

adducts called oxidation specific epitopes (OSEs), which are proinflammatory moieties present on oxidized low density lipoproteins and on apoptotic cells and, unless removed, cause extensive cell damage. Natural antibodies (NAb) produced by B-1 lymphocytes, bind OxPL and prevent their inflammatory activity. E06 is a NAb that recognizes the phosphocholine moiety of OxPL. We previously showed that transgenic expression of a single chain (scFv) form of the antigen-binding domain of E06 IgM (E06-scFv) increases cancellous and cortical bone mass in both male and female mice by increasing bone formation. Age-related bone loss is characterized by a decline in osteoblast number and bone formation, associated with increased oxidative stress and lipid peroxidation. These findings, together with the evidence that serum anti-OxPL IgM titers decrease with age, suggest that increased OxPL formation and decreased anti-OxPL antibodies may contribute to age-related bone loss. Like humans, mice exhibit an age-dependent worsening in glucose tolerance, mainly due to alteration in body composition and increased fat tissue. Chronic low grade inflammation and oxidative stress are associated with development of diabetes mellitus and B-1 lymphocytes have been shown to be protective against obesity associated inflammation, glucose intolerance, and insulin resistance. We tested the hypothesis that overexpression of E06-scFv could attenuate age-related bone loss and glucose intolerance. Serial BMD measurements by DXA of both female and male C57BL/6 E06-scFv transgenic mice (and their WT littermates) up to 22 and 24 months, respectively, showed that E06-scFv attenuated age-related bone loss at the spine and femur in both sexes. As revealed by microCT analysis, this effect was due to the attenuation of the age-associated decline in cancellous bone in both sexes. Additionally, both male and female E06-scFv transgenic mice accumulated less fat mass than WT littermates during aging. Intraperitoneal glucose tolerance test, at 15 months of age, revealed that glucose tolerance was greater in both male and female E06-ScFv mice than in respective WT littermates and did not differ from the glucose tolerance of young mice, indicating that E06-scFv improves glucose metabolism. These data suggest that OxPL impair both age-related bone loss and age-related glucose intolerance. Therefore, targeting OxPL with a neutralizing antibody such as E06, represents a prototypic therapeutic intervention that may simultaneously ameliorate important age-associated diseases.

Genetics and Development (including Gene Regulation)

GENETICS AND DEVELOPMENT AND NON-STEROID HORMONE SIGNALING II

The Chromatin Landscape of Glucocorticoid Regulated Genes in Mouse Embryonic Neural Stem / Progenitor Cells

Kimberly Berry, B.S., Uma Chandran, PhD, Fangping Mu, PhD, Donald DeFranco, PhD.

University of Pittsburgh, Pittsburgh, PA, USA.

MON-727

The Chromatin Landscape of Glucocorticoid Regulated Genes in Mouse Embryonic Neural Stem/Progenitor Cells

Antenatal administration of Dexamethasone (Dex), a synthetic glucocorticoid (GC), is a common

clinical intervention for women at risk for preterm birth or in preterm labor that effectively reduces fetal risk of mortality and bronchopulmonary-related comorbidities. Despite the therapeutic potential of Dex, excess GC act adversely in the developing central nervous system to reprogram distinct neural circuits in the brain by acting through the glucocorticoid receptor (GR). For example, prenatal exposure to excess GCs can impact neural stem and progenitor cell (NSPC) proliferation leading to long-term alterations in prefrontal cortical neuronal complexity, which could contribute to behavioral and cognitive impairments later in life. The GR is a member of the nuclear receptor superfamily that, when bound by a ligand, translocates from the cytoplasm to the nucleus and associates indirectly or directly with DNA elements (e.g. glucocorticoid responsive elements or GREs) resulting in the activation and/or repression of target genes. While GR-regulated transcriptomes have been identified in many NSPC models, the mechanisms responsible for programming these cells for GC-responsiveness remain largely unknown. We therefore used transposase accessible chromatin followed by genome-wide sequencing (Omni ATAC-seq) to characterize the chromatin landscape of primary embryonic mouse NSPCs in response to an acute *in vitro* treatment with Dex. We identified a small, yet distinct fraction (0.002%, $p < 0.05$) of open chromatin sites that were Dex-inducible. 95% of these Dex-induced changes in chromatin accessibility occur within intronic or intergenic regions, suggesting the presence of long-range enhancer-promoter contacts that mediate NSPC transcriptional responses to Dex. Motif enrichment analysis revealed putative GRE sites located in Dex-inducible open chromatin within -5kb/+2kb of a Dex-induced gene, providing possible DNA targets of GR for further validation. A number of other transcription factors implicated in neurodevelopmental processes were found to underlie both Dex-inducible and constitutively open chromatin regions. Characterization of the precise epigenetic and transcriptional response to excess GC *in-utero*, and its influence on acute and chronic neurological outcomes, will encourage the development of alternative GC treatment regimens that could protect the developing brain from insult while providing optimal health outcomes in neonates.

Tumor Biology

TUMOR BIOLOGY: GENERAL, TUMORIGENESIS, PROGRESSION, AND METASTASIS

An Uncommon Case of Squamous Cell Carcinoma of the Vulva with Metastasis to the Thyroid Gland

Laishiya Munshi, DO¹, Vishnu Priya Pulipati, MD¹, Susana Mascarell, MD².

¹Rush University Medical Center, Chicago, IL, USA, ²John H. Stroger Hospital of Cook County, Chicago, IL, USA.

SAT-128

Background: Distant metastasis from Squamous Cell Carcinoma (SCC) of the Vulva is very rare and typically associated with poor outcomes. In the literature, there have been no reported cases of vulvar SCC with metastasis to the thyroid, which augments the uniqueness of the case we are presenting.

Clinical Case: A 29-year-old female was hospitalized for abdominal pain & altered mental status. Labs showed calcium 21 (RR 8.5-10.5 mg/dL) with iPTH 4.3 (RR 12-88 pg/mL). Imaging revealed an 8.6 x 7.2 cm right thyroid mass (solid with cystic internal components, hyperechoic to isoechoic, wider than tall, lobulated margins, punctate echogenic foci occupying nearly the entire right lobe, minimal vascularity), mildly effacing the trachea. There were also extensive lesions consistent with systemic metastasis involving the left hilar lymph nodes, pre-tracheal lymph nodes, right hepatic lobe, head of pancreas, retroperitoneal lymph nodes, right inferior pubic ramus, proximal right humerus, left humerus, proximal femur & frontal lobe of the brain. Hypercalcemia of malignancy from an unknown cancer was diagnosed. FNA biopsy of the thyroid mass was consistent with atypia of undetermined significance. Liver biopsy showed evidence of high grade carcinoma with non-calcitonin producing neuroendocrine differentiation. Labs showed serum serotonin 11 (RR 56-244 ng/mL), CA 19-9 < 0.8 (RR 0-35 U/mL), alpha-fetoprotein 2.12 (RR 0-9 ng/mL), CEA 20.97 (RR 0-2.9 ng/mL), PTHrP 33 (RR 14-27 pg/mL), 1,25OH Vit D 18 (RR 18-72 pg/mL), chromogranin A 189 (RR 25-140 pg/mL), & calcitonin < 2 (RR < 5 pg/mL). A vaginal lesion was discovered on exam & biopsy showed squamous cells with cytopathic effect of Herpes Simplex Virus (confirmed with immunohistochemical stain). Subsequent biopsy of the brain & core needle biopsy of the thyroid showed morphology similar to a concurrent biopsy of a vulvar lesion also found on exam: poorly differentiated SCC. The patient was diagnosed with vulvar SCC with extensive metastasis. Her hospital course was complicated by atrial fibrillation, acute respiratory failure, & sepsis. She, unfortunately, passed away from her severe morbidities.

Discussion: Metastasis to the thyroid is an infrequent occurrence. It is commonly encountered in breast, lung & renal cell carcinomas. It can occur due to direct spread from adjacent tissues or by lymphatic or hematogenous spread. Thyroid gland metastasis is more commonly seen in patients with aggressive or widespread carcinomas, especially by hematogenous route, due to the thyroid's extensive vascularity.

Conclusion: Thyroid gland metastasis, particularly due to vulvar SCC, is a rare entity with a poor prognosis. In patients with extensive poorly differentiated carcinoma such as our patient, it is of utmost importance to identify suspicious thyroid nodules and perform comprehensive diagnostic testing to facilitate timely intervention for improved outcomes.

Diabetes Mellitus and Glucose Metabolism

DIABETES COMPLICATIONS II

Association of Serum Level of Omentin-1, Hs-CRP and Atherosclerosis in Patients with Type 2 Diabetes

Mohamed Fahmy Amara, M.D.

Faculty of Medicine, Fayoum university, Alexandria, Egypt.

MON-691

Abstract:

Omentin-1 has been identified as an interesting novel adipokine that may modulate the action of insulin. Serum omentin-1 levels were associated with endothelial dysfunction and cardiovascular diseases, which highly contribute to morbidity and mortality of patients with diabetes, however its exact biological function is still unclear. The aim of this study was to assess the level of circulating plasma Omentin-1 level in patients with type 2 diabetes compared to control subjects, and to investigate the relationship of circulating Omentin-1 levels with HOMA, BMI, lipid profile, epicardial fat, visceral fat and subcutaneous fat in early stages of atherosclerosis measured by carotid intima media thickness (CIMT). This is a cross-sectional observational study which included 45 patients with type 2 DM (not previously diagnosed as ACVD patients) and 30 (age and sex)-matched healthy control subjects. Patients with a history of recent acute infection, malignancy, metabolic or endocrinal diseases, cardiac failure, renal and hepatic impairment were excluded. Participants were subjected to measurement of FPG, HbA1c, lipid profile, calculation of HOMA2, hs CRP, serum omentin-1, CIMT, estimation of visceral, epicardial and subcutaneous fat through CAT scanning. There was no statistically significant difference between both groups in the mean circulating omentin-1 level, a mean of (793.86 ± 195.81) ng/ml in type 2 diabetes Vs (804.93 ± 205.76) ng/ml in the control group, (p=0.654). However, there was a highly statistically significant difference in hs-CRP between both groups, mean hs CRP is (4.29 ± 4.87 mg/l) vs (0.92 ± 0.53 mg/l) respectively. There was a statistically significant negative correlation between omentin-1 and hs CRP (r= -0.278, p= 0.016). There were no statistically significant correlations between omentin-1 with BMI, HbA1c, HOMA, lipid profile or adiposity. These findings may denote the anti-inflammatory effects of omentin-1 which maybe unrelated to insulin resistance and dyslipidemia. Further studies are required to confirm the cardioprotective role of omentin-1 in patients with type 2 diabetes, focusing on its local anti-inflammatory role.

Nothing to disclose: MA, NA, NK

No Sources of Research Support

Neuroendocrinology and Pituitary

CASE REPORTS IN UNUSUAL PATHOLOGIES IN THE PITUITARY

Langerhans Cell Histiocytosis: A Difficult Diagnosis in Cranial Diabetes Insipidus

Ivy Hoi Yee Ng, MBChB, Elaine Yun Ning Cheung, MD,

Grace Yee Wai Kam, MBChB.

United Christian Hospital, Kwun Tong, Hong Kong.

SUN-271

Background

Langerhans cell histiocytosis (LCH) is a myeloid neoplastic disorder that is rare in adults, with a reported incidence of 1-2 cases per million per year. Cranial diabetes insipidus (CDI) is the most common and often the first endocrine manifestation of LCH, when histiocytes infiltrate the pituitary. Anterior pituitary dysfunction, when present, usually develops after onset of CDI. Unlike most other etiologies of