Silent pituitary corticotroph tumors derive from the Tpit (aka TBX19) pituitary lineage. Accounting for ~ 30% of corticotroph tumors, they are not infrequently clinically aggressive and invade locally into adjacent sellar structures, making complete surgical resection challenging and contributing to their higher recurrence rates. How silent and active corticotroph tumor subtypes differ is not clear although some studies reported that silent corticotroph tumors exhibit reduced PC1 expression causing impaired POMC processing. We used single cell RNAseq to compare the transcriptome between silent (n = 2) and active (n = 4) corticotroph tumors at the single cell level. We obtained an average of 265 million reads, and 24,682 genes per patient with an average of 1,240 genes expressed and 3,5442 unique molecular identifiers (UMIs) detected per cell. We further defined 5 distinct cell populations from a total of 23,269 cells, namely tumor cells (62%), stromal cells (25%), immune cells (7%), progenitor cells (5%), and a minor population of erythrocytes (1%). Tumor cells clustered in an origin-dependent manner and all expressed POMC and TBX19. However, the gene signatures of silent and active corticotroph tumors differed in 3 major aspects. Firstly, and supporting prior studies, a series of hormone processing peptidase genes, including PC1 (aka PCSK1), PDIA3, SEC11C, SPCS1 and CTSB, were reduced in silent corticotroph tumors (p=5.54e-5) compared to active corticotroph tumors. Secondly, genes involved in organization of secretory vesicles such as SCG5, TIMP1, VGF, SYT17, LGALS3 and CALY were also reduced in silent corticotroph tumors, which could further compound their inability to secrete ACTH. Thirdly, the silent corticotroph tumors exhibited several features of endothelial-to-mesenchymal transition (EMT), including increased expression of the mesenchymal genes CDH2 (aka NCAD), COL1A1, PCDH9, FGF5, ID2 (p=8.4e-3), and loss of EPCAM, which regulate cell migration and movement. Upstream analysis suggested that aberrant STAT3 activation may be related to these changes. Consequently, we noted that the stromal content was higher in silent corticotroph tumors (47.5% vs. 18.13%), concordant with the observed EMT de-differentiation of tumor cells. In summary, our scRNAseq analysis provides an unprecedented precise investigation of the transcriptomic features of thousands of heterogenous corticotroph tumor cells simultaneously. We demonstrate that although silent corticotroph tumor cells still express the pituitary lineage markers PITX1 and TBX19, they exhibit EMT, potentially affording increased migratory capacity at the cost of reduced neuroendocrine function with inability to produce and secrete mature ACTH. Our findings provide novel insights into the pathogenesis of silent versus active corticotroph tumor, but may reveal novel molecular targets for treatment of these challenging tumors.

Neuroendocrinology and Pituitary
PITUITARY TUMORS

One Fourth of Adult Patients With Acromegaly Have Tall Stature With Similar Frequency in Males And Females

Anna Bogusławska, MD[1], Aleksandra Gilis-Januszewska, MD,PhD,AssocProf[1], Kesson Magdid, PhD[2], Magdalena Godlewska, MD[1], Marta Olszewska, MD[3], Andrzej Jerzy Nowak, MD[1], Jerzy Starzyk, MD,PhD,Prof[4], Marta Korbonits, MD,PhD,Prof[2], Alicja Hubalewska-Dydejczyk, MD,PhD,Prof[1].
[1]Department of Endocrinology, Jagiellonian University, Medical College, Krakow, Poland, Krakow, Poland, [2]Centre for Endocrinology, William Harvey Research Institute, Barts and the London School of Medicine and Dentistry, Queen Mary University of London, London, United Kingdom, [3]Department of Paediatrics, Jagiellonian University, Collegium Medicum, Cracow, Poland, Krakow, Poland, [4]Department of Paediatric and Adolescent Endocrinology, Paediatric Institute, Jagiellonian University Medical College, Cracow, Poland, Krakow, Poland.

Introduction: Tall stature (TS) is a manifestation of growth hormone (GH) excess, with higher prevalence reported for males. The aim of this study was (i) to evaluate the relationship between height of patients with GH excess related to midparental height (MPH) and population mean height; (ii) to test whether TS patients with acromegaly come from tall families. **Methods:** Single-centre, observational study on 101 consecutive adult patients with acromegaly and no family history of pituitary adenoma. Patients were analysed in two subgroups depending on height using country-specific data: 1) normal stature and 2) TS group, defined as either height above gender-specific 97 percentile or as >1.5 country-specific standard deviation (SD) from MPH. **Results:** Twenty-four percent of acromegaly patients (13 females/11 males) met one or both of the TS criteria. TS patients were significantly younger at the diagnosis (mean±SD, 33.6±13.4 vs 50.6±12.3 years) and at first symptoms (median 27.5, range 23-42 vs 41 (33-54) years) with greater tumour size and higher basal GH concentration than normal stature patients (p<0.01). The TS criteria based on the 1.5 SD above MPH identified more TS patients than the above 97 percentile height (92% vs 38%) and especially increased the diagnosis of TS in women (92% vs 31%). There was no difference in height of family members of acromegaly patients with or without TS. Height of family members were not taller than the population mean. **Conclusion:** One fourth of adult patients with acromegaly have TS with similar frequency in males and females. Based on our data TS patients with acromegaly do not come from tall families.

Neuroendocrinology and Pituitary
PITUITARY TUMORS

Prevalence of Abnormal Glucose Metabolism in Acromegaly & Impact of Treatment Modalities on Glucose Metabolism

Sajjad Ali Khan, MBBS[1], Nanik Ram, MD[1], Muhammad Qamar Masood, MD[2].
[1]AGA KHAN UNIVERSITY, KARACHI, Pakistan, [2]The Aga Khan University, Karachi, Pakistan.

Objective: To determine the frequency of diabetes mellitus impaired glucose tolerance and impaired fasting glucose in Pakistani patients with acromegaly and to establish the impact of the intervention (surgery/ medical) on glucose metabolism.
Methods: Eighty-nine patients fulfilling the endocrine society criteria for acromegaly diagnosis were included.