# Mutation of the TSH receptor gene: a longitudinal study in children with non-autoimmune subclinical hypothyroidism

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#### **BACKGROUND**

Neonatal screening strategies revealed an increase in hypothyroidism associated with an in-situ thyroid gland due to TSH receptor (TSHR) mutations.

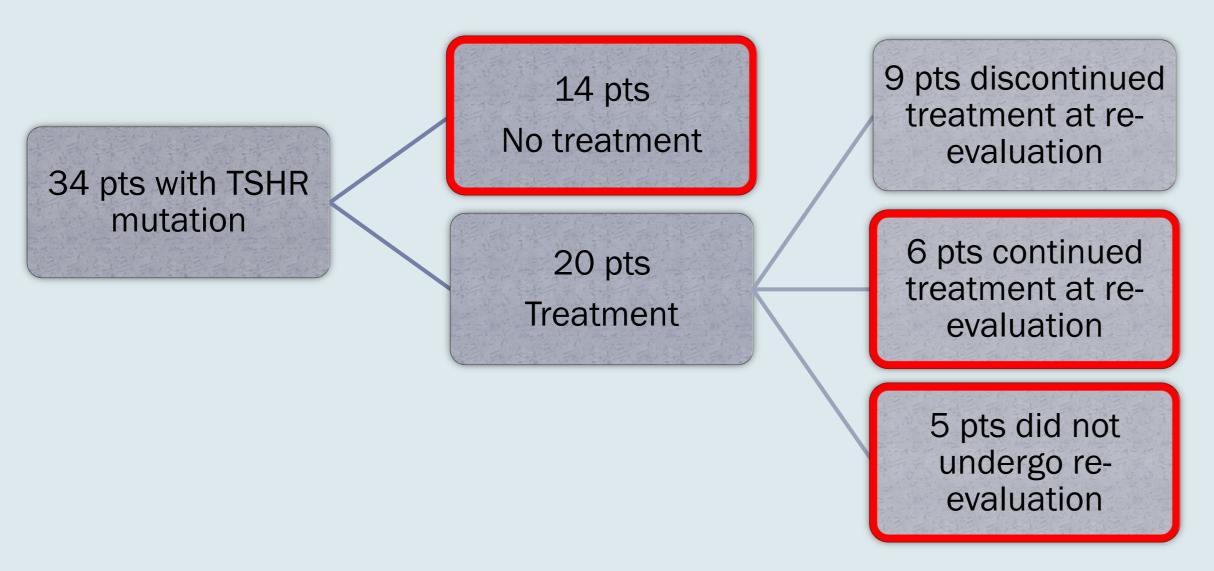
## **OBJECTIVE AND HYPOTHESIS**

Determine the impact of TSHR mutations on clinical course, biochemical parameters and therapeutic approach in children carrying this mutation.

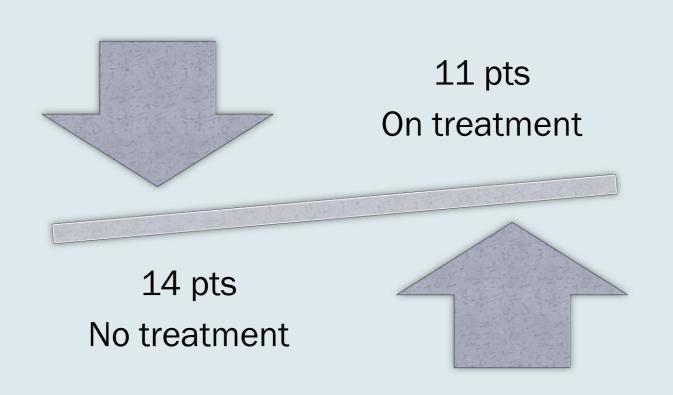
Hypothesis: therapy may be unnecessary in partial TSH resistance due to a TSHR mutation.

### **METHODS**

 We retrospectively evaluated diagnosis and re-evaluation parameters in 34 patients (pts) with non-autoimmune subclinical hypothyroidism and a diagnosed TSHR mutation.



Ultrasound exam (US), Auxological parameters, DEXA, Bone age, Biochemical parameters (total cholesterol, HDL, triglycerides, AST, ALT, ALP, CPK) and Developmental Quotient (DQ) ) were compared between pts



#### **RESULTS**

**Diagnosis** of all TSHR mutation pts:

• 53% at screening, 23% for familial thyroid disease, 15% for signs/symptoms, 9% casually.

Age range: 0 -11 years

• Mean I spot:  $8.4 \pm 4 \text{ mU/L}$ 

• Mean TSH:  $14.2 \pm 13$  mcU/ml (range 5.3 - 74.9) • Mean FT4:  $1.27 \pm 0.2$  ng/dl (range 0.27- 2.09)

**Ultrasound:** 

In treatment	Hypoplastic	Normal	Hyperplastic
First US	27%	72%	0%
Last US	55%	44%	0%

NO	Hypoplastic	Normal	Hyperplastic
treatment			
First US	15%	84%	0%
Last US	12%	75%	12%

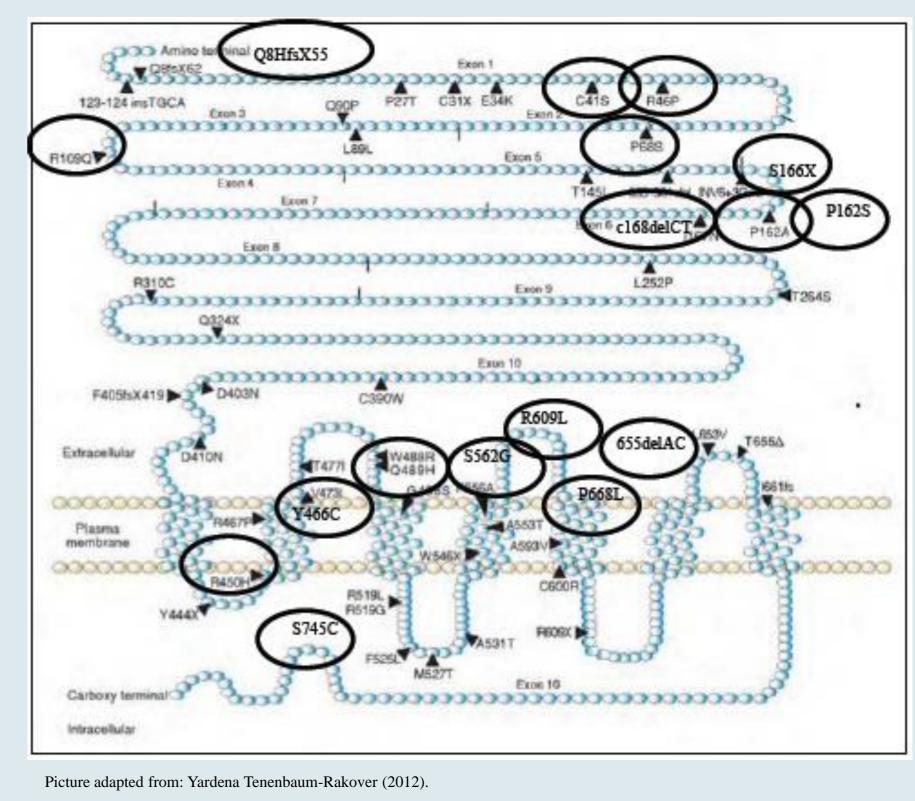
#### Therapy vs No Therapy:

height sds, weight sds, BMI sds, target height sds, bone	n.s.
mineral density z-score, chronological age-bone age and biochemical parameters.	
height sds-target height sds	p < 0.05
Mean DQ scores were within the average range in all pts	n.s.

Re-evaluation: 15 pts underwent etiological re-evaluation

- 60% discontinued treatment (mean TSH 7.6  $\pm$ 3.2 mcU/ml, mean FT4 1.16  $\pm$  0.2 ng/dl
- 40% resumed treatment (mean TSH 22.2  $\pm$ 10.2 mcU/ml, mean FT4 1.0  $\pm$  0.23 ng/dl
  - 4 pts: Compound heterozygote for a TSHR mutation
  - 1 pt: SGA

## Mutations found in our study:



## CONCLUSIONS

In conclusion, our data indicates that children diagnosed with non-autoimmune subclinical hypothyroidism due to a TSHR mutation might not be in need of treatment unless they are compound heterozygous for the mutation or in case of selected cases of single heterozygous children born SGA