Is the Glucocorticoid receptor, NR3C1, present in PIT1 progenitor cells?

Dale Ann Sunny[1], Sandria Athul, Pratyusa Das, Buffy Ellsworth PhD[2]

[1]SI Bridges to the Baccalaureate, School of Biological Sciences, Southern Illinois University Carbondale

[2]Department of Physiology, SIU School of Medicine.

Abstract

The pituitary gland is referred to as the "master" gland of the endocrine system because it controls the functions of many of the other endocrine glands. The pituitary gland itself consists of 2 major structures: anterior lobe and posterior lobe. Each lobe of the pituitary gland makes certain hormones. The anterior lobe produces growth hormone, prolactin, adrenocorticotropic hormone, thyroid-stimulating hormone, follicle-stimulating hormone, and luteinizing hormone. The posterior lobe releases antidiuretic hormone and oxytocin. In this experiment we optimized immunohistochemistry for the proteins NR3C1 and PIT1. NR3C1 encodes glucocorticoid receptors, which can function as a transcription factor that binds to glucocorticoid response elements in the promoters of glucocorticoid responsive genes to activate their transcription. PIT1 is a transcription factor that binds to the growth hormone gene to stimulate its expression in the anterior pituitary. Previous studies from the Ellsworth laboratory show that glucocorticoid signaling, presumably via NR3C1, is important for the development of growth hormone producing cells, known as somatotrophs (unpublished data, Das and Ellsworth). PIT1 marks the cells that will develop into somatotrophs. This experiment was conducted to see whether NR3C1 and PIT1 are both present in these somatotroph progenitor cells.

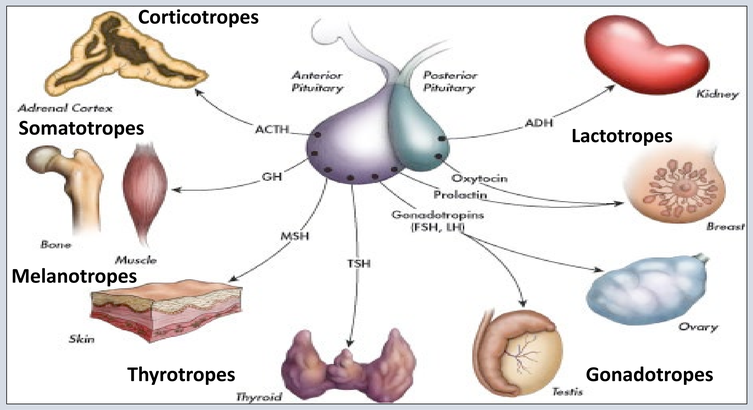

Figure 1: Different Cell Types in the Pituitary Gland.
The pituitary gland is composed primarily of five hormone-producing cell types. They are thyrotropes, lactotropes, corticotropes, somatotropes and gonadotropes, each secreting thyrotropin, prolactin, ACTH, growth hormone and gonadotropins (FSH and LH) respectively.

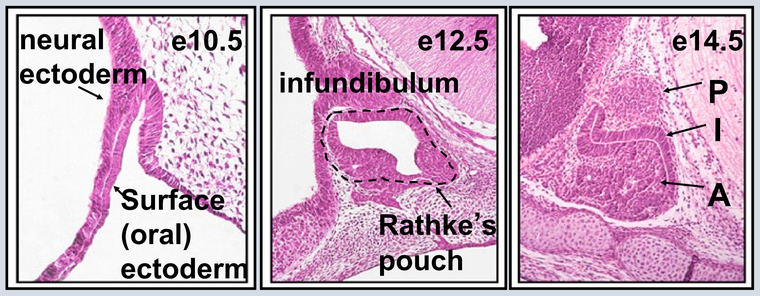

Figure 2: The development of the Pituitary Gland.
Rathke's pouch is the portion of the oral ectoderm that invaginates to form the putative pituitary during embryonic development and will become the intermediate and anterior lobes of the pituitary gland.

References

Ellsworth, B. S., & Stallings, C. E. (2018). Molecular mechanisms governing embryonic differentiation of pituitary somatotropes. *Trends in Endocrinology & Metabolism*, *29*(7), 510–523. https://doi.org/10.1016/j.tem.2018.04.009

Pfäffle, R., Kim, C., Otten, B., Wit, J.-M., Eiholzer, U., Heimann, G., & Parks, J. (1996). Pit-1: Clinical aspects. *Hormone Research*, *45*(1), 25–28. https://doi.org/10.1159/000184824

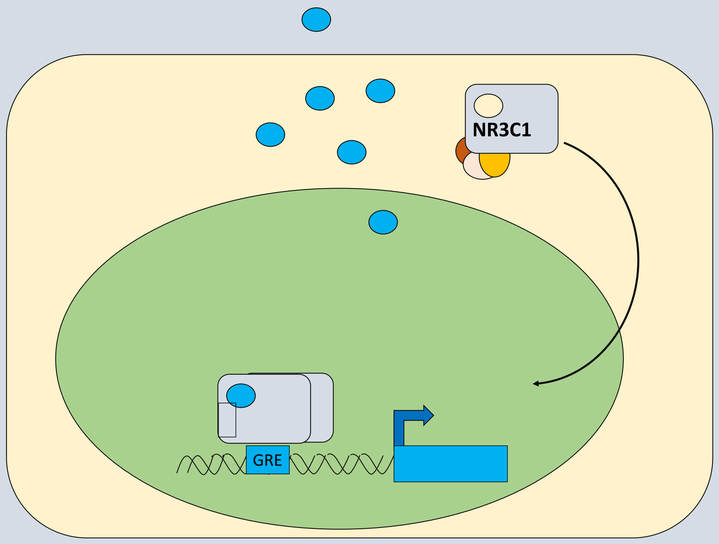

Figure 3: Glucocorticoid receptor signaling.
The glucocorticoid receptor also known as NR3C1 is the receptor to which cortisol and other glucocorticoids bind. The glucocorticoid receptor controls the genes that affect growth, metabolism, and immune response and is expressed in almost all body cells.

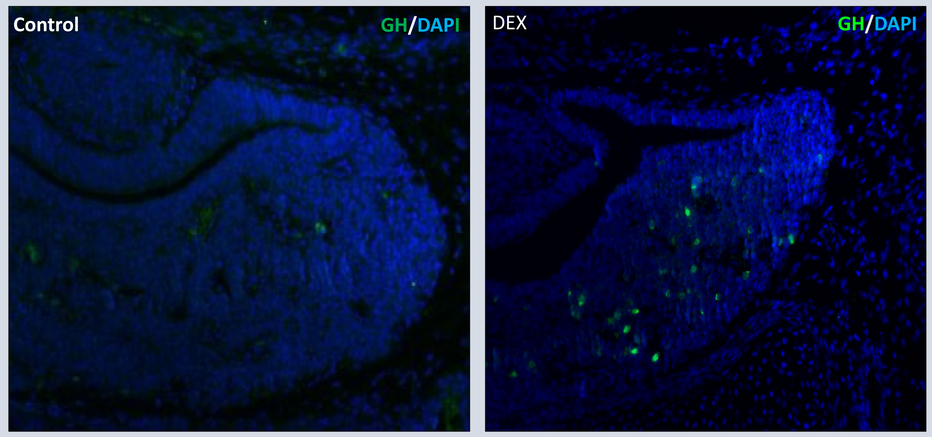

Figure 4: Glucocorticoids induce premature somatotrope maturation in the embryonic mouse pituitary gland.
Pregnant mice were given glucocorticoids (3 ug/mL dexamethasone) in their drinking water from embryonic day (e)13.75 to e15.75, when embryos were collected. Immunohistochemistry was performed for growth hormone (GH, green). Cell nuclei are stained with DAPI (blue). No GH is detected in the control pituitary, but several GH-positive cells are present in the pituitary from an embryo exposed to glucocorticoids (DEX). This shows that glucocorticoids can induce premature somatotrope maturation in mice. Scale bars represent 100 microns. (unpublished data, Das and Ellsworth).

Results

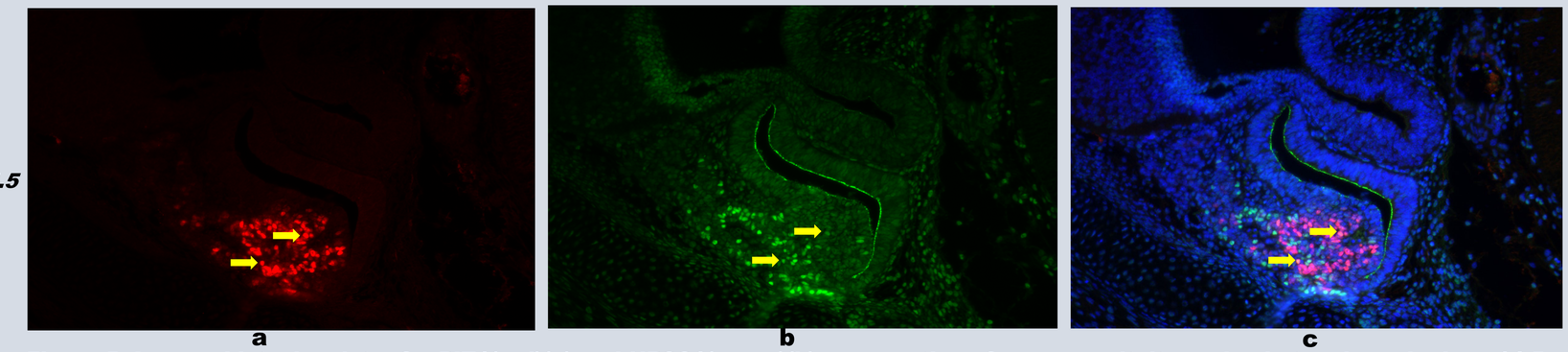

Figure 5: Immunohistochemistry for PIT1(red)(a) and NR3C1(green)(b) on a section of a mouse pituitary gland at embryonic day e14.5 at 200x magnification. The arrows indicate the colocalized cells.

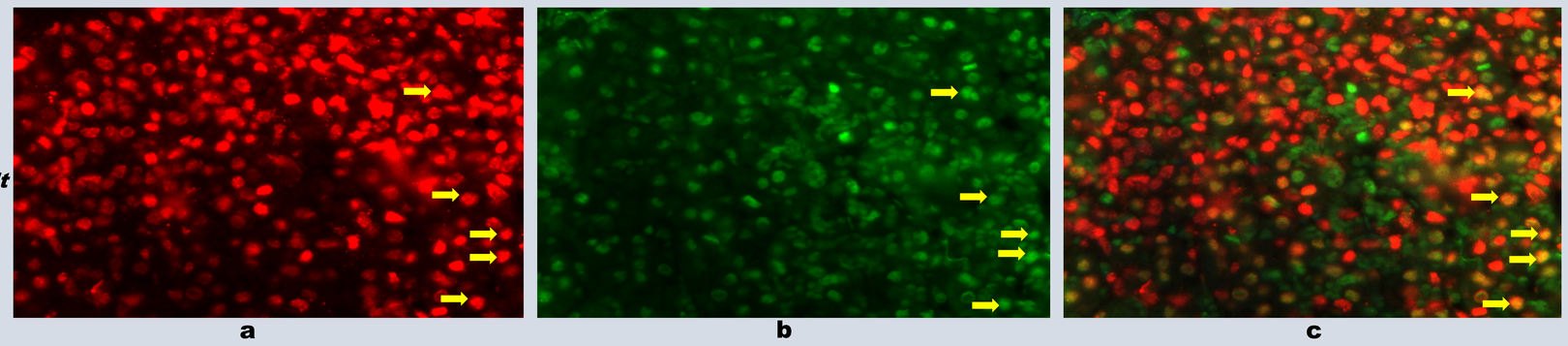

Figure 6: Immunohistochemistry for PIT1(red)(a) and NR3C1(green)(b) on a section of an adult mouse pituitary gland at 630x magnification. The arrows indicate the colocalized cells.

Conclusion

NR3C1 is present in a subset of PIT1 positive cells at embryonic day e14.5 and adult stages. In this experiment more colocalization was found between NR3C1 and PIT1 in adult embryos than in e14.5.

Acknowledgements

I would like to thank Dr.Laxmi Sagwan-Barkdoll and the Southern Illinois Bridges to the Baccalaureate Program at Southern Illinois University, Carbondale for giving me the opportunity to do the research and the National Institute of Health for funding the research. I would also like to thank Dr.Buffy Ellsworth, Sandria Athul and Pratyusa Das for their constant support and guidance throughout the research.