Diabetes Mellitus and Glucose Metabolism
LIPIDS, OBESITY AND METABOLIC DISEASE

Phosphatidylcholine Transfer Protein Interacts With PPARδ to Modulate Activity
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SAT-LB124
Obesity is one of the largest public health crises in the USA. Obesity can be lethal due to the development of cardiovascular complications such as, hypertension, heart attack, and stroke. Recently, peroxisome proliferator-activated receptor δ (PPARδ), the least-characterized member of the PPAR family of nuclear receptors (NRs), has shown great promise in treating obesity and associated cardiovascular complications. Recent reports have shown that PPARδ activation is tuned, in part, through an interaction with fatty acid binding protein 5 (FABP5) in a polyunsaturated Fatty acids (PUFAs) dependent manner. This enhancement is thought to occur due to ligand transfer, however, FABP5 only binds a subset of reported PPARδ ligands. To find other candidate lipid transport proteins (LTPs), we performed a protein complementation assay (PCA) between LTPs and NRs. We uncovered a novel interaction between PPARδ and phosphatidylcholine transfer protein (PC-TP), sensitive to cellular nutrient levels. Preliminary data show that this interaction opposes canonical PPARδ signaling, leading to a decrease in PPARδ transactivation in cells and isolated mice livers. This led me to hypothesize that PC-TP senses nutrient status through membrane composition. Specific PC molecular species drive PC-TP translocation to inhibit PPARδ transactivation of genes. Utilizing our novel PCA assay I have shown that the interaction is modulated in part by cellular levels of methionine and choline, as cells cultured in media depleted of methionine and choline (MCD) show a decreased in the interaction. Using the same assay, I have shown a requirement of full length PPARδ for the interaction with PC-TP. This analysis will be complimented by mutagenesis and chemical perturbations aimed to alter PC-TP and PPARδ function. Additionally, I have assayed the in vivo relevance of PC-TP interaction with PPARδ using livers harvested from PCTP−/− and littermate control mice fed a variety of diets. Preliminary RNA-seq characterization, show interesting alterations in gene expression that suggest more complex regulation between PC-TP and PPARδ in vivo. MCD, which was shown to reduce the inhibitory interaction between PC-TP and PPARδ in vitro, seems to lead to an increased effect on PPARδ transactivation when PC-TP is depleted. Analysis comparing the effect of diet within each genotype shows a loss of differential PPARδ regulation for both CHEA and KEGG analysis when comparing WT to PCTP−/− mice supporting a role for PC-TP in differential PPARδ regulation caused by MCD diet. These studies will further the understanding of how lipid homeostasis is sensed and maintained through PPARδ by interactions with two separate LTPs.

Bone and Mineral Metabolism
BONE DISEASE FROM BENCH TO BEDSIDE

Urine Phosphoethanolamine Is an Underutilized Biomarker for Hypophosphatasia
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SUN-LB64
Hypophosphatasia (HPP) is a rare disease caused by a loss-of-function mutation in the ALPL gene leading to a deficiency in the tissue-non-specific isoenzyme alkaline phosphatase (ALP) and excess of extracellular inorganic pyrophosphate (PPi) and pyridoxal 5-phosphate (PLP). Patients with HPP have a widely variable clinical phenotype, from neonatal seizures and hypomineralization to isolated dental or joint disease in adults. Patients present with ALP activity levels below their age-adjusted reference interval and elevations in PLP. This variable clinical phenotype leads to significant diagnostic challenges, particularly in those with minor disease manifestations. Biomarkers for diagnosing HPP and monitoring patients on enzyme replacement therapy (ERT) are limited. Low ALP activity is not specific for HPP; it can be low in other conditions including untreated hypothyroidism, and other skeletal dysplasias. Accurate PLP assessment is limited in patients on ERT due to hydrolysis of the substrate. Phosphoethanolamine (PEA) is a substrate hydrolyzed by TNSALP and elevated levels of PEA may be observed in HPP, supporting the diagnosis of HPP, but have been reported to be non-specific. We hypothesized that urine PEA levels could be used to diagnose HPP and as a surrogate marker for ERT compliance. We performed a retrospective analysis on 83 adult patients (63F: 20M)
Bone and Mineral Metabolism
PARATHYROID HORMONE TRANSLATIONAL AND CLINICAL ASPECTS

Relationship Between LC-MS/MS Measurements of PTHrP and Calcium in Patients With Compromised Renal Function
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SAT-LB70
Elevated concentrations of parathyroid hormone related peptide (PTHrP) may indicate hypercalcemia of malignancy and can prompt investigation into potential malignancy. Early studies using PTHrP radioimmunoassays suggested that PTHrP concentrations in normocalcemic renal failure patients were elevated due to assay cross-reactivity with C-terminal fragments present in this population [1]. At our institution, we developed a liquid chromatography-tandem mass spectrometry (LC-MS/MS) assay for PTHrP targeting a peptide in the middle of the PTHrP sequence (to avoid measuring terminal fragments). Given the high specificity of LC-MS/MS, our objective was to revisit the early observation that PTHrP concentrations are elevated in renal failure patients. We used retrospective chart review to investigate 1) whether PTHrP concentrations differed between adult patients with and without renal impairment and 2) how PTHrP and calcium concentrations were related in these patients. We excluded patients with cancer; the participants (n=93, 20-90yo, 56% female) were categorized based on eGFR using the 2009 CKD-EPI equation following KDIGO guidelines. We focused on patients with healthy kidney function (n=21, 20-73y, 43% female), stage 4 kidney disease (n=40, 23-90y, 63% female), and end stage renal disease (ESRD, n=19, 27-81y, 58% female), 7 of whom were on hemodialysis. When measured by LC-MS/MS, we observed higher PTHrP concentrations in ESRD and stage 4 patients compared to those with healthy kidney function (p<0.0001 for both). Overall, there was a strong negative correlation between eGFR and PTHrP (r=-0.768, p<0.0001). In contrast to the previous study documenting elevated C-terminal fragments of PTHrP in normocalcemic patients, we observed that 80% of patients with elevated PTHrP had hypercalcemia, in agreement with the positive association between concentrations of PTHrP and calcium (p=0.295, p=0.0178). No statistically significant difference was observed between distributions of PTHrP concentrations in stage 4 and ESRD patients with and without hypercalcemia. Among ESRD patients, higher PTHrP concentrations occurred in patients on dialysis compared to those not on dialysis (p=0.003). Our data suggest that elevated PTHrP concentrations are not solely due to decreased glomerular filtration; otherwise, patients on hemodialysis would have decreased PTHrP concentrations due to clearance. Considering the specificity of the LC-MS/MS method for the central portion of PTHrP, we conclude that elevated PTHrP concentrations may occur in patients with severe renal dysfunction; PTHrP elevations correlate with hypercalcemia in the majority of these patients. Clinicians should be cognizant of the method used to measure PTHrP when evaluating hypercalcemia, particularly in patients with renal insufficiency.

Reproductive Endocrinology
MALE REPRODUCTIVE HEALTH - FROM HORMONES TO GAMETES

Novel Hormonal and Metabolic Markers of Recovery From Overtraining Syndrome Unveiled by the Longitudinal ARM of the Eros Study - the Eros-Longitudinal Study.
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SAT-LB4
Background: Overtraining Syndrome (OTS) is an unexplained underperformance syndrome triggered by excessive training, insufficient caloric intake, inadequate sleep, and excessive cognitive and social demands. Investigations of markers of the challenging recovery from OTS have not been reported to date. The objective of the present study is to describe novel markers, and biochemical and clinical behaviors during the restoration process of OTS.Design: A 12-week interventional protocol in 12 athletes affected by OTS was conducted, including increased food intake, transitory interruption of the trainings, improvement of sleep quality, and management of stress.Methods: We assessed 50 parameters, including hormonal responses to an insulin tolerance test (ITT), basal hormonal and non-hormonal biochemical markers, body metabolism and composition. Results: In response to an ITT, early cortisol (p = 0.026),