

Deficiency of pituitary hormones

- a genetic national multicentre study -

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**Hormones and
Metabolism**

**Neurologic and
Neurovascular
Disorders**

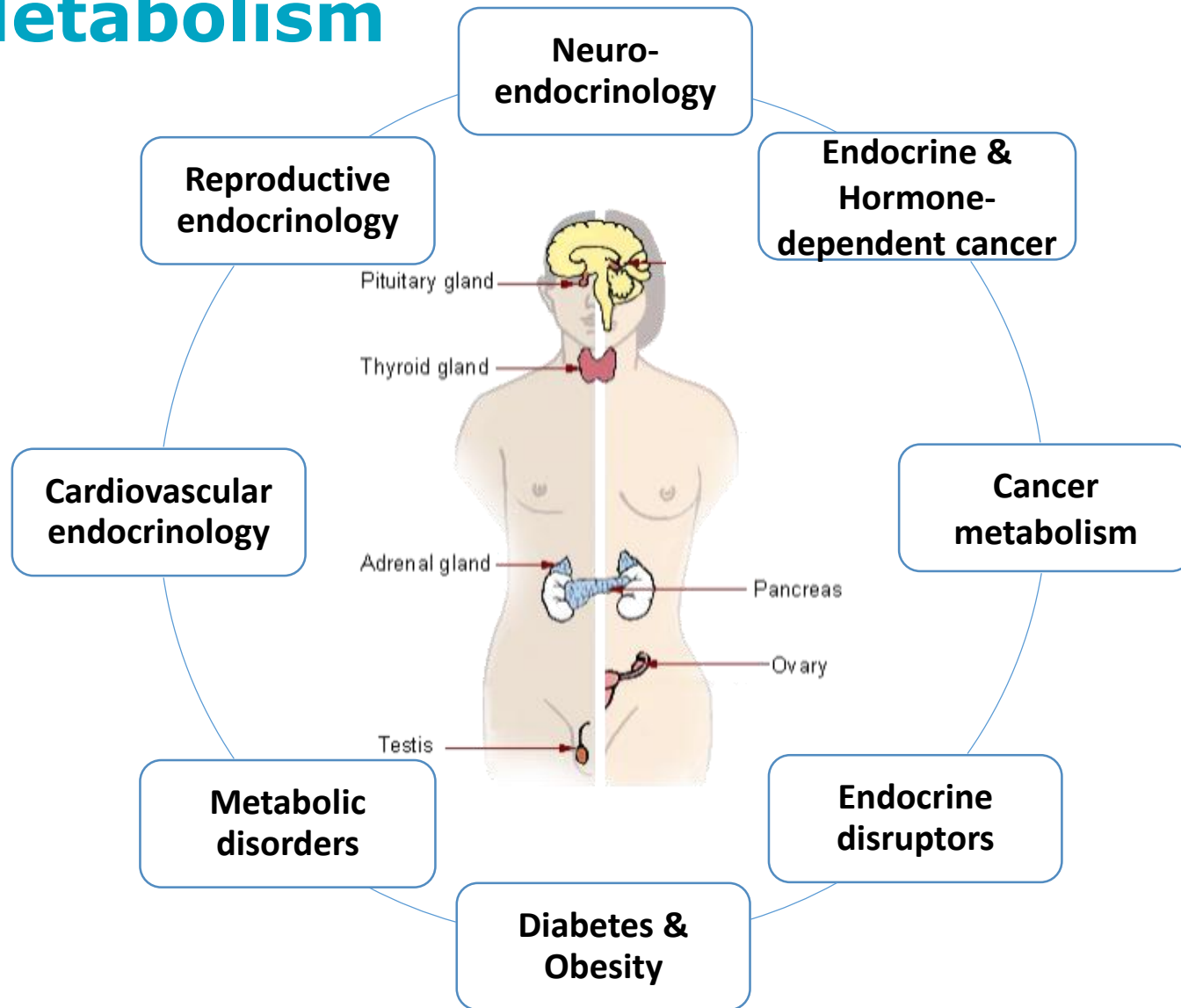


66 PhD Integrated Members

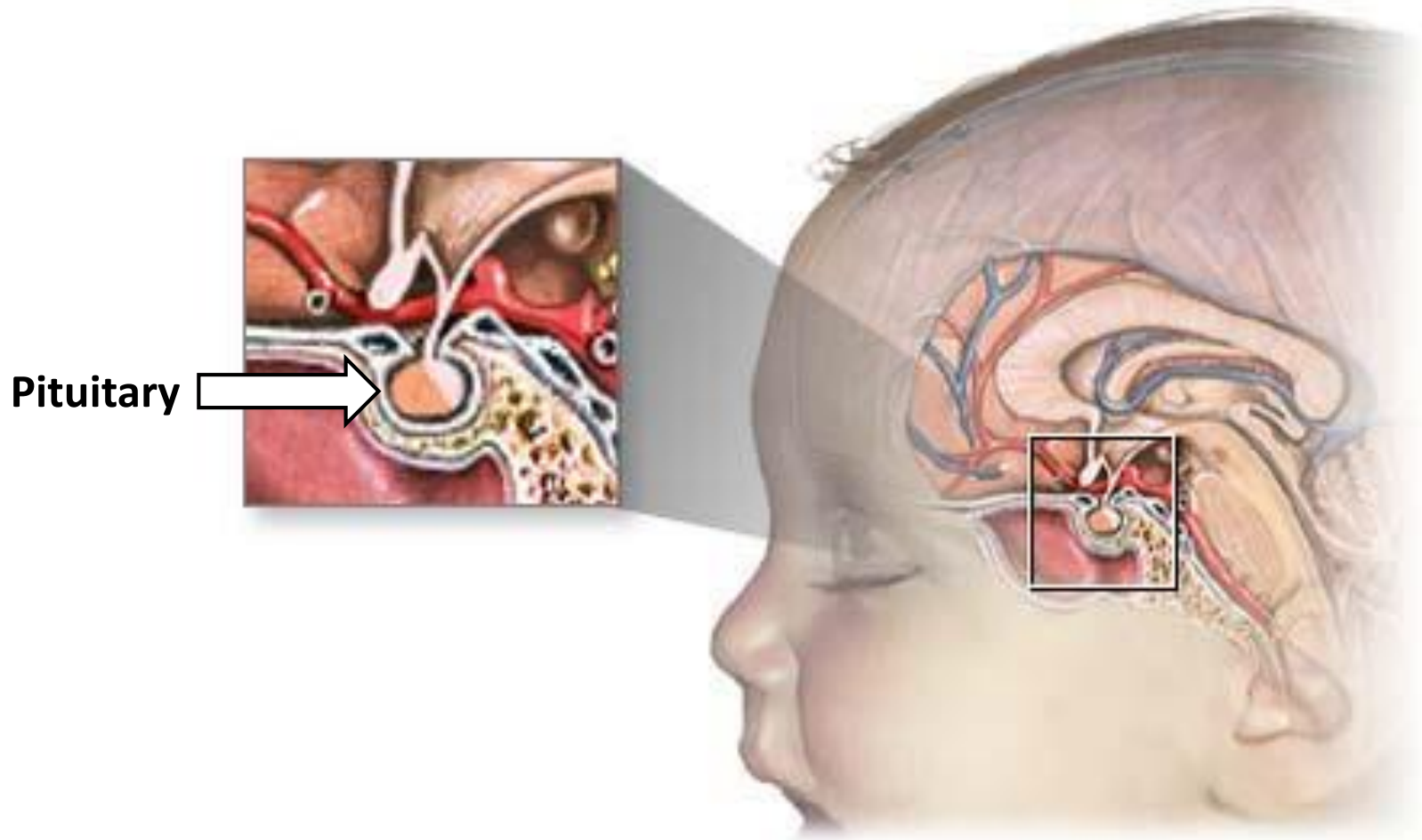
**Biopharmaceuticals
and Biomaterials**

**Biomedical
Chemistry and Drug
Research**

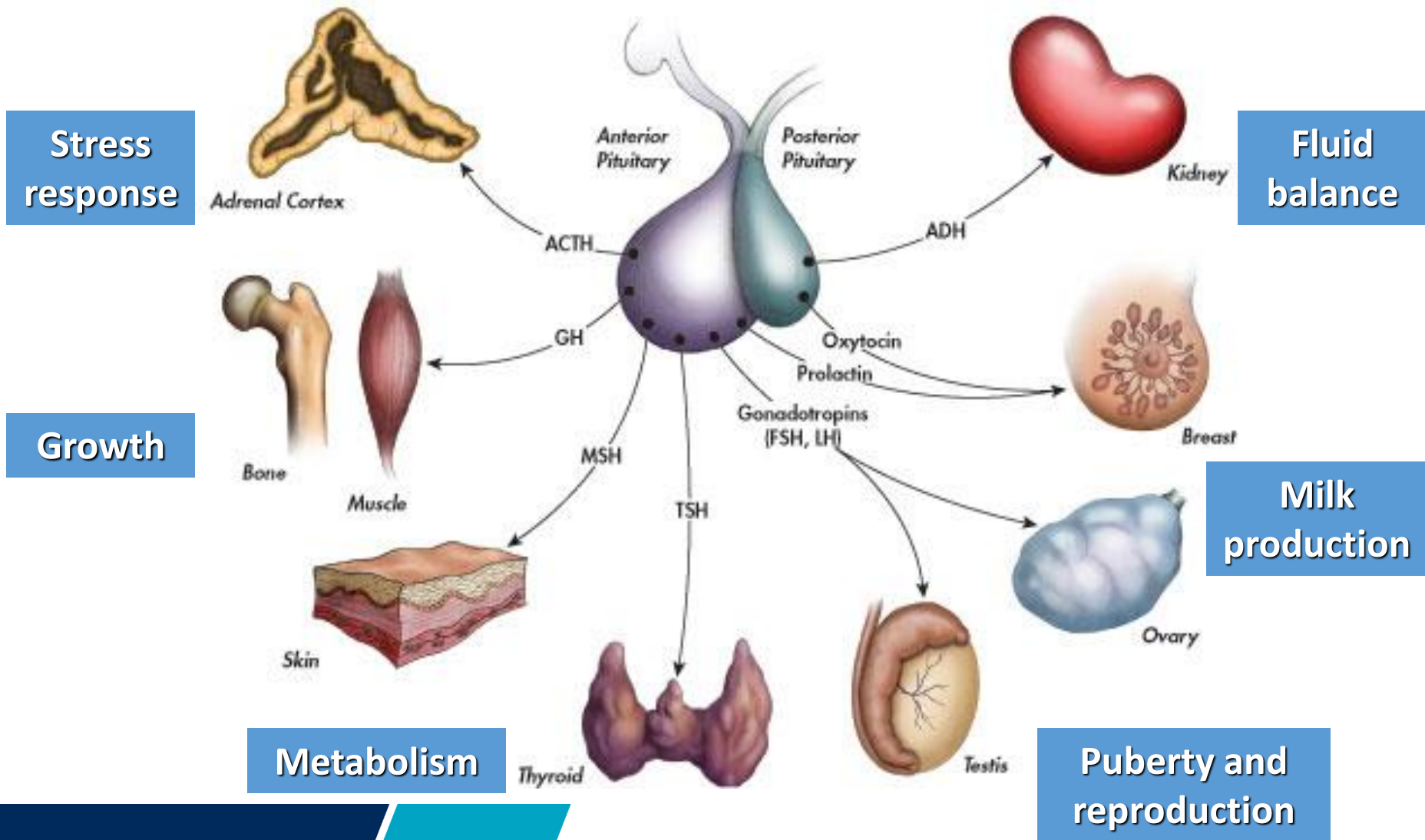
Hormones & Metabolism



Pituitary gland



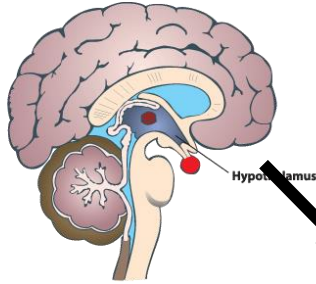
Pituitary hormones and actions



Cascade of pituitary hormone regulation and action

The example of growth hormone (GH)

Hypothalamus



GHRH (Growth Hormone Releasing Hormone)

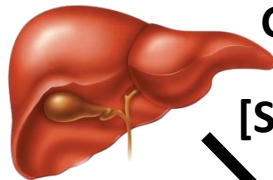
Pituitary



GHRHR (Growth Hormone Releasing Hormone Receptor)

GH (Growth Hormone)

Liver



GHR (Growth Hormone Receptor)

[STAT5b]

IGF1 (Insulin-like Growth Factor-1) +

{ IGFBP3
ALS

Target organ



IGF1R (Insulin-like Growth Factor-1 receptor)

Consequences of pituitary hormone deficiencies (hypopituitarism)

- Short stature (growth hormone deficiency)
- Mental retardation (hypothyroidism)
- Infertility (hypogonadism)
- Cardiovascular, metabolic and immune alterations (adrenal failure)
- Increased thirst and urine production (diabetes insipidus)

Causes of pituitary hormone deficiencies

Invasive

Infarction

Infiltrative

Injury

Immunologic

Iatrogenic

Infectious

Isolated

Idiopathic

Genetic?



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Braga



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Centro Hospitalar do
Tâmega e Sousa, E.P.E.



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HOSPITAL DAS
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Portuguese study of pituitary hormone deficiencies

- 20 clinical departments
- 264 patients
- 8 years
- DNA sequencing of genes involved in the development and function of the pituitary

Genetic mutations in 30% of cases

Total 264 patients

**Def. GH
(n=88)**

Genes

**GH1
(n=6)**

**GHRH
(n=6)**

**CHD7
(n=1)**

**Def. FSH/LH
(n=50)**

Genes

**FGFR1
(n=6)**

**GNRHR
(n=5)**

**KAL1
(n=3)**

**CHD7
(n=8)**

**others
(n=8)**

**Def. ADH
(n=12)**

Genes

**AVP
(n=5)**

**Multiple def.
(n=114)**

Genes

**PROP1
(n=29)**

**LHX3
(n=7)**

**LHX4
(n=6)**

**GLI2
(n=2)**

**others
(n=3)**

Pituitary Hormone Deficiency

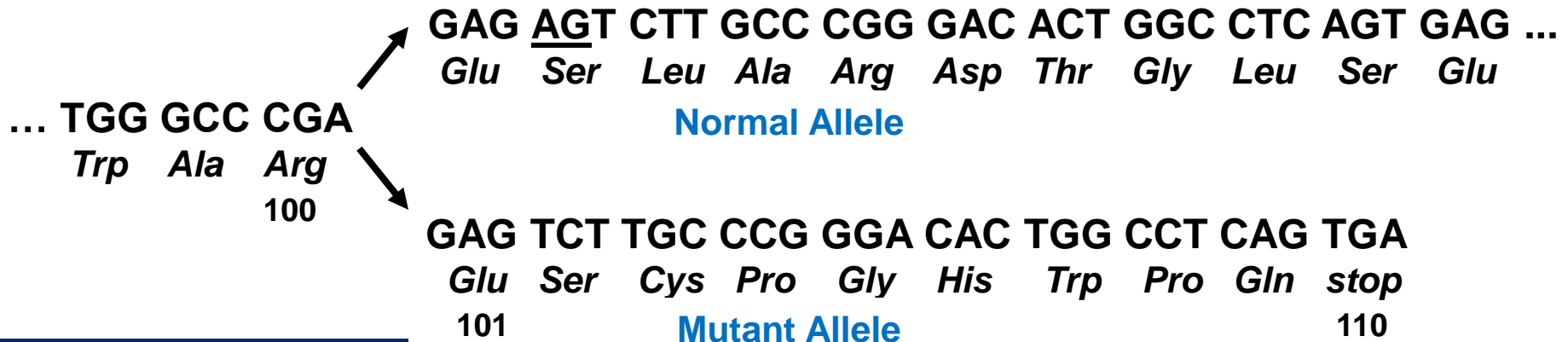
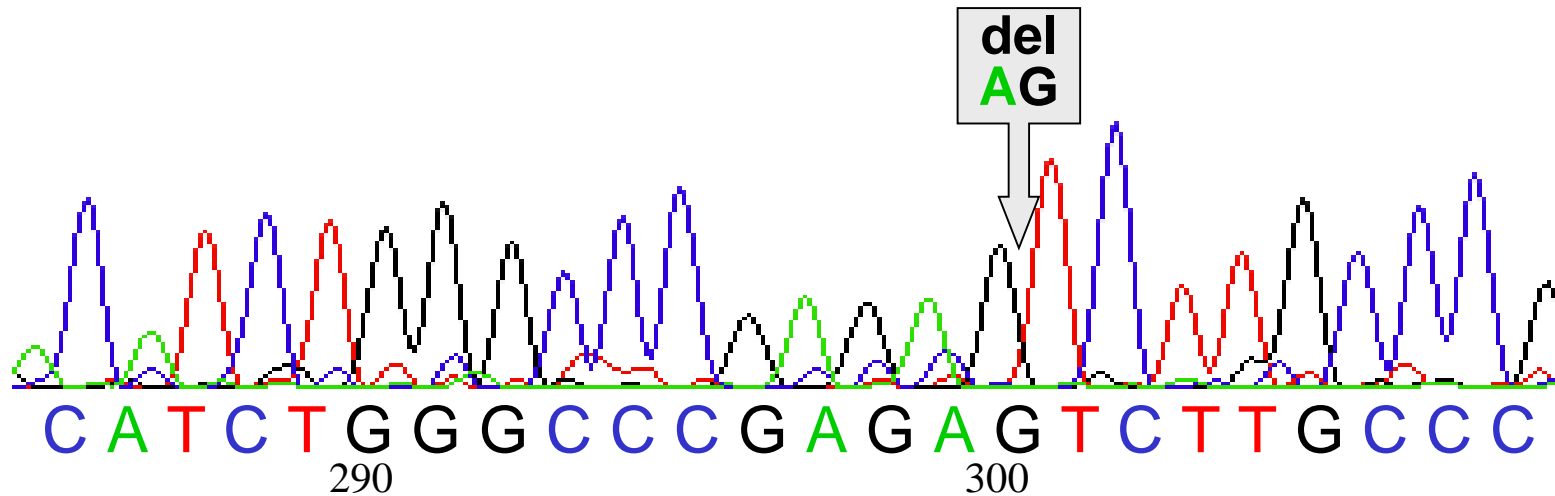
- Practical example -



- Female, 64 years old
- Short stature
- No pubertal development
- Hypothyroidism
- Deficiency of multiple hormones (GH, TSH, FSH, LH, Prolactin)
- Idiopathic (i.e. unknown cause)

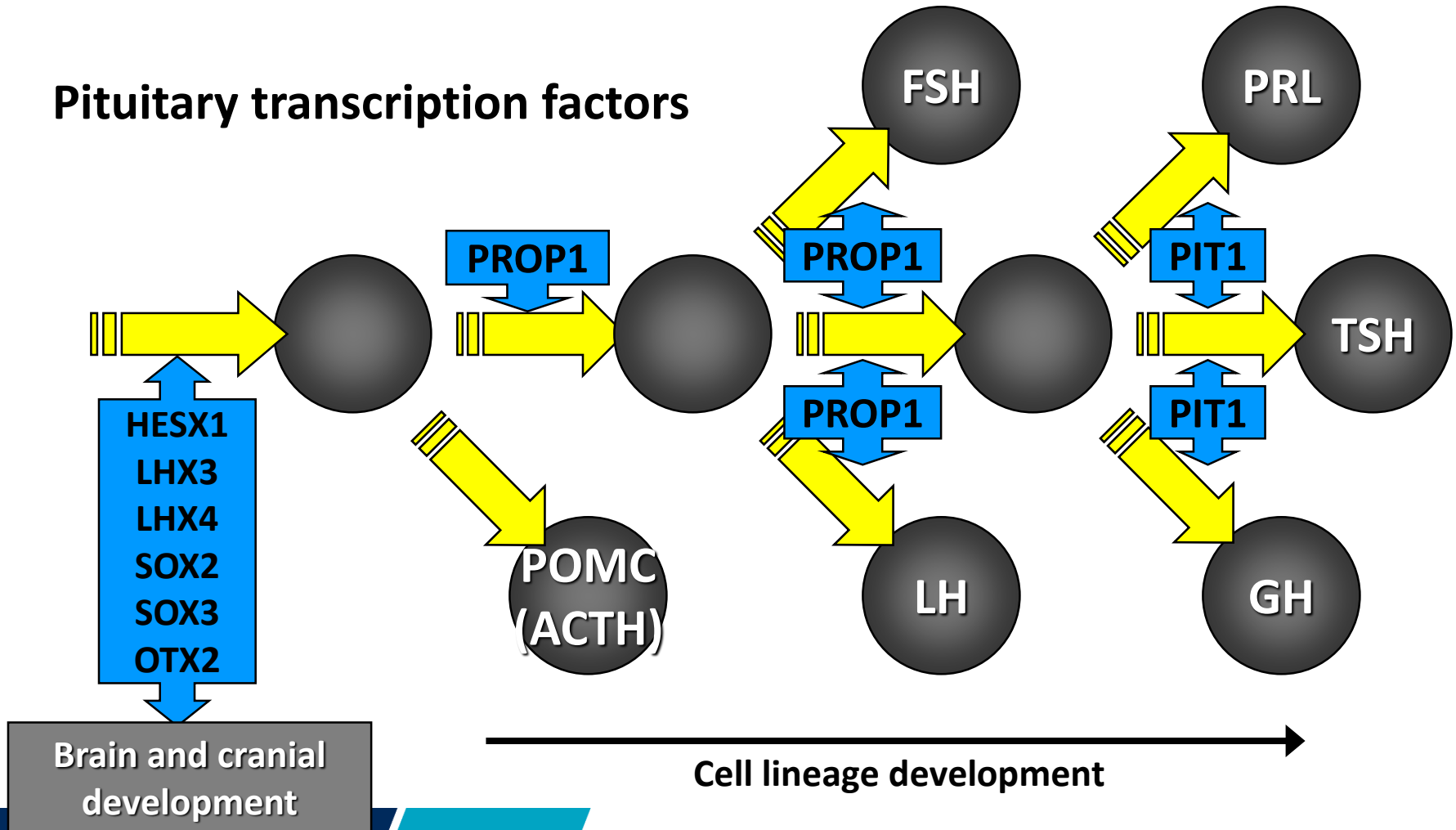
Genetic testing

- *PROP1* gene mutation (301_302delAG) -



PROP1 gene: the most common genetic defect in Portuguese patients

Pituitary transcription factors



Impact of the genetic studies

- Allow a definite diagnosis based on the precise molecular defect
- Allow appropriate clinical decisions
 - Prognosis
 - Treatment and follow-up
 - Genetic counselling
- Provide insight into the mechanisms of pituitary disorders

Acknowledgements

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