

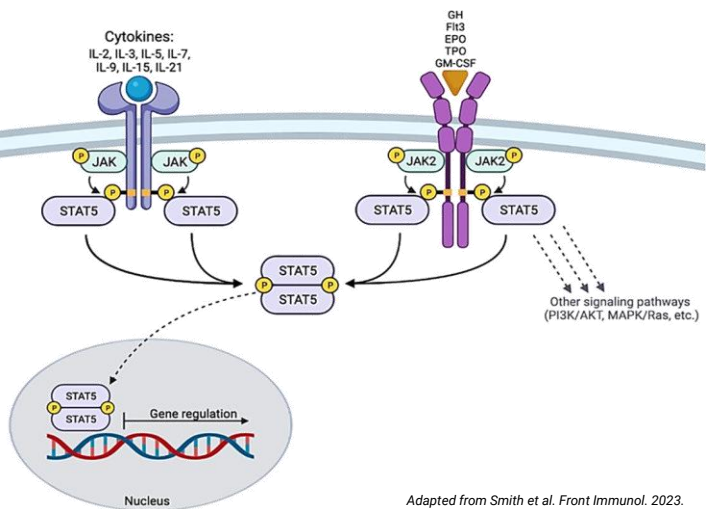
# STAT5B haploinsufficiency presenting with severe atopic dermatitis without immune dysregulation

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## Rationale

STAT5B is a critical mediator of multiple cytokines and growth hormone signaling, playing a key role in lymphocyte development, proliferation, and survival



Adapted from Smith et al. Front Immunol. 2023.

## STAT5B

### LOF

### DN

### GOF

Atopic dermatitis

Growth delay

Autoimmunity

CID  
Pulmonary  
disease

Hyper IgE

Urticaria  
Eosinophilia  
Diarrhea  
LGL leukemia

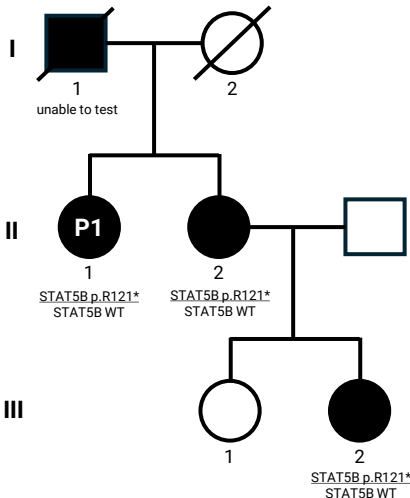
## STAT5B haploinsufficiency

**Table 1.** Clinical features of P1 (II.1) with STAT5B haploinsufficiency

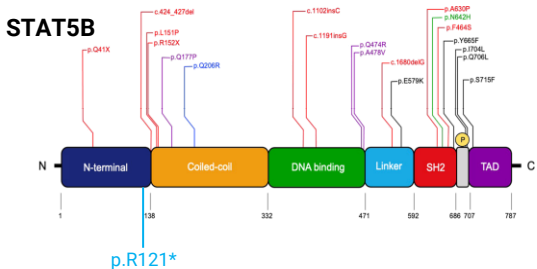
| Clinical feature | Description   |
|------------------|---|
| Age of onset     | Neonatal  |
| Previous Tx      | Moisturizers, bleach baths, topical corticosteroids, topical tacrolimus |
| Other allergies  | Moderate asthma, allergic rhinitis, peanut allergy                      |
| Complications    | Adrenal insufficiency, ulnar fracture                                   |
| AD severity      | SCORAD: 59, QoL score: 27   |
| Growth           | Slight height reduction (145 cm)  |

**Table 2.** Laboratory findings of P1 (II.1) with STAT5B haploinsufficiency

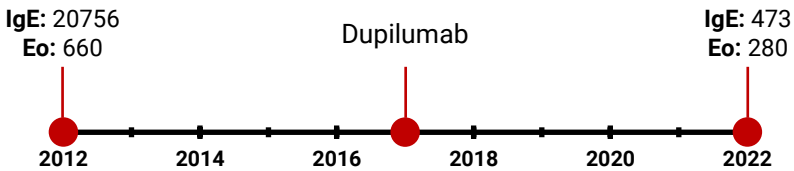
| Laboratory findings   |
|---|
| ↓ CD4+ and CD8+ T <sub>CM</sub> cells, ↑ CD4+ T <sub>EM</sub> cells |
| ↑ CD4+ T <sub>EM</sub> cells  |
| ↑ % TEMRA CD4+ and CD8+ cells                                       |
| Normal Treg cells   |
| ↓ IGF-1, normal GH and IGFBP-3                                      |



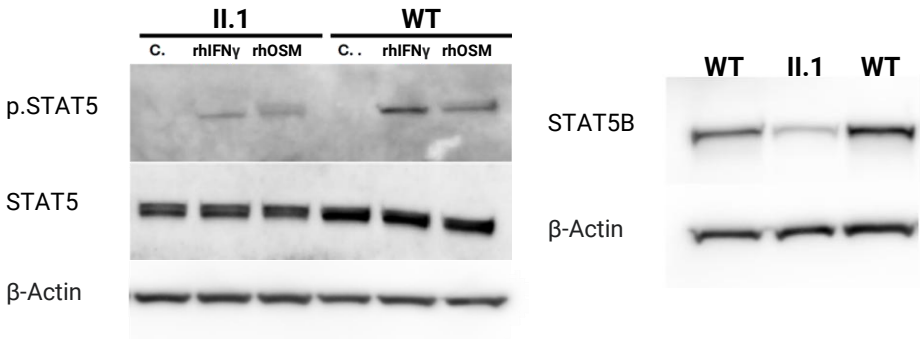
**Figure 1.** Family pedigree of affected family



**Figure 2.** Reported STAT5B variants including from P1 (II.1)



**Figure 3.** Timeline of eosinophil and IgE levels pre- and post-dupilumab from P1 (II.1)



**Figure 4.** Reduced p-STAT5 and STAT5B expression in dermal fibroblasts

## Conclusion

This study identifies a novel heterozygous nonsense pathogenic variant in the STAT5B gene, resulting in haploinsufficiency associated with severe atopic dermatitis and mild growth impairment with notably absent autoimmune endocrinopathy or other immune dysregulation, expanding the phenotypic spectrum of STAT5B-associated disorders

## Reference

- Smith MR, Satter LRF, Vargas-Hernández A. STAT5b: A master regulator of key biological pathways. Front Immunol. 2023;13:1025373.
- Scalco RC, Hwa V, Domené HM, Jasper HG, Belgorosky A, Marino R, et al. STAT5B mutations in heterozygous state have negative impact on height: another clue in human stature heritability. Eur J Endocrinol. 2015;173(3):291-6.