laboratory testing. We removed albumin from serum with immunoprecipitation using anti-albumin antibody and measured cortisol with LC-MS/MS. The decrease of cortisol was 4% in control serum but 38% in the patient serum after removing albumin, suggesting the binding rate of cortisol to mutant albumin in the patient was increased, leading to false hypercortisolemia.
Conclusion: This is the first case demonstrating the false hypercortisolemia in a FDH patient. Clinicians should consider the possibility of the abnormal cortisol binding to albumin in differential diagnosis of hypercortisolemia with normal ACTH level.
Reference: (1) Norio Wada, et al: A Novel Missense Mutation in Codon 218 of the Albumin Gene in a Distinct Phenotype of Familial Dysalbuminemic Hyperthyroxinemia in a Japanese Kindred. Journal of Clinical Endocrinology and Metabolism 1997;82;3246–3250

Adipose Tissue, Appetite, and Obesity

CNS, INFLAMMATORY, AND THERMOGENIC INFLUENCES OF BODY WEIGHT

Calcitonin Receptor Expressing Neurons in the PVH Regulate Feeding Behavior

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The paraventricular nucleus of the hypothalamus (PVH) is a brain region crucial for energy homeostasis. Abnormal PVH development or damage leads to hyperphagic obesity and energy expenditure deficits underscoring the importance of PVH neuronal activity in energy balance control. Application of salmon calcitonin (sCT) to the PVH suppresses feeding and calcitonin receptor (CalcR) is highly expressed in the PVH of rodents suggesting that CalcR-expressing PVH neurons contribute to energy homeostasis. In situ hybridization reveals that many $CalcR^{PVH}$ neurons express melanocortin-4 receptor (MC4R), a receptor required for normal feeding behavior. To investigate the physiologic roles of $CalcR^{PVH}$ neurons, we generated CalcR-2a-Cre knock-in mice to manipulate CalcR-expressing cells. Deletion of MC4R from CalcR expressing cells using Cre-loxP technology resulted in profound obesity in both male and female mice by 16 weeks of age. This weight gain was attributable to hyperphagia, as cumulative food intake of the MC4R deleted mice was significantly greater than the controls and energy expenditure measurements acquired through CLAMS analysis were not significantly different. To determine the brain regions engaged by $CalcR^{PVH}$ neurons, we used anterograde Cre-dependent viral tracing reagents injected into the PVH of CalcR-Cre mice, and found that $CalcR^{PVH}$ neurons project to brain regions implicated in energy balance control, including the nucleus of the solitary tract and the parabrachial nucleus. To assess the acute effects of activating $CalcR^{PVH}$ neurons, we used DREADD technology to chemogenetically activate $CalcR^{PVH}$ neurons. $CalcR^{PVH}$ neuron activation suppressed feeding but had no significant effect on energy expenditure. To determine if the activity of $CalcR^{PVH}$ neurons is required for energy homeostasis, we silenced them using Cre-dependent tetanus toxin virus. Male mice with tetanus toxin silenced $CalcR^{PVH}$ neurons were obese 7 weeks following injection in part due to greater cumulative food intake; CLAMS analysis revealed no differences in energy expenditure. Mice with silenced $CalcR^{PVH}$ neurons as well as mice with CalcR deleted from the PVH had normal anorectic responses to sCT, suggesting sCT-induced anorexia does not require $CalcR^{PVH}$ neurons or CalcR expression in the PVH. Taken together, these findings suggest $CalcR^{PVH}$ neurons are an essential component of feeding and energy homeostatic circuitry.

Genetics and Development (including Gene Regulation)

GENETICS AND DEVELOPMENT AND NON-STEROID HORMONE SIGNALING II

Abundant Circulation of Functional Short Non-Coding RNAs Expressed from the Intergenic Area in Mouse Serum

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The human genome expresses numerous and different forms of non-protein-coding (nc) RNAs from over 80% of its sequence in addition to mRNAs. Although their overall functions and biological importance are still under intensive investigation, they appear to be important for supporting complex human biology. Some of these ncRNAs are recently identified in several human fluids, such as serum, urine and saliva. Here we present a comprehensive analysis on the short RNAs presented in mouse serum by employing three organs, adrenal gland, liver and ovary, as controls. We found that serum has numerous sRNAs. Among them, short ncRNAs (sncRNAs) expressed from the intergenic area (intergenic sncRNAs) dominated the majority (~97%) in serum with their read numbers equivalent to those found in three control organs. In contrast, known sncRNAs, such as ribosomal RNA fragments, transfer RNAs, micro RNAs, piwi-interacting RNAs, small nuclear and small nucleolar RNAs, were very minor components in serum, and were significantly low compared to control organs. Few short RNA fragments derived from mRNAs or long non-coding RNAs were also identified. The principal component analysis for the intergenic sncRNAs found in serum and three control organs revealed that the former was distinct from the latter. Indeed, ~90% of serum intergenic sncRNAs were not identified in each control organ in one-by-one comparisons. Multiple comparison between serum and all three control organs demonstrated a similar tendency: ~75% of the serum intergenic sncRNAs were distinct from the intergenic sncRNAs found in the three control organs, whereas these control organs shared 53% of them. The genomic areas encoding these intergenic sncRNAs tended to distribute around -20 - +20 kbs from the transcription start site of their nearby protein-coding genes. Among four selected serum intergenic sncRNAs,