. 2016. PubMed PMID: 27472900.
3. Bravo A, Kavanaugh A. Bedside to bench: defining the immunopathogenesis of psoriatic arthritis. Nature reviews Rheumatology. 2019. PubMed PMID: 31485004.
4. Singh JA et al. Special Article: 2018 American College of Rheumatology/National Psoriasis Foundation Guideline for the Treatment of Psoriatic Arthritis. Arthritis & rheumatology. 2019. PubMed PMID: 30499246.