ImmunoTools *special* Award 2019

Dr. Eirini Meimaridou

School of Human Sciences,
London Metropolitan University,
North Campus,
166-220 Holloway Road,
London, N7 8DB

Redox perturbations in adrenal redox homeostasis and its effect on chronic inflammation

Background:

Glucorticoids (GCs) are essential to life, and they respond acutely to metabolic and inflammatory stress. Under the control of the hypothalamus, the pituitary releases ACTH, which acts on the adrenal via the ACTH receptor (MC2R) to produce GCs, mainly cortisol in humans and corticosterone in mice. Therefore, normal adrenal function to ensure correct physiological levels of GC to regulate important adaptive responses of human body is required. In 2012 I showed by that loss-of-function mutations in nicotinamide nucleotide transhydrogenase (NNT) cause familial glucocorticoid deficiency (FGD), a potentially fatal, adrenal-specific disorder characterised by increased ACTH and reduced cortisol levels [1]. Specifically, I have shown that knockdown of NNT in human adrenocortical cells (H295R) cells results in oxidative stress, reduced GSH/GSSG ratio, increased mitochondrial superoxide production and a high NADP/NADPH ratio indicating insufficient NADPH availability to maintain the antioxidant capacity for ROS detoxification. Similarly by using an in vivo model I demonstrated that a substrain of C57BL/6J mice that contain a spontaneous Nnt mutation (an in-frame 5 exon deletion) display glucocorticoid deficiency. It has previously been reported that the same substrain of mice display glucose intolerance, reduced insulin secretion and exhibited greater resistance to acute pulmonary infection with Streptococcus pneumonia.

The immuno Tools award will give me the opportunity:

- To investigate whether glucocorticoid deficiency due to oxidative stress mediated by loss of NNT expression is associated with inflammation of the mouse adrenal gland. Requested inflammatory cytokines will be tested in Nnt-KO mouse adrenals and will be compared to the adrenals of wild type.

- To determine the effect of Nnt knockdown in human monocytic (THP1) cell differentiation. Specifically I will investigate whether loss of Nnt expression in THP1 promote M1 or M2 macrophage differentiation

This award will give me the opportunity to obtain strong preliminary data to apply for further funding from research councils; BBSRC and MRC.

ImmunoTools *special* AWARD for **Dr. Eirini Meimaridou** includes 25 reagents:

mouse ELISA-sets	GM-CSF, IL-6, IL-17A, TNF-alpha
recombinant human cytokines	rh IL1alpha, rh CXCL9, rh CXCL10, rh TNFalpha, rh IL-12, rh IL-8, rh CCL3
FITC - conjugated anti-human	CD14

DETAILS more AWARDS