free T4, mildly elevated free T3, and elevated TSI/TRAb, overall consistent with early Graves' hyperthyroidism. His pretibial myxedema was treated with high-dose topical steroids with improvement of his dermopathy. For his hyperthyroidism, he was started on low dose methimazole and never developed Graves' ophthalmopathy.
Discussion:
Although the exact pathophysiology of pretibial myxedema is unknown, it is thought to be mediated by TSH receptor expression on fibroblasts, similar to Graves' ophthalmopathy. It is usually seen in patients with active or longstanding Graves' disease, often with high levels of thyroid receptor antibodies and concomitant Graves' ophthalmopathy. However, there are a few cases of pretibial myxedema occurring in euthyroid patients with or without ocular symptoms, usually in the setting of elevated TSI, TRAb, or TPO antibodies. Our patient is a rare case of pretibial myxedema preceding active thyroid disease without ophthalmologic manifestations. Patients with hyper-pigmented, non-pitting plaques or nodules on pretibial regions should prompt providers to consider pretibial myxedema and test for thyroid studies, even in those without symptoms of hyperthyroidism or Graves' ophthalmopathy.

Tumor Biology

TUMOR BIOLOGY: GENERAL, TUMORIGENESIS, PROGRESSION, AND METASTASIS

Nuclear Receptor 4A1 (NR4A1) Acts as a Tumor Suppressor in Anaplastic Thyroid Cancer

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SAT-123

The nuclear orphan receptor NR4A1 has been demonstrated to play important roles in development and progression of various cancers. However, the biological roles and its underlying mechanisms of NR4A1 in anaplastic thyroid cancer (ATC) are largely unknown. Here, we showed that the expression level of NR4A1 was robustly down-regulated in ATC cell lines and human ATC tissues as compared to Nthy-ori 3-1 cells and normal thyroid tissues, respectively, using in silico analysis, qRT-PCR and immunohistochemistry analyses. Gain-of-function experiments were carried out to understand the NR4A1's responsiveness to apoptotic inducers. The results showed that ectopic over-expression of NR4A1 reduced cell viability and promoted cell apoptotic rate induced by UV irradiation or Adriamycin. Moreover, the activities of caspase-3 and PARP were elevated in NR4A1 overexpression cells in response to apoptotic inducers. Furthermore, we found that down-regulation of XIPA was involved in the pro-apoptotic role of NR4A1 in ATC cells. Collectively, these findings suggest that the nuclear orphan receptor NR4A1 acts as a tumor suppressor in ATC via regulating XIPA, providing a potential therapeutic target against ATC.

Cardiovascular Endocrinology

PREVALENCE, DIAGNOSIS, AND MECHANISMS OF HYPERALDOSTERONISM

11C Metomidate PET-CT Identifies More Unilateral Primary Aldosteronism Than Adrenal Vein Sampling

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OR34-01

Introduction. Adrenal vein sampling (AVS) is the current reference test to identify unilateral, surgically-curable primary aldosteronism (PA). However, AVS is invasive and technically difficult. Even in AVS-proven unilateral PA, up to 6% of patients with fail to have biochemical cure after surgery using the PASO criteria. 11C-Metomidate PET-CT offers a non-invasive alternative. We compared the accuracy of both PET-CT and AVS using post-surgery cure (PASO criteria) as the reference.
Methods. This multi-centre prospective trial recruited 25 patients with confirmed PA, and all underwent CT, AVS, and PET-CT tests. Sequential AVS under ACTH-stimulation was done by an experienced interventionalist, and cortisol gradient of >5 was taken to be successful cannulation. Lateralization ratio >4 was consistent with unilateral PA. All results were reviewed at a multidisciplinary meeting to decide on the diagnosis (unilateral or bilateral PA) and management (secondary outcome). Primary outcome was biochemical cure using PASO criteria at 6 months post-surgery (ClinicalTrials.gov: NCTxxxxxxxx).
Results. Recruitment for the study has been complete with 25 patients, 49.2 ± 9.5 yr, 14 females (56.0%). All 25 patients had successful AVS. 22 of 25 patients (88.0%) had unilateral PA, and 3 patients (12.0%) had bilateral PA. PET-CT identified unilateral PA in 18 of 22 patients (sensitivity 81.8%), while AVS identified unilateral PA in 15 of 22 patients (sensitivity 68.2%). In one patient, repeat AVS done simultaneously without ACTH-stimulation aided to identify unilateral PA, when initial AVS failed to do so. Other cases where AVS failed to identify unilateral PA were due to venous anomalies, and limitation of the lateralization cut-off of 4. 18 of 22 patients have undergone surgery, with 3 patients awaiting surgery, and 1 opting for medical treatment. Post-surgery, all patients had complete normalization of aldosterone-renin ratio, and hypokalemia (if present). 2 patients had bilateral PA on both PET-CT and AVS. 1 patient had discordant AVS

and PET-CT results, with AVS lateralizing to right, and PET-CT to left. This patient was classified as bilateral PA and treated medically.

Conclusion. This is the first study to demonstrate that 11C-Metomidate PET-CT may identify cases of unilateral PA not detected with AVS, using the stringent PASO criteria for post-operative biochemical cure.

Thyroid

THYROID NEOPLASIA AND CANCER

The Anti-Cancer Agent, Homoharringtonine, Induces the Sodium Iodide Symporter (NIS) Gene Expression in Culture Cells from Papillary Thyroid Cancer, as Well as Non-Thyroid Cancers.

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MON-512

Background: The therapeutic effect of thyroid cancer by radioiodide treatment is dependent on enhancement of *NIS* expression by TSH, especially its much greater magnitude in target tissue(s) compared to other healthy tissues. We preliminarily found that a protein synthesis inhibitor cycloheximide (CHX) markedly enhanced *NIS* mRNA expression, followed by increased iodide uptake, in several cancer cell lines, though CHX is highly toxic for clinical use.

Aims: To evaluate the possibility of clinical application of such a pathway to enhance *NIS* expression, we tried another weak protein synthesis inhibitor, homoharringtonine (HHT), a natural plant alkaloid already utilized as an anti-leukemia agent, in several human cancer cell lines, including thyroid cancer.

Methods: BHP 2-7 papillary thyroid cancer cells, MCF7 breast cancer cells, and MKN gastric cancer cells were treated with HHT and/or a p38 inhibitor, and harvested for quantitative RT-PCR of *NIS*.

Results: HHT significantly induced the *NIS* mRNA expression in all of the cell lines tested, up to 298-fold in BHP cells, 38-fold in MCF7 cells, and 235-fold in MKN cells. Time course experiments indicated a biphasic induction of *NIS* in BHP cells with two peaks at 48 hours and 96 hours, with the EC_{50} of 664 ng/mL and 767 ng/mL, respectively. In contrast, *NIS* induction by HHT was monophasic in MCF7 cells at 24 hours with EC_{50} of 24.6 ng/mL, as well as MKN cells at 96 hours with EC_{50} of 255.7 ng/mL. Roles of p38 MAPK in the *NIS* induction has been reported previously, however, p38 inhibitors, SB239063 (10μM), as well as ML3403 (30μM), did not significantly reduce the *NIS* expression in HHT-treated BHP cells.

Conclusion: These results indicated that HHT has a potential to enhance *NIS* expression in some *NIS*-expressing cancer tissues, including papillary thyroid cancer, although its functionality and efficacy are to be validated. The heterogeneity of response in the *NIS* expression to HHT in three cell lines could be due to differential mechanisms of *NIS* gene regulation in different tissues.

Adipose Tissue, Appetite, and Obesity

OBESITY TREATMENT: GUT HORMONES, DRUG THERAPY, BARIATRIC SURGERY AND DIET

GPR142 Expression Levels Were Correlated with Plasma Ghrelin Levels and Heights in Morbidly Obese Patients

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MON-603

Recently, aromatic amino acids, especially tryptophan were discovered to be the strongest ligands for GPR142, which was previously known as an orphan GPCR. GPR142 is expressed in the digestive tract and pancreas in mice and human. Previously we found that GPR142 is highly expressed in the ghrelin-producing cell line, MGN3-1 cells, and that tryptophan strongly stimulated ghrelin secretion in vitro.

In this study, we measured the mRNA expression levels of GPR142 in the gastric samples of 6 morbid obese patients undergone laparoscopic sleeve gastrectomy and compared its level with their clinical parameters. GPR142 expression levels were negatively correlated with plasma desacyl ghrelin levels (p=0.011) and positively correlated with heights (p=0.08).

The current results that GPR142 expression levels were correlated with plasma desacyl ghrelin levels may confirm the link between GPR142 signal and regulation of ghrelin secretion demonstrated in our in vitro study. Regarding to the correlation with heights, there are some reports that plasma ghrelin levels were inversely correlated with heights in children[1-3], although, as far as we know, there are no reports demonstrating the relationship between plasma ghrelin levels and heights in adults. Considering that ghrelin strongly stimulates growth hormone secretion, GPR142 signaling may have influence on height through regulating ghrelin-growth hormone axis.

Conclusion

GPR142 mRNA expression levels were negatively and positively correlated with plasma desacyl ghrelin levels and heights in morbid obese adults undergone bariatric surgery. Current results may help understanding the pathophysiological role of GPR142 in the regulation of ghrelin secretion and heights.

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