JAK Inhibition for treatment of psoriatic arthritis in Down syndrome

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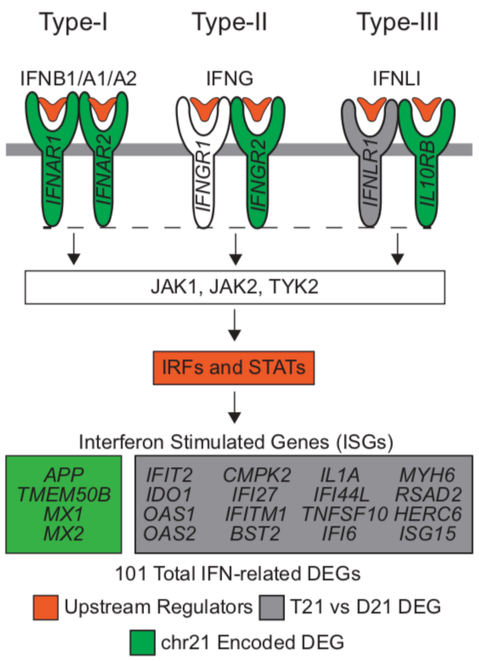
Background

- People with Down syndrome (DS) are predisposed to autoimmune conditions including inflammatory arthropathies[1]
- Trisomy 21 (T21) hyperactivates interferon (IFN) and downstream Janus kinase (JAK) signaling[2]
- Dysregulated innate and adaptive immunity cause psoriatic arthritis (PsA): ↑ production of Type I IFN, TNF alpha, IL-17, IL-12, IL-22, IL-23[3]
- First-line treatments for PsA are IL-17 and IL-23 inhibitors that have not been studied in DS[4]
- Tofacitinib is also FDA-approved to treat PsA (as a second-line agent) and targets JAK signaling[4]



IFN receptors and downstream IFN stimulated genes are upregulated in T21.

Adapted from Sullivan et al., 2016, eLife.

Case Report

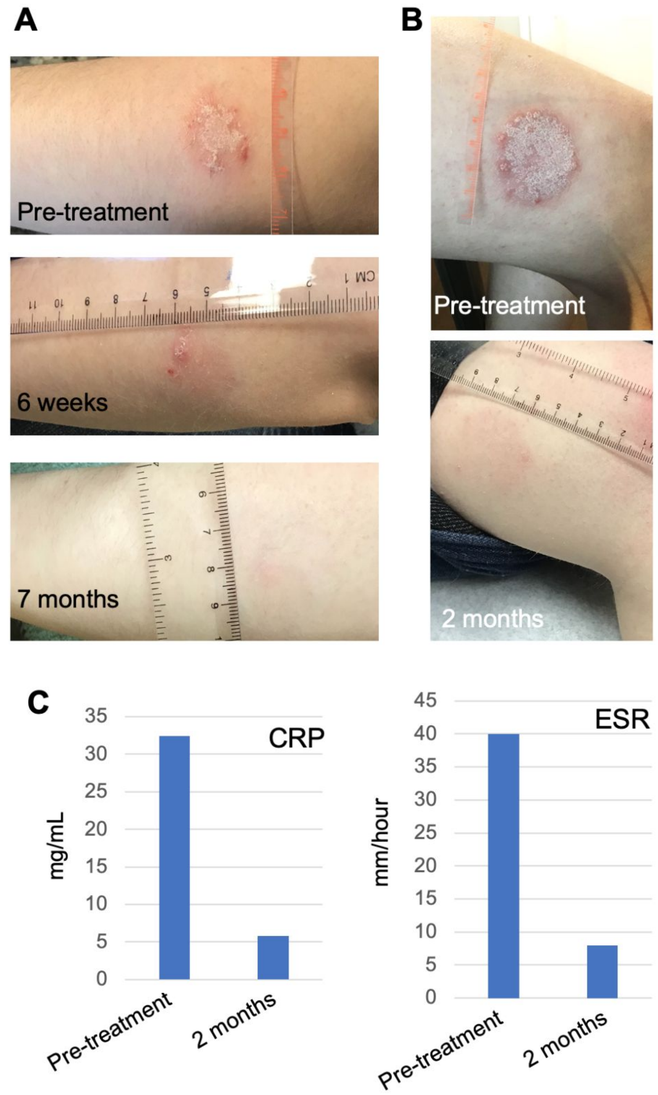
27yo female with DS, psoriasis, hypothyroidism, and celiac disease who presents with persistent left shoulder pain

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)

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

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References

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