weight as well as adipocyte hypertrophy. Interestingly, cold-acclimatized mice showed a marked reduction in GC-induced weight gain, hyperphagia, and fat accumulation. Moreover, the GC-induced rise in blood glucose and serum insulin concentrations - readily observed when mice were maintained at thermoneutrality - was absent in cold-exposed animals. In addition, GC treatment at thermoneutrality resulted in increased lipid deposition and decreased UCP1 expression in BAT, the 'whitening' of BAT. This GC-induced loss of thermogenic capacity was profoundly reduced in cold-adapted mice. Across all groups, UCP-1 protein levels in BAT closely correlated ($r^2 = 0.70$, $p < 0.0001$) with those of tyrosine hydroxylase (TH), the rate-limiting enzyme of catecholamine synthesis. These results indicate that cold-acclimation prevents the development of GC-induced metabolic dysfunction in mice. Thus, environmental temperature is a potent modulator of GC-induced adiposity and body weight gain, potentially via an interaction between SNS and GC signaling.

Steroid Hormones and Receptors

STEROID BIOLOGY AND ACTION

Expression of SLC35F1 in the Plasma Membrane of Cells of Aldosterone Producing Cell Clusters (APCCs) and Its Possible Role in Aldosterone Synthesis

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Background Genetic mutations and histological appearances suggest that APCCs are precursors to some aldosterone producing adenomas (APA). They are hypothesised to contribute to post-operative non-cure and recurrence of primary aldosteronism (PA) but are currently undetectable pre-operatively. SLC35F1 is a possible nucleotide sugar transporter. On microarray it is highly expressed in APCCs, but not in the rest of the adrenal cortex (1). Our aim was to investigate the role of SLC35F1 in APCCs, determine its subcellular localisation and establish whether expression is consistent with pathological APCC subtypes (as suggested by recent evidence from *in situ* metabolomic studies (2)). **Methods** Comparative bioinformatic analysis of the SLC35F1 amino acid sequence was carried out. *Ex vivo* 4uM adrenal sections, from 6 PA patients in the MATCH study, were stained on serial sections with anti-CYP11B2 (Gomez-Sanchez) or anti-SLC35F1 (Novus NBP1-86755). *In vitro*, H295R cells were transfected with SLC35F1 cDNA. Subcellular localisation of SLC35F1-GFP was studied by comparison to organelle markers (golgin 97, RAB11, wheat germ agglutinin, calnexin and Tom20) using confocal microscopy. Overexpression and siRNA knockdown in H295R cells was correlated to aldosterone production. **Results** SLC35F1 is a decamembrane-spanning transporter molecule predicted to have a negatively charged pocket in the substrate binding site, implying a transport substrate with a positive charge. Strong staining of CYP11B2 in clusters of cells in adrenal cortex, consistent with APCCs, were present in all six adrenal glands (25 APCCs). Serial sections showed specific SLC35F1 staining of APCCs, in cytoplasm and plasma membrane. SLC35F1 staining was absent from normal cortex. 12 APCCs (48%) were SLC35F1-negative. Visualisation of transiently expressed SLC35F1 demonstrated localisation to the endoplasmic reticulum in H295R cells (Pearson's coefficient r=0.758) with no plasma membrane localisation (r=-0.07). Preliminary transfection data suggest direct involvement in aldosterone production. **Conclusions** Expression of SLC35F1 in the plasma membrane and cytosol of APCC cells supports a role in pathological aldosterone production by APCCs. The inferred transport substrate of SLC35F1 is the NAD(P)(H) precursor, nicotinamide riboside, a positively-charged nucleotide sugar. If confirmed, the essential requirement for NAD(P)H in steroidogenesis, and heterogeneity of SLC35F1-staining in APCCs, is consistent with a metabolically active, possibly pathological, subtype of APCCs. Detection of SLC35F1 in vivo may therefore facilitate sub-classification of PA patients.

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2). Murakami et. al. 2019 Hypertension. In press.

Diabetes Mellitus and Glucose Metabolism

TYPE 1 DIABETES MELLITUS

The Lesser Evil: Pembrolizumab Induced Remission of Metastatic Melanoma with Autoimmune Diabetes, Hypothyroidism, and Colitis

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SAT-661

Background: Immune checkpoint inhibitors (ICI) are a new class of immunotherapy agents that empower the innate immune system to destroy cancer cells by overcoming checkpoints against autoimmunity and self-tolerance. ICI use against certain cancers has yielded impressive results. Pembrolizumab, an ICI approved by the FDA in 2014 for treatment of metastatic melanoma, is a monoclonal antibody which binds the programmed cell death protein 1 (PD1) receptor, blocking it's activation. Recent case reports have demonstrated a link between pembrolizumab and severe immunotherapy related adverse events including the incidence of autoimmune disorders.

Clinical Case: A 68-year-old male with hypertension and a past medical history of cutaneous melanoma treated fifteen years earlier with tumor resection was started on pembrolizumab after identification of new metastases to the lung and bones. After 3 cycles of therapy he began to experience dizziness, lightheadedness, and vision changes with diarrhea. Outpatient labs demonstrated hyperkalemia with hyponatremia. He was directed to the emergency department by his oncologist for presumed adrenal insufficiency, where he received one dose of IV dexamethasone (4 mg). Repeat labs demonstrated severe diabetic ketoacidosis with elevated blood glucose 981 (70-99 mg/dL), pH 7.19 (7.32-7.42), anion gap of 37 (4-15 mmol/L), and betahydroxybutyrate > 9.00 (0.00-0.40 mmol/L). Following endocrinology consultation steroids were discontinued