SAT-446

Thyroid hormones (TH) act mainly on the expression of the genome. It is well accepted that differential gene expression following treatment with TH recapitulates the expression profiles taking place during natural processes induced by these hormones. Although both processes seem to correlate at the scale of a few target genes, this hasn't been addressed in a systematic manner. Our objectives were first to compare transcriptome variations after TH treatment with transcriptome variations during a TH controlled natural process and second to evaluate the proportion of the direct TH-response. The measurement of gene expression at genome scale (transcriptome) is obtained by sequencing all the messenger RNAs (RNA-seq). Direct response was sorted out by linking the transcription start sites of target genes using RNA-PET analysis with TR binding sites mapping using chromatin interaction analysis by paired-end tag sequencing (ChIA-PET). Indeed, ChIA-PET not only allow to map TR binding sites but also the physical interactions between them and transcription start sites of regulated genes. Our model is one of the striking developmental processes orchestrated by TH: amphibian metamorphosis. Tadpole transformation is marked by dramatic changes including *de novo* morphogenesis (limb), tissue remodelling (brain, intestine...) and organ resorption through apoptosis (tail). These changes involve cascades of gene regulation initiated by TH and their receptors. Because metamorphosis has close and interesting parallels with the perinatal period in mammals (including human), metamorphosis is thus an attractive model to analyze in a physiological context, the functions and mechanisms of action of TH. Here, we have focused on one *Xenopus tropicalis* organs, the tail fin skin which will disappear through cell death. We have compared natural metamorphosis with 24h of 10nM triiodothyronine (T_3) treatment. We were able to observe several differences between T_3 treatment and natural development. First, the genes regulated by T_3 only correspond to a proportion of genes differentially expressed during metamorphosis. Second, T_3-response genes start to be regulated well before tail regression (several days). Finally, T_3-direct target genes represent a few percent of all the genes differentially expressed during tail regression. In conclusion, the comparison of transcriptomes of natural and induced metamorphosis allow us to reach a more precise understanding of TH action

Pediatric Endocrinology

PEDIATRIC PUBERTY, TRANSGENDER HEALTH, AND GENERAL ENDOCRINE

A Guide to Professional Development: Funding Your Research Through NICHD

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SUN-075

The *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) leads research and training efforts to understand human development, improve reproductive health, enhance the lives of children and adolescents, and optimize abilities for all. Under the "New Strategic Plan 2020", NICHD will focus on priorities to: 1. Understand the Molecular, Cellular, and Structural Basis of Development; 2. Promote Gynecologic, Andrologic, and Reproductive Health; 3. Set the Foundation for Healthy Pregnancies and Lifelong Wellness; 4. Improve Child and Adolescent Health and the Transition to Adulthood; and 5. Advance Safe and Effective Therapeutics and Devices for Pregnant and Lactating Women, Children, and People with Disabilities. Cross-cutting topics include health disparities, prevention, infectious disease, nutrition and global health. NICHD is committed to funding the largest number of meritorious projects, while allowing flexibility to support high program priorities and respond to emerging scientific opportunities. Mechanisms to support individual research and training include research project grants (RPGs), training and career development awards (K awards) and fellowships (Pre and Postdoctoral). There are specific eligibility requirements for each of these mechanisms. Applicants are advised to contact a program officer (PO) and discuss the idea, its relevance to program priorities of NICHD, and potential funding opportunities available. While preparing your application, receive guidance on the grantsmanship from the PO, in addition to peers working at your institution. The PO can help you to understand the peer review process at NIH and suggest study sections with a good fit to review your application. The peer review process is independent of the program administration at NIH. Applicants can avoid some common errors in writing applications by reviewing the NIH website and understanding the NIH grants process. The NIH has recently revised its approach to the review and monitoring of vertebrate animal and human subject research. Applicants may receive guidance both at their institution (from which the application is submitted) and NIH. NICHD has developed new guidelines and processes to enhance and improve clinical trials. Currently, applications may be submitted to separate funding opportunity announcements for "clinical trials required" and "clinical trials optional". The goal is to ensure adequate clinical trial-specific information in the grant applications for thorough review. Additional new review criteria consider training in good clinical practice and expanded registration and results reporting in ClinicalTrials.gov.

Cardiovascular Endocrinology

ENDOCRINE HYPERTENSION AND ALDOSTERONE EXCESS

Endoscopic Ultrasound-Guided Radiofrequency Ablation (EUS-RFA) as an Alternative to Adrenalectomy for the Treatment of Aldosterone-Producing Adenomas (APAs)

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SAT-546

Primary Aldosteronism (PA) carries significant cardiometabolic risk, over and above those attributable to hypertension alone. The Endocrine Society guidelines recommend adrenalectomy in those with unilateral disease. However surgery is likely to become unsustainable in public healthcare systems as more patients are diagnosed with PA. Already, surgery may not be feasible in some patients due to co-morbidities, others are reluctant to have the whole adrenal gland removed when excess aldosterone can be localised to small APA(s) in 1 gland.

The FABULAS Study explores if EUS-RFA is a safe alternative to left-sided adrenalectomy (ClinicalTrials.gov ID NCT03405025). This multicentre phase-1 study comprises 3 groups of 10 patients with proven PA and left APAs. Successive groups have an increasing benefit:risk ratio for surgery. The first 4 ablation procedures are assessed by an independent safety committee before progression into the next, overlapping group. The primary outcomes are safety and feasibility of EUS-RFA. Safety is assessed throughout the study, including measures of intra-procedure adrenomedullary activation. Efficacy is evaluated by biochemistry, home / clinic BPs, and quantitative ^{11}C-metomidate PET-CT at baseline and 6 months post-ablation.

RFA is performed using a Starmed catheter, small enough to pass through a 19-gauge needle, through the stomach. Ablation has been performed in 6 patients (median age 63-years). Mean tumour size was 17mm (range 12-36mm). Plasma metanephrine levels remained stable during RFA. 2 adverse events occurred within the first 48hours post-ablation: AF in a patient with known paroxysmal AF, and an episode of pyrexia and raised CRP attributed to tissue infarction. Both events were deemed 'not unexpected' by the safety committee. Most patients have benefited clinically post-ablation. This is illustrated by a 65-year-old man with previously uncontrolled hypertension despite 4 antihypertensive medications, including spironolactone. Baseline aldosterone/renin ratio (ARR) was >200 (PA likely if ARR>60). PET CT revealed a 15mm left adrenal nodule with avid metomidate uptake and an SUVmax ratio of 1.92 (SUVmax ratio >1.25 suggestive of unilateral disease). He underwent uneventful EUS-RFA. 6 months post-ablation his ARR has normalised to 26. On repeat PET CT the metomidate avid adenoma is no longer hot, with a drop in both the SUVmax measured over the APA (31 pre-, and 5 post-ablation) and a reduction in the SUVmax ratio to 1.04. Most importantly, his home BP averages 124/83mmHg and he is thrilled to be off all treatment.

Retrospective reports exist of successful percutaneous and retroperitoneal RFA of APAs. FABULAS is the first prospective study, using a minimally invasive, endoscopic route. If proven to be safe and

effective EUS-RFA will open the doors for more patients to receive definitive treatment, potentially even those with bilateral disease.

Diabetes Mellitus and Glucose Metabolism

DIABETES COMPLICATIONS II

Use of Metabolic Syndrome Severity to Assess Treatment with Vitamin-E and Pioglitazone for Non-Alcoholic Steatohepatitis

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MON-673

BACKGROUND: Non-alcoholic steatohepatitis (NASH) represents inflammatory and fibrotic changes in the setting of non-alcoholic fatty liver disease (NAFLD) and can progress to cirrhosis. While clinical management of NASH has proven difficult, the Pioglitazone, Vitamin E or Placebo NASH study (PIVENS) demonstrated that treatment with either pioglitazone or vitamin-E increased odds of NASH-resolution. NASH is strongly associated with insulin resistance and the metabolic syndrome (MetS) as both a predictor and an outcome, though this has only been studied using dichotomous MetS criteria (e.g. ATP-III). We previously formulated a sex- and race/ethnicity-specific MetS severity Z-score (MetS-Z) that serves as a continuous measure of metabolic dysregulation. We hypothesized: 1) there would be a decrease in severity of MetS over the course of intervention in PIVENS and 2) the degree of decrease in MetS-Z early in the course of treatment would be a predictor of future NASH resolution. METHODS: Participants in PIVENS (n=201) had biopsy-confirmed NASH at baseline and were randomized to receive pioglitazone, vitamin E or placebo for 96 weeks, when they received repeat biopsy to assess for NASH resolution. We compared levels of MetS-Z and its standardized effect size (the absolute observed difference in MetS-Z for an individual divided by the overall baseline standard deviation of MetS-Z) at baseline, 48 weeks and 96 weeks and used logistic regression to determine associations between baseline MetS and the change in MetS from 0–48 weeks on ultimate NASH resolution—both overall and by intervention group. RESULTS: During the 96 weeks of intervention, 73 participants (363%) exhibited NASH resolution. Baseline MetS-Z was inversely associated with odds of NASH resolution, such that those with higher MetS severity at baseline were less likely to experience NASH resolution (odds ratio [OR] per 1-SD of MetS-Z-score: 0.54, 95% confidence interval [CI] 0.33,0.88). Of the three intervention groups, the decrease in MetS-Z during initial 48 weeks of intervention was greatest for pioglitazone treatment (effect-size: -0.31, CI -0.15,-0.48). During treatment with vitamin E, those with significant 48-week changes in MetS-Z tended to be those with vs. without ultimate NASH resolution (-0.18 vs. -0.05). In the group overall, 48-week change in MetS-Z was inversely associated with NASH resolution (OR of per 1-SD change: 0.56, CI 0.35,0.88). CONCLUSION: Individuals with more severe metabolic derangement at baseline were less likely to exhibit NASH resolution, suggesting that individuals may have a threshold of MetS-severity beyond which successful treatment is unlikely. As hypothesized, a decrease in MetS-Z over time was associated with improved odds