Proceedings of the Nutrition Society (2015), **74 (OCE3)**, E190 doi:10.1017/S0029665115002165

Scottish Section Meeting, 25–26 March 2015, Diet, gene regulation and metabolic disease

A novel hypothalamic protein regulated by high fat diet and leptin

D. Sergi, A. C. Morris, J. E. Drew, F. M. Campbell, P. Nicol and L. M. Williams
Rowett Institute of Nutrition and Health, Greenburn road, AB21 9SB, University of Aberdeen

Obesity is a global health issue. Treatment or prevention of obesity via lifestyle change remains elusive, particularly due to the lack of patient compliance and the subsequent weight regain following the cessation of dietary intervention. The hypothalamus is pivotal in regulating energy homeostasis by matching up energy intake and expenditure. Therefore, identifying novel mechanisms underlying these processes will provide new insights into the treatment of obesity. High-fat feeding has been reported to induce functional and structural impairment of the hypothalamus[1–3] leading to leptin[4] as well as ghrelin resistance[5]. As a consequence regulation of energy homeostasis is disrupted.

Microarray analysis identified a novel gene, *SerpinA3N*, highly up regulated in hypothalamic neurons of mice in response to consumption of a high-fat diet (HFD) and intraperitoneal (IP) injections of leptin[6]. We sought to investigate whether *SerpinA3N* plays a role in energy balance by using a hypothalamic cell line model.

Initial results confirm that *SerpinA3N* is expressed in the hypothalamic neuronal cell line as assessed by PCR (Fig. 1). Its expression is up regulated by both leptin ($P < 0{\cdot}001$) and palmitic acid ($P < 0{\cdot}001$) challenge (Fig. 2). Statistical analysis was carried out using one-way ANOVA.

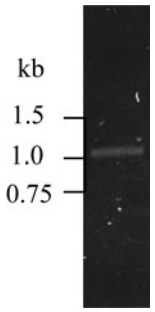

Fig. 1. Electrophoresis on 1% agarose of *SerpinA3N* PCR product amplified using specific primers. Product size 1·02 kb.

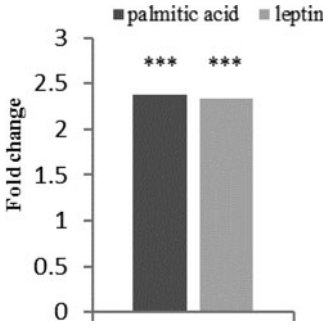

Fig. 2. *SerpinA3N* gene expression in the hypothalamic neuronal cell line in response to palmitic acid and leptin. Gene expression normalized to *B2M*. Fold change relative to vehicle treated cells. ***$P < 0{\cdot}001$

Western blot revealed that alpha-1-antichymotrypsin (the protein encoded by *SerpinA3*) is secreted into the cell culture medium. Further studies are required to identify its role in hypothalamus as well as its downstream target(s) and post-translational modifications.

1. Thaler JP, Yi CX, Schur EA, *et al.* (2012) Obesity is associated with hypothalamic injury in rodents and humans. *J Clin Invest* **122**, 153–162.
2. Milanski M, Degasperi G, Coope A, *et al.* (2009) Saturated fatty acids produce an inflammatory response predominantly through the activation of TLR4 signaling in hypothalamus: implications for the pathogenesis of obesity. *J Neurosci* **29**, 359–370.
3. Zhang X, Zhang G, Zhang H, *et al.* (2008) Hypothalamic IKKbeta/NF-kappaB and ER stress link overnutrition to energy imbalance and obesity. *Cell* **135**, 61–73.
4. Koch CE, Lowe C, Pretz D, *et al.* (2014) High-fat diet induces leptin resistance in leptin-deficient mice. *J Neuroendocrinol* **26**, 58–67.
5. Briggs DI, Enriori PJ, Lemus MB, *et al.* (2010) Diet-induced obesity causes ghrelin resistance in arcuate NPY/AgRP neurons. *Endocrinology* **151**, 4745–4755.
6. Williams LM, Grant C, Morris AC, *et al.* *SerpinA3N* expression in the hypothalamus is regulated by nutritional status, age and leptin. (Neuroscience conference Washington 2014).