How Tpit alters a diagnostic algorithm

Clarifying the Classification Problem in Pituitary Adenoma Diagnosis with Simple Supervised and Unsupervised Methods

# Abstract:

*Context.*—Disease classification depends upon the sensitivity and specificity of tests, which change depending upon disease prevalence. Pituitary adenoma classification is complex, and diagnostic strategies vary between institutions. An optimal diagnostic strategy has not been defined. We previously examined pituitary adenomas with immunohistochemical stains (IHC) for steroidogenic factor 1 (SF-1), Pit-1, anterior pituitary hormones, cytokeratin CAM5.2, alpha subunit of human chorionic gonadotropin and found that a screening panel comprised of SF-1, Pit-1 and adrenocorticotropic hormone successfully classified the majority of cases and reduced the overall number of stains performed.

*Objective.*— To update the IHC panel used to classify pituitary adenomas at our institution and clarify the degree to which the new panel improved the classification process.

*Design.*— We examine 157 pituitary adenomas from two institutions with immunohistochemical stain for Tpit. Immunostains were scored using the Allred system. Adenomas were assigned to a gold standard class based upon IHC and available clinical and serological information. Correlation and cluster analyses and classification and regression tree analyses were used to update our previous classification strategy.

*Results.*—text \*\*\*\*\*\*\*\*\*\*\*\*

*Conclusions.*—Tpit IHC improves upon our prior algorithm by reducing the number of false negatives and false positives incurred by ACTH immunostaining. This reduces the overall incidence of IHC null cell adenoma and increases the incidence of silent corticotroph adenoma.

# INTRODUCTION

Pituitary neuroendocrine tumors are uncommon neoplasms of the anterior pituitary gland. Their phenotype usually emulates the developmental program of the anterior pituitary, which can be organized into three families, each mediated by a principle transcription factor: gonadotrophs with steroidogenic factor 1 (SF-1), corticotrophs with T-box transcription factor (Tpit), and the diverse acidophil family including prolactin, growth hormone, and thyroid-stimulating hormone (TSH) with Pit-1.

We previously validated an algorithm for immunohistochemical (IHC) characterization of pituitary adenoma that used stains for the major anterior pituitary hormones as well as IHC stains for CAM5.2, SF-1 and Pit-1[7]. At that time, reliable reagents for use in formalin-fixed, paraffin-embedded (FFPE) material were not available for Tpit. In this work, we explore the impact on our algorithm of a monoclonal antibody to Tpit that is suitable for use in FFPE.

Cases were drawn from Allina Health Laboratory and University of Pennsylvania files. Diagnoses were checked against available serologic and clinical information in order to render a gold standard diagnosis, as previously described[7].

T-box transcription factor , product of the *TBX19* gene, also known as Tpit, is \*\*\*

# MATERIALS AND METHODS

## Case Selection and Recording of Preoperative Data

Text

## TMA Construction, Immunohistochemistry and Scoring

We used a mouse\*\*\* monoclonal antibody to Tpit (\*\*\*HG3-31 (sc-268), \*\*\*Santa Cruz Biotech, 1:100\*\*\* dilution) to examine 157 adenomas in tissue microarrays (TMAs). TMA construction, IHC staining and quantification, and adenoma classification were performed as previously described[7]. Allred scoring[1] was performed in a blinded fashion to semi-quantify IHC staining.

## Data Analysis

Text

# RESULTS

Text

# DISCUSSION

Text

References