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

David Diaz-Jimenez, PhD, Maria-Grazie Petrillo, PhD, Jonathan T. Busada, PhD, John A. Cidlowski, PHD.
NIEHS/NIH, Durham, NC, USA.

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

Tanner A. Slayden, MD[1], Elizabeth M. Bauer, MD[2], Mohamed K.M. Shakir, MD[2], Thanh Duc Hoang, DO[2].
[1]Walter Reed National Military Medical Center, SILVER SPRING, MD, USA, [2]Walter Reed National Military Medical Center, Bethesda, MD, USA.

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 μIU/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 mcIU/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

Maria Chang Villacreses, MD[1], Rudruidee Karnchanasorn, MD[2], Horng-Yih Ou, MD & PhD[3], Wei Feng, MD[4], Raynald Samoa, MD[5], Lee-Ming Chuang, MD, PhD[6], Ken C. Chiu, MD[7].
[1]City of Hope National Medical Center, West Covina, CA, USA, [2]The University of Kansas Medical Center, Kansas City, KS, USA, [3]National Cheng-Kung University Medical Center, Tainan, Taiwan, [4]City of Hope National Medical Center, San Gabriel, CA, USA, [5]City of Hope National Medical Center, Duarte, CA, USA, [6]National Taiwan University, Taipei, Taiwan, [7]City of Hope National Medical Center, Santa Monica, CA, USA.

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,