

(pGRTH) in *in vitro* studies. GRTH knock-in (KI) mice with insertion of the human mutant GRTH gene show loss of the cytoplasmic 61 KDa phospho-species with preservation of the non-phospho nuclear form. KI mice are sterile, lack elongated spermatids and spermatozoa with arrest at step 8 of round spermatids (RS) which contain chromatoid bodies (CB) markedly reduced in size. CB is a non-membranous, cytoplasmic organelle present adjacent to the nucleus of RS, where mRNAs bound to GRTH transported from nucleus to cytoplasmic sites are temporarily stored, translationally repressed for later transport to polyribosomes for translation at specific stages of spermiogenesis. Owing to the specific function of CBs and importance of pGRTH in spermatid elongation, CBs isolated from germ cells of WT and GRTH KI mice were used for subsequent experiments. CBs isolated from GRTH KI mice are smaller, highly condensed and lack the nuage texture of CBs in WT mice. We observed the absence of pGRTH in CB of round spermatids of GRTH KI mice. Also, MVH protein (recognized CB marker protein) was decreased in the CB of GRTH KI mice. Expression of genes related to spermatid regulation, chromatin compaction, remodeling (TP1 and 2, PRM1 and 2, GRTH, TSSK6, HMG2, GCNF, RNF8, TDRD 1, 6, 7 and 9) analyzed by qPCR were markedly reduced in the CB of GRTH KI mice compared to WT. No change was observed in the expression of bromodomain mRNAs and protein, indicating that pGRTH does not participate in the translational regulation of this protein class at the level of this organelle. Notably, mRNAs of TP2, PRM2 and GRTH which associated with GRTH protein were co-localized with MVH protein in the CB. This indicated the relevance of GRTH as a binder/transport protein of key chromatin remodelers for ensuring their mRNA repression/stability within the CB. In addition, GRTH binding to genes essential for spermatid development and regulation (TP1 and 2, PRM1 and 2, GRTH, TSSK6, RNF8 and GCNF) were also found to be markedly decreased in the CB KI mice. These results demonstrate the importance of pGRTH in the maintenance of biochemical composition/structure of the CB and role in spermatid regulation, chromatin compaction, spermatid development and completion of spermatogenesis.

## Adrenal

### ADRENAL - HYPERTENSION

#### *Cardiovascular Risk Factors, Morbidity, and Overall Mortality in Patients with Adrenal Adenomas:*

##### *A Population-Based Study of 1,003 Patients*

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### MON-222

**Background:** Benign adrenal tumors are frequently diagnosed on imaging and may pose health risks to patients regardless of functional status. Both non-functioning adrenal tumors (NFAT) and tumors with mild autonomous cortisol secretion (MACS) have been associated with

increased cardiovascular events and risk factors. However, limited data exist on the association of adrenal adenomas with cardiometabolic outcomes in the population-based setting.

**Aim:** 1) To determine the prevalence of cardiovascular co-morbidities and events and 2) to assess mortality in a population-based cohort of patients with adrenal adenomas.

**Methods:** We identified adult patients living in the community diagnosed with an adrenal tumor from 1995-2017 using a medical records linkage system. Adrenal tumors were classified as MACS if cortisol was  $\geq 1.8$  mcg/dL after 1 mg dexamethasone suppression test, NFAT if cortisol was  $< 1.8$  mcg/dL, and adenoma with unknown cortisol secretion (AUCS) if dexamethasone suppression test was not performed. Cardiovascular co-morbidities and events were assessed at baseline. Patients were then followed until death, migration out of the community, or through December 31, 2018. Results were compared to age and sex matched reference subjects without adrenal tumors and adjusted for tobacco use and BMI.

**Results:** A total of 1,003 patients had adrenal adenomas with 136 (14%) NFAT, 86 (9%) MACS, and 781 (78%) AUCS. The median age of diagnosis was 63 years (range, 20-96) and 581 (58%) were women. At baseline, patients with adrenal adenomas were more likely to have hypertension (92% vs 81%,  $p < 0.001$ ), overweight/obesity (89% vs 82%,  $p < 0.001$ ), pre-diabetes/diabetes (82% vs 70%,  $p < 0.001$ ), dyslipidemia (89% vs 82%,  $p < 0.001$ ), and chronic kidney disease (11% vs 7%,  $p = 0.004$ ) than age and sex matched reference subjects. Myocardial infarctions (13% vs 8%,  $p < 0.001$ ), coronary intervention (9% vs 6%,  $p = 0.007$ ), heart failure (12% vs 6%,  $p < 0.001$ ), peripheral vascular disease (26% vs 15%,  $p < 0.001$ ), and thromboembolic disease (7% vs 3%,  $p < 0.001$ ) were more prevalent in patients with adrenal adenomas, whereas overall survival was lower compared to reference subjects (60% vs 65%,  $p$  value = 0.013). Subgroup analysis (adjusted for age, sex, BMI, and smoking) demonstrated prevalence of cardiovascular events including peripheral vascular disease was highest in those with MACS (44.7%), followed by AUCS (40.1%), and then NFAT (36.6%), although differences between groups were not significant. Overall survival was lower in patients with MACS (62%) and AUCS (59%) compared to NFAT (71%),  $p < 0.001$ .

**Conclusions:** Adrenal adenomas are associated with significantly higher prevalence of cardiovascular risk factors and morbidity at the time of diagnosis and with increased mortality during follow-up. Results are potentially related to abnormal cortisol secretion but are limited by suboptimal evaluation for hormone excess.

## Adipose Tissue, Appetite, and Obesity

### ADIPOSE TISSUE BIOLOGY AND OBESITY II

#### *MED1 Is a Lipogenesis Coactivator Required for Postnatal Adipose Tissue Expansion*

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### SUN-589

Mediator is a multi-subunit transcription coactivator complex that controls gene activation by connecting enhancer-binding transcription factors (TFs) with RNA