

Endocrine Society of Australia Postdoctoral Award 2018 – Report

Recipient: Dr Luba Sominsky, School of Health and Biomedical Sciences, RMIT University

Project title: The role of microglia in mediating the neuroendocrine responses in diet-induced obesity

Summary:

Microglia, a key brain immune cell population, are acutely and chronically activated by a diet that is high in fat, yet if this response contributes to or counteracts the development of obesity with prolonged exposure to high fat diet (HFD), is currently unknown.

We have shown that rodents suckled in small litters, where they have greater access to their mother's milk, maintain an overweight phenotype throughout their life. This early life overfeeding is associated with acute and long-term changes in the levels of the major metabolic hormones, leptin and ghrelin, as well as in the brain (hypothalamic) appetite-regulatory circuitry. We have also seen that these overweight rats have increased microglial proliferation and activation throughout the brain. However, it is still not known whether this acute neuroinflammatory response is adaptive or detrimental in the context of HFD feeding and the associated neuroendocrine changes.

The Endocrine Society of Australia has supported my research into the role of microglia in the development of obesity.

Aims:

This project had two aims:

Aim 1: To test, in a rat model, if microglia mediate the hypothalamic inflammatory response to an acute HFD (3 days).

Aim 2: To test if microglia mediate hypothalamic sensitivity and the development of an obesogenic phenotype after a long-term high fat diet (3 months).

Progress:

We have completed experiments showing that as little as 3 days of HFD feeding induce hypothalamic microgliosis, and that a conditional ablation of microglia in our *Cx3cr1-Dtr* rats leads to an immediate suppression of food intake and temporary weight loss.

We have also conducted experiments examining the role of microglia in the development of obesogenic phenotype after a long-term HFD (3 months), and whether microglial ablation in the context of HFD feeding is beneficial in counteracting the negative effects of acute HFD exposure. Neuroimmune assessments, as well as the assessments of circulating metabolic factors and hypothalamic appetite circuitry are currently underway.

Conclusions:

Our studies show that microglia have an important role in the regulation of satiety and are thus a potential target for the control of satiety. These findings have important implications for the management of overweight and obesity.

Conference presentations:

2018 - Endocrine Society of Australia Annual Meeting, Adelaide, Australia. *Activation and suppression of microglia during early development similarly disrupt neuroendocrine function in the female rat.*

Publications relevant to the award:

Fuller EA, Younesi S, Xavier S, **Sominsky L.** (2019) Neuroimmune regulation of female reproduction in health and disease. *Current Opinion in Behavioral Sciences.* 28:8-13.