

associated to hyperinsulinism in the context of gestational diabetes. Micropenis was noted on physical exam. As part of the study for hypotonia, serial thyroid function tests were obtained revealing central hypothyroidism. A low dose ACTH stimulation test was performed which revealed adrenal insufficiency. The patient was started on cortisol and thyroid hormone replacement. Brain MRI showed an ectopic neurohypophysis located along the floor of the hypothalamus, a small anterior pituitary gland, and a partially absent infundibulum, findings consistent with pituitary stalk interruption syndrome. The patient received testosterone injections for micropenis and is being followed for development of other pituitary hormone deficiencies. PSIS is a rare congenital condition that is increasingly recognized in neonates manifesting with signs of hypopituitarism.

## Neuroendocrinology and Pituitary PITUITARY TUMORS II

### *Cancer Incidence in 1,296 Patients with Acromegaly Is Not Increased: A Nationwide Population-Based Study*

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### MON-330

**Background:** Single- and multi-center studies have shown an increased incidence of malignancies in patients with acromegaly. These findings may be affected by selection bias. Our aim was therefore to investigate the incidence of malignancies in a nationwide unselected cohort of patients with acromegaly.

**Methods:** Adult patients diagnosed with acromegaly due to a pituitary tumor between 1987 and 2017 were identified in the Swedish National Patient Registry. All malignancies following the diagnosis of acromegaly were identified in the Swedish Cancer Registry that has a coverage of over 96%. Standardized incidence ratios (SIRs) for malignancies, with 95% confidence intervals (CI), were calculated by using the Swedish general population as a reference. Incidence of malignancies was also analyzed in sub-groups of patients treated with radiotherapy and in those having diabetes mellitus and hypopituitarism.

**Results:** A total of 1,296 patients with acromegaly were included (621 men, 675 women). The mean age ( $\pm$ SD) at diagnosis was 51.6 $\pm$ 14.7 years. The mean follow-up was 12.7 $\pm$ 8.3 years, with a total of 16,395 person years at risk. Pituitary surgery was performed in 842 (65%) patients and radiation therapy in 152 (12%) patients. The diagnosis of hypopituitarism and diabetes mellitus was recorded in 29% and 16% of patients, respectively. Overall, 186 malignancies were identified in patients with acromegaly as compared to 179 expected malignancies in the general population (SIR 1.04; 95% CI 0.90-1.20). Incidence of malignancies was similar in men and women [SIR 1.08 (95% CI 0.88-1.32) vs 1.00 (95% CI 0.80-1.23)]. Incidence of colorectal cancer (SIR 1.12; 95% CI 0.75-1.62) or malignancies of the respiratory system (SIR 1.22; 95% CI 0.76-1.84) was not increased. Incidence of kidney and ureter cancer (n=17)

was, however, increased (SIR 3.81; 95% CI 2.22-6.11). In the entire study cohort, only three cases of thyroid cancer were recorded. SIR for malignancies in patients treated with radiotherapy (1.12; 95% CI 0.56-2.01) and in patients with hypopituitarism (SIR 0.91; 95% CI 0.68-1.18) or diabetes (SIR 1.08; 95% CI 0.78-1.45) did not differ from the general population.

**Conclusions:** This large nationwide population-based study showed that the overall incidence of malignancies in patients with acromegaly was not different from the general population. In particular, incidence of colorectal and thyroid cancer was not increased. Incidence of malignancies of the urinary tract was, however, increased.

## Tumor Biology

### TUMOR BIOLOGY: GENERAL, TUMORIGENESIS, PROGRESSION, AND METASTASIS

#### *Cholesterol Uptake as a Critical Vulnerability in Triple Negative Breast Cancer*

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### SAT-145

Triple Negative Breast Cancer (TNBC) is an aggressive subtype of cancer with poor prognosis due to high metastatic potential and lack of targeted therapies. Normal epithelial cells express the microRNA-200c (miR-200c), a potent suppressor of epithelial-to-mesenchymal transition (EMT). However, miR-200c is silenced or lost in TNBC, allowing a de-differentiated, non-epithelial phenotype and aberrant expression of genes conferring invasive and chemoresistant characteristics. Recent literature has demonstrated that EMT promotes altered tumor cell metabolism, creating novel vulnerabilities that can be exploited therapeutically. In addition to driving global metabolic changes, miR-200c-induced reversal of EMT alters key cholesterol metabolism genes that support the uptake of dietary cholesterol from the bloodstream. Intracellular cholesterol homeostasis is critical for cell survival and is carefully regulated, but how these homeostatic mechanisms adapt during tumor progression is poorly understood. Based on preliminary data, I hypothesize that TNBCs depend on exogenous cholesterol uptake and availability to maintain cell viability and an invasive phenotype. This work aims to identify novel cholesterol-related targets in breast cancer and delineate mechanisms regulating cholesterol homeostasis in normal and cancer physiology. Restoration of miR-200c in TNBC leads to alteration of the cholesterol uptake components low- and very-low-density-lipoprotein receptors LDLR and VLDLR, through direct and indirect mechanisms previously unexplored in cancer. miR-200c further inhibits Niemann-Pick Type C (NPC1), a lysosomal protein necessary for utilization of exogenous cholesterol. Interestingly, expression of NPC1 in TNBC correlates with a unique inability of cells to proliferate in the absence of exogenous LDL supply, suggesting defects in de novo cholesterol biosynthesis. Further, NPC1 inhibition leads to cell death in TNBC but not more epithelial-like breast cancers. Whether this cell death is due to disruption in critical cholesterol supply or due to defective lysosome dysfunction is currently being investigated. Overall, this work suggests a role of