Spatial and Temporal Expression of Immunoglobulin Superfamily Member 1 (IGSF1) in the Rat

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Introduction

X-linked IGSF1 deficiency syndrome*

- Central hypothyroidism (CeH)
- Delayed puberty (but normal testis growth)
- Macroorchidism (adults)
- Variable PRL/GH-def and ↑BMI/fat%

IGSF1*

- Plasma membrane glycoprotein
- Known mutations impair protein trafficking to cell membrane
- Function and expression profile unknown

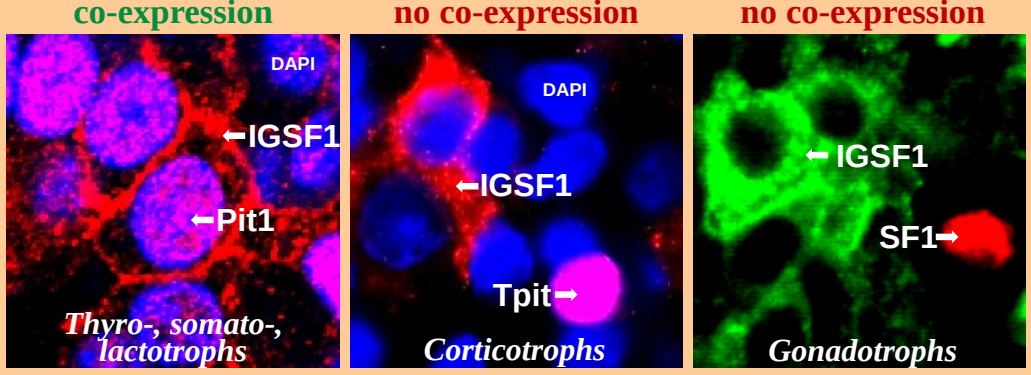
Aim

To investigate spatial + temporal expression of IGSF1 in rat hypothalamus, pituitary gland, and testis, at the protein and mRNA levels.

Results

Pituitary gland

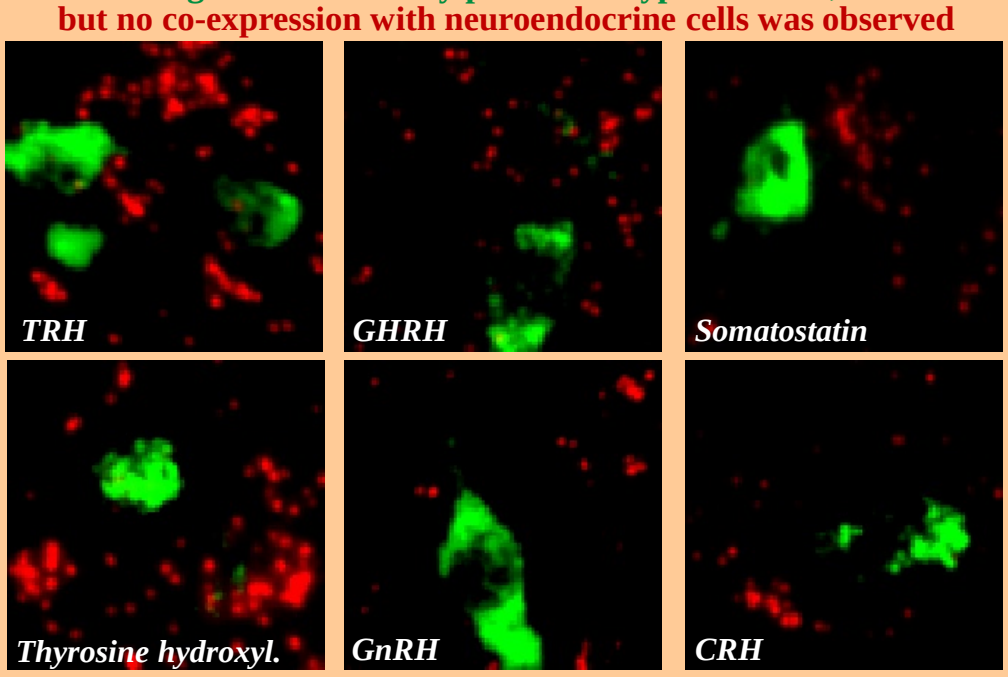
co-expression | no co-expression | no co-expression



IF antibodies against Igsf1 (cytoplasm), DAPI, Pit1, Tpit, or SF1 (all nucleus)

Hypothalamus

Igsf1 is abundantly present in hypothalamus, but no co-expression with neuroendocrine cells was observed

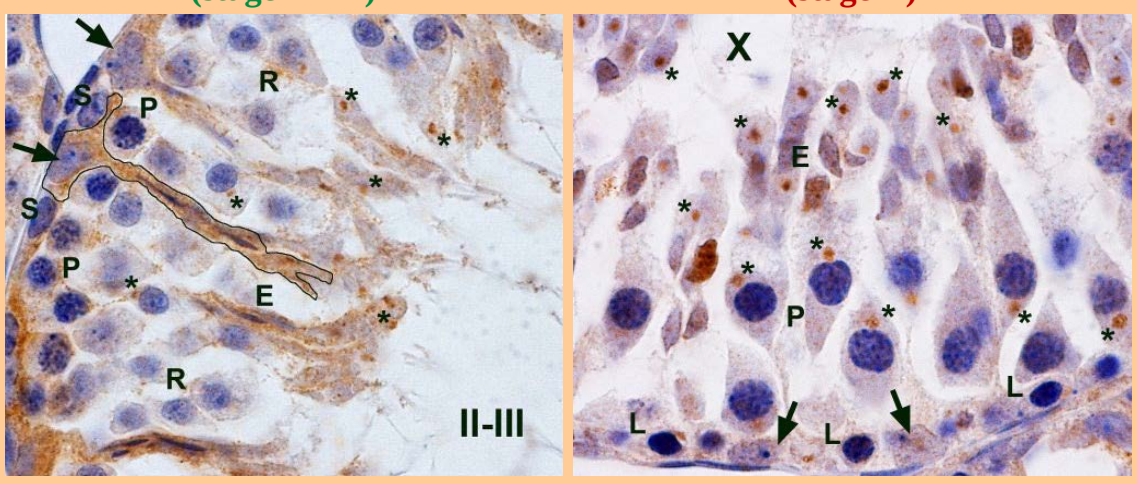


*In situ hybridisation for Igsf1 (**red probe**) and neuroendocrine cells (**green probe**)*

In all cases, specificity of IGSF1 protein expression was corroborated by *in situ* hybridization and real-time PCR for the *Igsf1* mRNA.

Testis

Igsf1 present in Sertoli cells '→' (stage II-III) | Igsf1 not present in Sertoli cells '→' (stage X)



Stages of the seminiferous epithelium in which Igsf1 is present in Sertoli cells and in the nucleus of spermatids

Igsf1 present in Leydig cells

Immunohistochemistry. Germ cell legend: spermatogonia (S), leptotene- (L), zygotene- (Z), pachytene- (P), and diplotene spermatocytes (D), round (R) and elongated spermatids (E), chromatoid bodies (*)

Discussion

- The central hypothyroidism might be dysfunction of the thyrotropic cells of the pituitary, rather than TRH production by the hypothalamus.
- The delayed puberty and macroorchidism are likely caused by a local defect in the testis, rather than gonadotropin deficiency.

Conclusion

IGSF1 expression observed in

- *Hypothalamus*; outside neuroendocrine cells
- *Pituitary*; specifically GH-, TSH-, and PRL-producing cells
- *Testis*; both in Sertoli cells (during specific stages of seminiferous epithelium) and Leydig cells.

* Sun et al., Nat. Genet. 2012; 44(12):1375-81
Joustra et al., JCEM 2013; 98(12):4942-4952