Imaging and manipulating the growth hormone axis

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Pituitary growth hormone (GH) is released in a pulsatile fashion in response to stimuli from its hypothalamic regulators. For efficient generation of hormone pulses, both the hypothalamic mechanisms and the pituitary target cells need to be highly coordinated in their secretory activity. This is particularly important for the GH axis since the physiological responses in target tissues depend on the pattern of GH exposure, as well as on the amount of GH released. Recent strudies have shown that the pituitary GH cell populations are highly dynamic and show a remarkable degree of plasticity, with both cell number and hormone reserves varying in response to demands at different stages of life. In order to study this, we are exploiting a variety of genetic approaches to image, manipulate or ablate single or multiple populations of hypothalamic or pituitary cells, either during development or postnatally. Studies of mice with disruption of genes involved in pituitary development have shed light on mechanisms underlying similar problems in children with pituitary deficits and have led us towards the identification of a precursor cell population in the adult pituitary gland. We have also targeted fluorescent proteins to cytoplasmic or secretory granule compartments in the GH and prolactin (PRL) axes, allowing the application of a variety of fluorescence imaging techniques to study the fate of these hormones from the single vesicle level, to the entire pituitary population of cells, *in vitro*, *ex vivo* and even *in vivo*. By targeting transgene products that selectively alter specific cellular functions (*e.g.*, receptor signaling, ion-transport, RNA stability, vesicle packaging) we can manipulate selectively, populations of neuroendocrine and pituitary cells. These provide new models of somatotroph loss and compromised pituitary function, that extend our understanding of pituitary endocrine deficits, and enable us to test more specific novel therapeutic interventions.