Introduction and Background

The tumorigenesis of pituitary adenomas

Objective

The objective of our study was to identify somatic genetic abnormalities in TSHomas.

Methods and overview of the Study Design

SNP Array Analysis (indels)

Whole Exome Sequencing

Candidate Driver Genes

SNP Array

Discovery Set

Validation Set (indels)

Validation Set (SNPs)

Sanger Sequencing

Result 1: Copy number Variations in TSHomas

The molecular mechanisms underlying their tumorigenesis and the molecular nature of these tumors are not well understood.

Next generation sequencing technology is increasingly being used in identification of somatic mutations in humans and mouse models, using this technology. Somatic mutations in the desmoplakin gene, USP8, have been identified in ACTH-secreting adenomas.

Thyrotropin-secreting pituitary adenomas (TSHomas)

TSHomas are rare form, representing less than 5% of all adenomas. The molecular mechanisms underlying their tumorigenesis and the molecular nature of these tumors are not well understood.

Result 2: Loss of Heterozygosity (LOH) in TSHomas

Chromosomal deletion at 15q and 20q harboring the PRKAR1A gene, which is critical for the development of pituitary adenomas.

Representative Plots of loss of Heterozygosity

- Six candidate somatic DNA variants were found in TSHomas. But no recurrence of DNA variants was seen in 12 TSHomas.
- Whole exome sequencing revealed a low mutation rate of TSHomas, thereby highlighting their benign nature.
- Further studies on a larger cohort of TSHomas, in combination with epigenetic and transcriptomic approaches, may reveal the underlying genetic lesions.