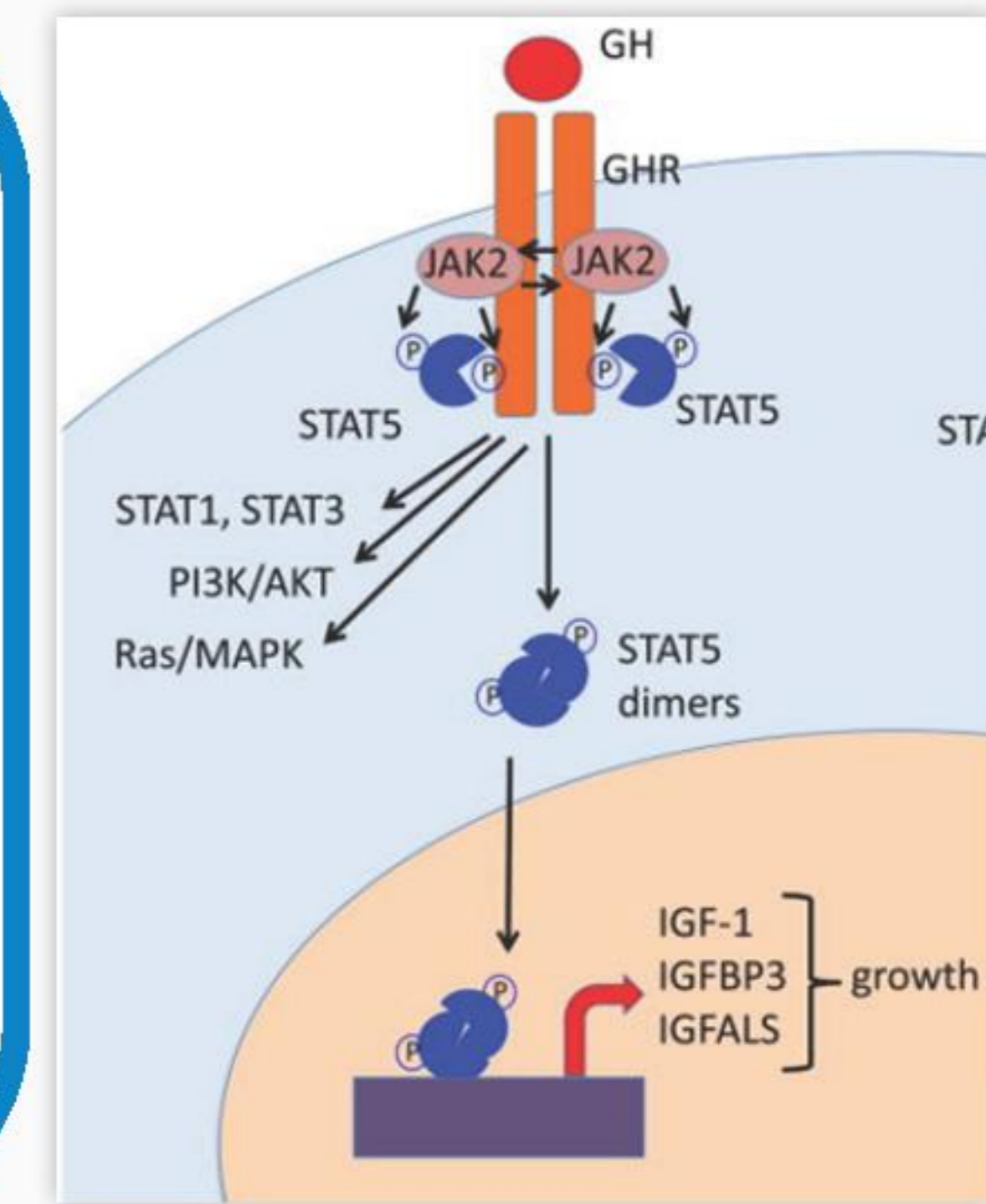


# Clinical and Biochemical Characteristics of a Female Patient with a Novel Homozygous STAT5B Mutation but Lack of Pulmonary Disease

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## BACKGROUND

STAT5B deficiency is characterized by severe postnatal growth failure, low IGF-1 level, elevated levels of GH and prolactin, and immunodeficiency. To date, only 10 patients with 7 different mutations have been described.

## OBJECTIVE

Describe clinical characteristics of a novel homozygous frameshift mutation in STAT5B.

## CASE REPORT

A 17-year-old female was referred for proportionate short stature and primary amenorrhea. She was born at term with a normal birth weight; her short stature became evident after 2 years. She had no history of severe or recurrent infections, or pulmonary disease. Parents were first cousins and target height was 152.2 cm (-1.3 SDS).

### On physical examination;

At first evaluation (chronological age: 15.2 years)

Weight: -4.1 SDS

Height SDS: -6.2 SDS

•Bone Age: 11 years

•Pubertal development was delayed (Tanner stage B2P2)

•She had midface hypoplasia, frontal bossing, high-pitched voice, and normal intelligence.

•Examination of the skin revealed generalized ichthyosis and erythema and papules on hands. A biopsy of the lesions led to a diagnosis of chronic dermatitis.

### On laboratory examinations,

•Serum IGF-1 was undetectable

•Serum IGFBP-3 was 0.5 mg/L,

•Persistently elevated prolactin (97-139 ng/mL).

•Results of two GH provocation tests showed GH peaks of 0.7 and 3.8 ng/mL.

### Imaging

Cranial and pituitary MRI were normal.

### GH Treatment

rhGH treatment, however, did not significantly improve serum IGF-1 levels or increase growth rate.

### Genetic analyses

Targeted gene analysis identified a novel homozygous frameshift mutation in the STAT5B gene, exon 12: c.1453del, p.Asp485Thrfs\*29, which segregated appropriately. Exome sequence analysis for homozygous recessive rare variants that could explain the growth hormone deficiency, were unrevealing (genes: HESX1, OTX2, LHX3, LHX4, SOX3, FGF8, FGFR1, GLI2, PROP1, POU1F1, IGSF1, GHRH, GHRHR, BTK, GH1, RIEG, GLI3, RNPC3).

### Immunological Evaluation

Absolute lymphocyte counts were in normal ranges. However, she had low CD3<sup>+</sup> T cell, elevated CD19<sup>+</sup> B cell and normal NK cell counts. FOXP3<sup>+</sup> expression on CD4<sup>+</sup>CD25<sup>+</sup> cells was normal. *In vitro* T lymphocyte proliferative blastogenesis in response to stimulation with CD3 were also normal.

## CONCLUSION

Severe immunodeficiency, chronic pulmonary fibrosis and elevated GH secretion, present in all but two previously reported patients, are not obligatory features in patients with STAT5B deficiency.



Figure 1. Phenotypic appearance of the patient

Table 1. Clinical and demographic features of index patient and family

	Patient	Mother	Father	Brother	Aunt 1	Aunt 2
Age	17.2	46	51	21	49	48
Height SDS	-5.18	-1.37	-1.27	-0.66	-1.87	-1.95
BMI SDS	26 (1.54)	46	22	31	31	26
Fat percent (%)	21.3	48.2	12.8	24.4	36.6	31.3
Birth weight (g)	2800	?	?	2800	4500	?
Puberty	Delayed	Normal	Normal	Normal	Normal	Normal
Eczema	Yes	No	No	No	Yes	Yes
Varicella (Age/severity)	3 year /N	10 years /N	?	7 years /N	?	8 years /N
Chronic Pulmonary disease	No	No	No	No	No	No
Type of mutation	homozygous	heterozygous	heterozygous	heterozygous	heterozygous	heterozygous
Basal GH (ng/mL)	0.74	2.1	0.34	1.5	0.08	0.54
IGF-I SDS	-4.5	-2.4	-1.6	-1.1	-1.5	-1.1
IGF-BP3 SDS	-6.16	-0.24	-2.04	-1.0	-0.63	-0.54
ALS SDS	-5.95	-1.72	-2.13	0.2	-0.63	-0.7

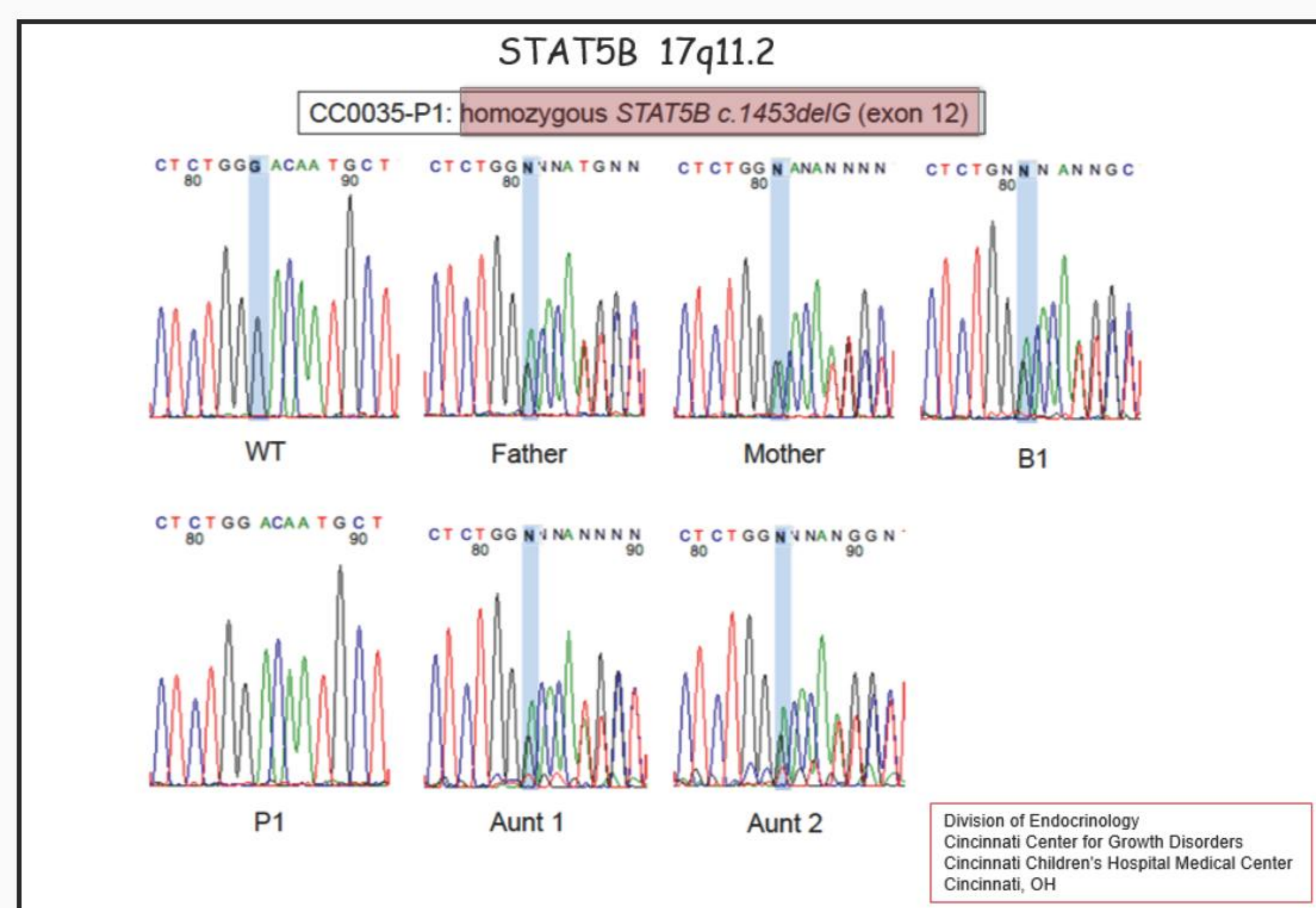


Figure 2. Results of molecular analyses

