Introduction/objectives: Our long-term goal is to determine molecular pathogenesis of pituitary tumors and to exploit these insights for diagnostic and therapeutic benefit. We have identified new molecular targets in these tumors and have developed a novel molecular-targeted imaging agent—Folatescan, to identify them.

Methods: Tumor specimens from surgery were used in the molecular and cell-culture studies. GeneChip arrays were performed and verified by RT-qPCR. Western analysis, immunochemistry and folate-binding studies were performed to determine folate expression. Cell culture and cytotoxicity studies were performed with MTT assays. In vivo imaging was performed by injection of Folatescan followed by planar and SPECT/CT imaging.

Results: Several genes, including GATA3, GATA2, PITX2, HLF, SMARCD3, and Histone deacetylase HD1 were upregulated in non-functional pituitary adenomas. The cyclin-dependent kinase inhibitor 1C (p57, Kip2), insulin-like growth factor binding protein 3 (IGFBP3), and frizzled homolog 7 (FZD7) were strongly downregulated in non-functional pituitary adenomas.

In particular the folate-receptor (FR) was significantly and uniquely upregulated in nonfunctional pituitary adenomas. Folatescan successfully imaged folate receptor expressing tumors and was validated by Westerns. Similarly, non-FR expressing tumors were not imaged by Folatescan.

Folate-targeted liposomes containing doxorubicin induced cell-death in folate-receptor expressing pituitary tumors in vitro, as measured by MTT assays.

Conclusions: These preliminary data demonstrate that Folatescan can successfully target FR+ pituitary tumors and provide preliminary evidence that folate can be used as a delivery system for successful tumor-targeted delivery of drugs into non-functional pituitary tumors opening the possibility of novel chemotherapy and molecular imaging of these tumors.