Population-based cohort study: *PROP1* gene mutations are the most prevalent cause of congenital multiple pituitary hormone deficiency in Lithuania

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Background. Congenital multiple pituitary hormone deficiency (MPHD) may result from defects of transcription factors that govern the early pituitary development. The most prevalent are two mutation of *PROP1* gene: the 296delGA and 150delA[1,2].

Methods:

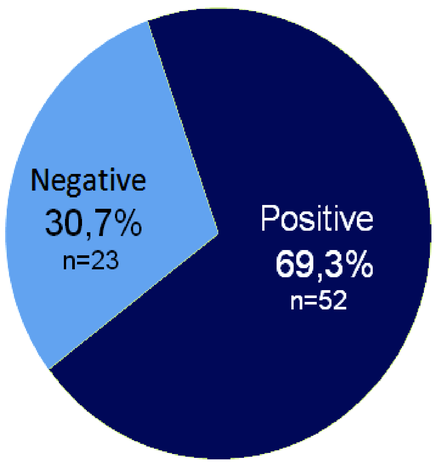
- Seventy five Lithuanian MPHD patients were tested for *PROP1* defects by Sanger sequencing.
- Perinatal/postnatal growth data, hormonal profiles and pituitary size were analyzed.

Conclusions:

1. The population-based cohort of patients with *PROP1* gene mutation is the largest described so far.
2. High prevalence of *PROP1* defects in Lithuania is due to a founder effect of 296delGA mutation.
3. The 296delGA mutation of Lithuanian patients originating earlier than in another European countries patients[3]
   (187.9 *vs.* 112 generations ago).

Results:

DNA analyses results of *PROP1* mutation

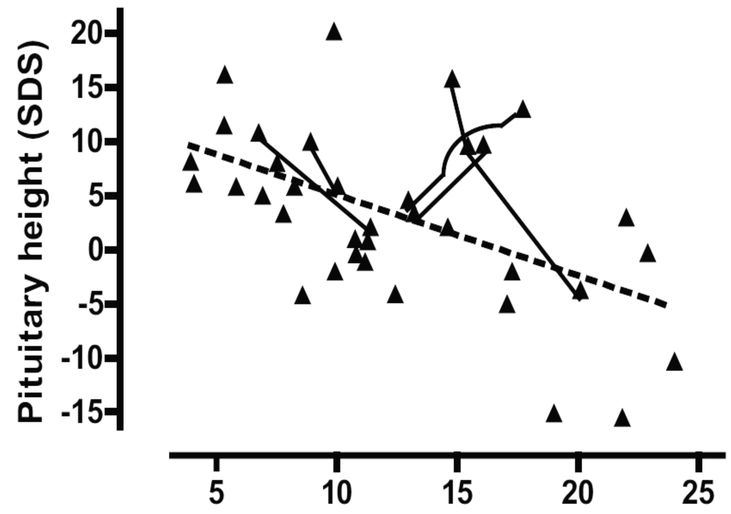


Genotypes:
50 patients – homozygote of 296delGA
1 patient – heterozygote of 296delGA/R71H
1 patient – heterozygote of 296delGA/150delA

- **50%** familial cases (ten sibling pairs and two sibling triples).
- The highest rate of *PROP1* mutations among MPHD patients from populations studied so far (**17.5** per million).
- The mutation carriers were found to share a common ancestor with the 296delGA mutation having arisen about **187.9** generations ago (range 156.8-229.5 generations).

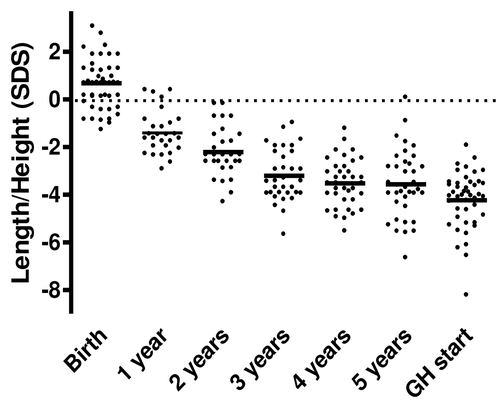
Pituitary size

- Pituitary height ranged from 16.6 mm (+20.2 SD) to 1.4 mm (–15.5 SD) and declined with age (r^2=0.27, P=0.001)

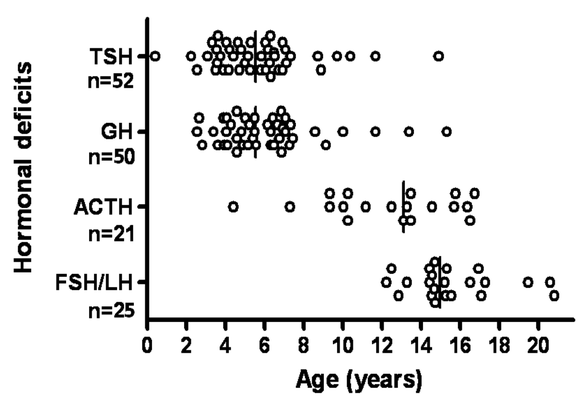


Perinatal and postnatal data

- Patients' birth lengths and weights were normal.



- Ages at diagnosis of hormones deficiencies.



References:

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2. Böttner A, Keller E, Kratzsch J, et al. *PROP1* mutations cause progressive deterioration of anterior pituitary function including adrenal insufficiency: a longitudinal analysis. *J Clin Endocrinol Metab*. 2004;89:5256–5265.
3. Dusatkova P, Pfäffle RW, Obermannova B et al. Ancestral origin of two most prevalent mutations in the *PROP1* gene causing combined pituitary hormone deficiency in selected European populations. [Abstract]. *Horm Res*. 2013:50.