Project Title: **The role of G-protein coupled bile acid receptor (Gpbar1, Tgr5) in the regulation of growth hormone.**

Authors: Sneha Limaye ([slimaye@neomed.edu](mailto:slimaye@neomed.edu)), Jessica M. Ferrell, Ajay Donepudi, Shannon Boehme, John Y.L. Chiang

Abstract:

Bile acid signaling through G-protein coupled bile acid receptor (Gpbar1, Tgr5) is known to regulate gene expression and hormone secretion. Tgr5 is expressed in several tissues and regulates several cellular pathways. Neuronal expression of Tgr5 increases during pathological conditions such as hepatic encephalopathy. Although studies have shown Tgr5 expression in different regions of the hypothalamus, Tgr5 function in the brain remains unclear. Recent studies from this lab show that lack of the Tgr5 gene increased serum growth hormone (GH) levels in mice. GH is secreted from the anterior pituitary gland, and its secretion is regulated by the hypothalamus via secreting somatostatin and growth hormone releasing hormone. It was hypothesized that Tgr5 expressed in the brain regulates growth hormone release. To identify the role of Tgr5 in GH secretion, pituitary and hypothalamic gene expression in male wild-type (WT) and Tgr5 knockout (Tgr5-/-) mice was analyzed using qPCR. Additionally, rat pituitary adenoma cells (GH-3 cells) were treated with a Tgr5 agonist, and GH regulatory genes were analyzed. Serum GH levels in mice and cell culture supernatants were analyzed using ELISA assays. Though serum GH levels and pituitary GH gene expression increased in Tgr5-/- mice compared to WT, *in vitro* experiments with rat pituitary adenoma cells suggest that Tgr5 activation has no effect upon GH secretion or expression of GH regulatory genes. Hypothalamic GH regulatory genes were altered in Tgr5 knockout mice. The results suggest that Tgr5 employs an indirect mode of action in regulating GH secretion.

Objectives:

* Determine the relationship between the bile acid receptor Tgr5 expression in the brain and growth hormone secretion and regulation.
* Localize Tgr5 expression in the animal brain.