**COMBINED CLINICAL AND GENE EXPRESSION PROFILING IN HUMAN ACTH-SECRETING PITUITARY TUMORS**


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**Introduction**

We have previously reported on the considerable variability in ACTH-secreting pituitary adenomas as regards responses to major modulators in vitro (Pecori Giraldi et al Journal of Neuroendocrinology 2011).

**Aim** of this study is to correlate transcriptome expression pattern in archival human ACTH-secreting adenomas with clinical features of patients prior to and after surgery.

**Methods.** Forty human ACTH-secreting pituitary adenoma formalin-fixed paraffin-embedded specimens were cut into 20 µm thick sections and RNA extracted using Recover All Total Nucleic Acid Isolation Kit (Invitrogen, Carlsbad CA, USA). RNA (300 ng) was hybridized to Human HT-12V4 expression bead Chip (approx 29000 transcripts) and analyzed with WG-DASL-HT assay (Illumina, San Diego CA, USA). Patients’ clinical charts were reviewed and data analyzed by Principal Component Analysis (JMP, Statistical Discovery, SAS Institute, Cary NC, USA). Combined clinical and expression analysis was performed on R-studio and functionality of identified genes assessed by DAVID and Cytoscape.

**Results**

Clinical and expression data clustered in three major groups, with 18, 4 and 18 patients, respectively. 1259 genes were significantly expressed (p<0.001) and clinical variables which proved predictive of clustering were adenoma size and plasma ACTH concentrations.

Differential expression analysis among clusters revealed significant expression of genes annotated to functions including granule lumen (enrichment score 2.6), phosphorylation (enrichment score 2.07), aminoacid ligase (enrichment score 2.08) and ubiquitin pathway (enrichment score 1.8).

**Conclusions.** Combined clinical and gene expression analysis of human ACTH-secreting adenomas allowed the identification of three major clusters. Functional annotations revealed the involvement of distinct pathways in individual clusters, pving the way to a greater understanding of the variability of human corticotrepe tumors.