

## Randy J. Seeley, PhD

Professor

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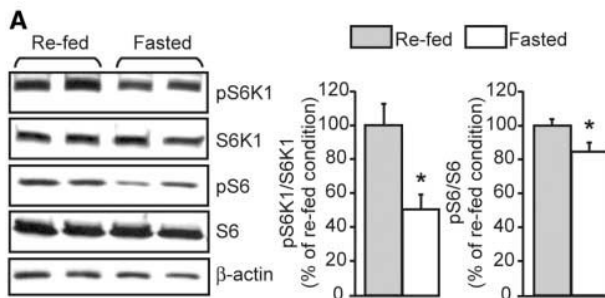
### Description of Research:

Under normal circumstances, caloric intake is precisely matched to caloric expenditure such that the amount of stored calories in the form of body fat remains stable. The evidence suggests that this is accomplished via a hormone (leptin) that is produced directly in fat cells that circulates back and has potent effects on the central nervous system (CNS). Dr. Seeley's research group focuses on understanding the effects leptin has on behavior and the CNS in service of regulating food intake. Specifically, they have been interested in hypothalamic neuropeptide systems (NPY, CRH and melanocortins) that might mediate the effects of leptin. Additionally, they have been exploring how these neuroendocrine systems are altered in a number of obesity models. Dr. Seeley's work has two major areas of clinical relevance. The first and most obvious is obesity. A deeper appreciation of the way in which leptin acts in the CNS to produce weight loss should provide a number of new targets for the development of pharmaceutical interventions for obesity. Dr. Seeley's has an active collaboration with Procter & Gamble to help leverage the discoveries into new treatment options for the obese population. The second area of clinical relevance is wasting which accompanies AIDS and some tumors. Weight loss is a major contributor to the mortality associated with these conditions. Both the length and quality of patients' lives could be substantially increased by effective treatments for wasting. They have developed a model of tumor anorexia that they are using to measure changes in neuroendocrine systems and attempting to reverse the anorexia with a variety of agonists and antagonists for identified receptors.

### Collaborations:

Dr. Seeley collaborates with Dr. Woods studying the control of obesity by the gut-brain axis, with Dr. Sakai evaluating stress and body weight regulation, and with Dr. D'Alessio studying GLP-1 and glucose tolerance. As a new member, Dr. Seeley has not used DHC cores.

### Representative Figure:



Modulation of hypothalamic mTOR signaling by energy status. Left: Representative Western blot from re-fed rats or rats fasted for 48 hours.  $\beta$ -actin was the loading control. Right: Quantification by image analysis of hypothalamic S6K1 and S6 phosphorylation. Error bars indicate SEM. \* $P < 0.05$  versus rats in the re-fed condition. Five brains were examined for each condition. Fig. 2 from Science, 2006; 312:927-930.