

## Steroid Hormones and Receptors STEROID AND NUCLEAR RECEPTORS

### *Induction of the Pro-Diabetic Gene DPP4 by Glucocorticoids: New Evidence of Pro-Inflammatory Effects in Macrophages*

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#### SUN-737

Glucocorticoids are potent endogenous anti-inflammatory molecules, with its receptor (GR) expressed in nearly all immune cells. Macrophages are heterogeneous cells having a central role in both tissue homeostasis and inflammation. Paradoxically glucocorticoids have a limited efficacy controlling these processes and inflammation resolution of macrophage-related diseases, such as type 2 diabetes, atherosclerosis and rheumatoid arthritis. To address this issue, we explored new glucocorticoid target genes in macrophages with potential clinical and therapeutic implications for these diseases. Analysis of genomic platforms identified the pro-diabetic exopeptidase dipeptidyl peptidase 4 (DPP4) as a novel glucocorticoid-responsive gene. GR directly induces its expression by binding to two glucocorticoid-responsive elements within the DPP4 promoter. Unexpectedly, DPP4 mediated the glucocorticoid-induced spontaneous macrophage migration. These actions were blocked by both GR and DPP4 siRNA knockdowns. Furthermore, two DPP4 inhibitors, Sitagliptin and Linagliptin, used clinically for the treatment of diabetes inhibited glucocorticoid-induced mobility of macrophages. DPP4 induction by glucocorticoids was also observed in murine peritoneal macrophages and pro-inflammatory M1 polarized macrophages and was associated with an increase in their migratory properties. Provocatively, DPP4 has been shown to be involved in the inflammatory macrophage profile associated with type 2 diabetes, obesity and atherosclerosis. Since macrophages require efficient cell movement for all their functions, such as sensing of Pattern Associated Molecular Patterns (PAMPs), phagocytosis and the antigen presentation, the DPP4 induction by glucocorticoids could potentiate the macrophage infiltration and their activation in chronic inflammatory tissues and diabetes.

## Thyroid

### THYROID DISORDERS CASE REPORTS II

#### *Alpha Gal Allergy in a Hypothyroid Patient*

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#### SAT-511

**Background:** The IgE-mediated allergy to galactose-alpha-1,3-galactose (alpha-gal), a carbohydrate expressed on nonprimate mammalian proteins, has gained more clinical significance as it can present with serious, potentially fatal anaphylaxis or angioedema. In general, recognizing a specific allergy is the first step in prescribing avoidance; but with delayed symptoms, uncertain prevalence, and

unclear diagnostic approach, alpha-gal allergies are difficult to recognize and prevent. To further complicate the clinical picture, some patients can tolerate small portions of nonprimate mammalian meat or tolerate one kind of meat over another. We hereby present a case that highlights the lack of guidance and resources currently available to treat a patient with alpha-gal allergy and hypothyroidism. **Case Presentation:** A 45-year-old woman with a history of an alpha-gal allergy and follicular thyroid neoplasm status post right hemithyroidectomy presented with postoperative hypothyroidism. After the surgery, she had undetectable serum thyroglobulin levels; her thyroid stimulating hormone (TSH) levels were ranging 5–6  $\mu$ IU/mL (not on thyroid replacement). The goal was to prescribe thyroid replacement to initiate cancer suppressive strategy. The American Thyroid Association (ATA) recommends a TSH of 0.5-to-2 mIU/mL in low risk patients postoperatively. The standard treatment of choice for correcting hypothyroidism is synthetic thyroxine (T4, levothyroxine). Commercially available levothyroxine, liothyronine, combo, and desiccated thyroid formulations - whether brand name, generic, tablet, soft gel capsule, or liquid - all contain meat byproducts and can be a concern for anaphylaxis or angioedema if one has an alpha gal allergy. Because of the possible reactions with all common formulations of thyroid hormone replacement in this patient, choosing a safe option was complicated and involved a multidisciplinary team, including allergy and immunology consultation. Daily parenteral synthetic thyroid hormone therapy was considered; however, it is not practical and was not feasible for the patient. She was eventually prescribed pure Levothyroxine, with a plant-based filler and vegetarian capsule. She tolerated this pure levothyroxine well without any adverse reactions, and the TSH goal was achieved. **Conclusion:** This case emphasizes the importance of recognizing various risk factors and common drugs associated with the alpha-gal allergy. Further research and pharmaceutical attention to this allergy is needed.

## Diabetes Mellitus and Glucose Metabolism

### IMPACTS OF METABOLISM ON CLINICAL CHALLENGES

#### *The Correction Factor for A1C in Anemic Patients*

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#### OR26-05

Diabetes can be defined by hemoglobinA1c (A1c), fasting plasma glucose (FPG), and 2-hour plasma glucose (2hPG). Despite that A1c has a tendency for underestimation of the prevalence of diabetes and overestimation of the prevalence of normal glucose tolerance, A1c is the most convenient method, since no preparation required. However,

various factors could affect A1c. The objective of this project is to identify the covariates that affect A1c. The study sample included 9,952 adults (age  $\geq 20$  years old) from the 2005–2016 NHANES. Subjects with established diabetes were excluded, and we analyzed subject's documented BMI, A1c, FPG, 2hPG, Hemoglobin (Hgb), race/ethnicity, age, education, poverty index, family history of diabetes, and tobacco and alcohol consumption to determine their impact on A1C measurement. Continuous data were expressed as means with standard deviation. Either t-test or ANOVA was used to examine the influence of covariates on continuous variables. We examined the relation of A1c with FPG, 2hPG, and other covariates. With backward regression analysis, we excluded the covariates without significant impact on A1c. All the analyses were conducted in SYSTAT 13, Systat Software, Inc. In the univariate analysis, A1c was significantly correlated with FPG ( $r=0.5692$ ,  $P<0.0001$ ) and 2hPG ( $r=0.5122$ ,  $P<0.0001$ ). In the backward regression analysis, education, poverty index, and family history of diabetes were excluded for their low impact on A1c. In addition to FPG and 2hPG, gender ( $r=-0.0527$ ,  $P<0.0001$ ), age ( $r=0.1746$ ,  $P<0.0001$ ), BMI ( $r=0.0978$ ,  $P<0.0001$ ), race/ethnicity ( $r=0.0478$ ,  $P<0.0001$ ), current alcohol consumption ( $r=0.0542$ ,  $P<0.0001$ ), current smoker ( $r=-0.0806$ ,  $P<0.0001$ ), and Hgb ( $r=-0.1526$ ,  $P<0.0001$ ) had significant impact on A1c. Due to the significant difference in Hgb between gender, gender-based analyses were performed. In male gender, the impact of other covariates (age, BMI, race/ethnicity, current alcohol consumption, and current smoker) than FPG and 2hPG could be explained at least partially through their impact on Hgb ( $P<0.0001$ ). Each 1 g/dL decrease of Hgb would falsely decrease A1c by 0.053% ( $P<0.0001$ ). In female gender, the impact of covariates other than FPG and 2hPG on A1c could be explained by their impact on Hgb ( $P<0.0001$ ) except for BMI. Each 1 g/dL decrease of Hgb would falsely decrease A1c by 0.047% ( $P<0.0001$ ). In addition to FPG and 2hPG, A1c could be affected by gender, age, BMI, race/ethnicity, current alcohol consumption, and current smoker through their impact on Hgb, except for BMI in female gender. A1c will be falsely decreased by 0.053% in male gender and 0.047% in female gender for each 1 g/dL decrement of Hgb. Thus, A1c should be interpreted with caution in anemic patients. We propose using the gender specific correction factors for more accurate interpretation of A1c.

## Adrenal

### ADRENAL CASE REPORTS I

#### *Lifestyle Modifications or Adrenalectomy?*

#### ***Pheochromocytoma Presenting with New Onset Diabetes Mellitus***

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#### **SAT-226**

##### Introduction

When clinicians think of pheochromocytomas, diabetes might not be the first thing that comes to mind. Pheochromocytomas elicit deterioration in glucose tolerance

in 20% to 40% of affected individuals. Size of the pheochromocytoma could be an independent risk factor for developing diabetes, as larger pheochromocytomas often present with diabetes mellitus in 23% to 33% of patients with symptomatic pheochromocytomas. Evidence suggests that pheochromocytoma proposes a risk for development of diabetes. There is no consensus or recommendations on which patients with new onset diabetes should be screened for pheochromocytoma or how to manage hyperglycemia in these patients.

##### Clinical Case

42 YO F with PMH of HTN presented to primary care clinic c/o polyuria, fatigue, 25-pound weight loss, epigastric pain and worsening hypertension over 3 months. Initial work up showed a HbA1C of 9%. The patient was diagnosed with type 2 diabetes mellitus and started on Metformin 1g BID with no improvement of glucose levels or symptoms. As part of initial work up for suspicion of pancreatic malignancy patient had an abdominal CT scan showing a 5.6 x 4.8 cm well-circumscribed left adrenal mass. Patient was referred for endocrine evaluation. Initial workup showed negative GAD Ab, normal 1mg Dexamethasone suppression test, normal aldosterone/renin ratio, elevated Free Normetanephrine of 17,921 pg/mL and elevated chromogranin A of 3,427 ng/mL. Based on biochemical evidence of catecholamine excess and left adrenal mass on imaging, patient was diagnosed with Pheochromocytoma. MIBG showed no evidence of metastatic disease. She was started on insulin therapy, Doxazosin 1mg BID which was titrated to 2mg BID and Amlodipine 5mg was increased to 10mg daily. Pt was referred to surgery for adrenalectomy. On pre-op evaluation patient had significant improvement of glucose levels and symptoms. Propranolol 20mg BID was started for BP optimization. A laparoscopic left adrenalectomy was performed without complications. Patient did not require anti-hypertensive medications or insulin during hospitalization and was discharged on metformin 500mg daily with no anti-hypertensive medications. At one-month Post-adrenalectomy follow up patient had normal BP of 116/72 mmHg and A1C of 5.4% with normal glucose logs indicating resolution of diabetes and HTN post adrenalectomy.

##### Conclusion

Diabetes is a multifactorial disease that has direct impact on patient's quality of life, morbidity and mortality. It is important to consider pheochromocytoma as a risk factor for development of diabetes, especially in young patients with atypical presentation, uncontrolled hypertension or without evidence of antibodies or insulin resistance. Screening and early diagnosis of pheochromocytoma could mean significant reduction on long term diabetes complications as diabetes seems to improve or even resolve after adrenalectomy.

## Adipose Tissue, Appetite, and Obesity

### ADIPOSE TISSUE BIOLOGY AND OBESITY

#### ***Assessment of Thermoregulatory Pathways Induced in Male and Female Mice Lacking Pituitary Adenylate Cyclase Activating Polypeptide (PACAP) in Response to Cold Acclimation***

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