The IGF1 resistance syndrome is caused by genomic or genetic defects affecting the IGF1R locus (15q26.3). It is characterized by intrauterine and postnatal growth failure associated with microcephaly and some degree of intellectual retardation, in the face of normal or supranormal IGF1 and IGFBP3 levels.

**Introduction**

- A 3.5 years old girl, born at 36.5 weeks by vaginal delivery with birth weight 1.935 g (-3.2 SDS), height 41 cm (-4.4 SDS) and cephalic perimeter (CP) 29 cm (-5.2 SDS). She was followed-up in the neuropaediatric clinic because of mild psychomotor retardation.

**Exploration at age 3.5 years:**
- Normal phenotype. Bone age: 2.5 years.
- Body Weight: 10.5 Kg. (-2.4 SDS);
- Height: 87.4 cm (-3.0 SDS); CP: 46.5 cm (-2.5 SDS)
- IGF1: 95.4 ng/ml (-0.8 SDS);
- IGFBP3: 3 µg/ml (0.51 SDS)
- GH test (glucagon), peak of: 2.9 ng/ml
- Further analyses and explorations were normal.

**Mutation screening of GHR, IGFALS, and IGF1R genes by HRM and sequencing.**
- A novel point mutation, c.2155C>T, was detected in heterozygosis in IGF1R exon 10. The mutation alters a highly phylogenetically conserved residue p.Arg719Cys, located in the fibronectin type III and Tyrosine-protein kinase domains (Fig. 1).
- The family study was positive for the maternal grandfather, the mother, and two siblings of the mother (Family Pedigree & Table 1).

This novel mutation, not reported in the literature, was previously detected in our lab in a non-related patient presenting with growth failure from the first year of life, associated with high levels of IGF1 and IGFBP3.

**Family Pedigree**

**Family History**

- We present a familial case of IGF1 resistance syndrome due to a novel heterozygous IGF1R mutation with good response to rhGH treatment, showing bone age acceleration and increased growth rate.
- It is recommended to screen for IGF1R mutations in cases with short stature associated with IUGR, microcephaly and intellectual deficit, especially if there is a familial clustering, and evaluate the indication of rhGH, adjusting or maintaining it according to the observed response.

**Fig.1:** Detection by HRM, DNA sequence and domain location of the IGF1R mutation c.2155C>T, p.Arg719Cys.