Leptin and Energy Availability

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By Brittany Bostic, Office of Research Editorial Assistant

Professor Myers’ research focuses on the adipose-derived hormone, leptin, which signals the repletion of long-term energy stores to suppress feeding, permit energy expenditure, and control a variety of processes that must be modulated in line with energy availability. The Myers lab utilizes mouse models to understand roles for individual leptin receptor (LepRb)-mediated signals (including STAT3) and populations of LepRb neurons in leptin action. Neurons in the lateral hypothalamic area (LHA) that control reward-driven processes, those in the medial hypothalamus that control feeding, and those in the brainstem that control glucose metabolism represent areas of ongoing research. Research in the Myers lab depends upon a number of BRCF cores, including the Transgenic Animal Model Core (TAMC), the Vector Core, the DNA Sequencing Core, and the Bioinformatics Core.

“We would have to shut down the lab without the Transgenic Core,” Dr. Myers said. “Our bread and butter is the generation of knock-in models to express a variety of genes (cre recombinase, molecular reporters) in a cell-specific way by gene targeting in mouse ES cells. I think the core has helped us make at least two dozen such models in the decade since I arrived at Michigan. Their technical skill, knowledge base, attention to detail, and willingness to work with you when you need something a bit out of the ordinary set them up as the best core in the country, I think.”

In one recent study, TAMC helped to generate a neurotensin-ires-cre line to permit the ablation of LepRb specifically in the LHA, revealing the role for leptin action in these neurons for energy balance (the animals were obese) and the control of the brain reward system. Furthermore, many such mouse lines permit the cell-specific interrogation of the neural circuitry in combination with cre-dependent viral tracers, such as several new conditional rabies vectors produced by Tom Lanigan, Ph.D., in the Vector Core.

In addition to standard DNA sequencing by the DNA sequencing core, RNAseq by the core, together with analysis by Dr. Jim Cavacolli’s team in the Bioinformatics Core is becoming more and more important for the Myers lab. Currently, the lab is investigating the mechanisms by which leptin controls cell-autonomous gene expression by RNAseq of polysome-associated mRNA isolated from LepRb-expressing neurons. While still in its infancy, the initial analyses have already revealed new genes enriched in these neurons, including several neuropeptides likely to contribute to neuronal signaling downstream of leptin action.