

## Introduction

Pituitary adenomas occur in 10% to 15% of the general population as determined by autopsy studies (Ezzat et al., 2004; Scheithauer et al., 2006). Although relatively rare (one case per 1000 people (Daly et al., 2009), clinically significant pituitary tumors are associated with significant morbidity and decreased quality of life. Pituitary adenomas are usually benign. However, a significant number of pituitary adenomas show an aggressive behavior, with local invasion, increased risk of recurrence after surgery and lack of therapeutic response (Buchfelder, 2009; Zada et al., 2011). The pathogenic mechanisms responsible for the invasive behavior in pituitary adenomas remain largely unknown although differences in the expression of genes such as VEGF and E-cadherin have been reported (Sánchez-Ortiga et al. 2013; (Fougner et al., 2010). The association between these molecular differences in gene expression and clinical features of tumor behavior might be useful as prognostic markers.

## Objective

- To determine whether invasive and non-invasive pituitary adenomas display differences in clinical features and molecular parameters

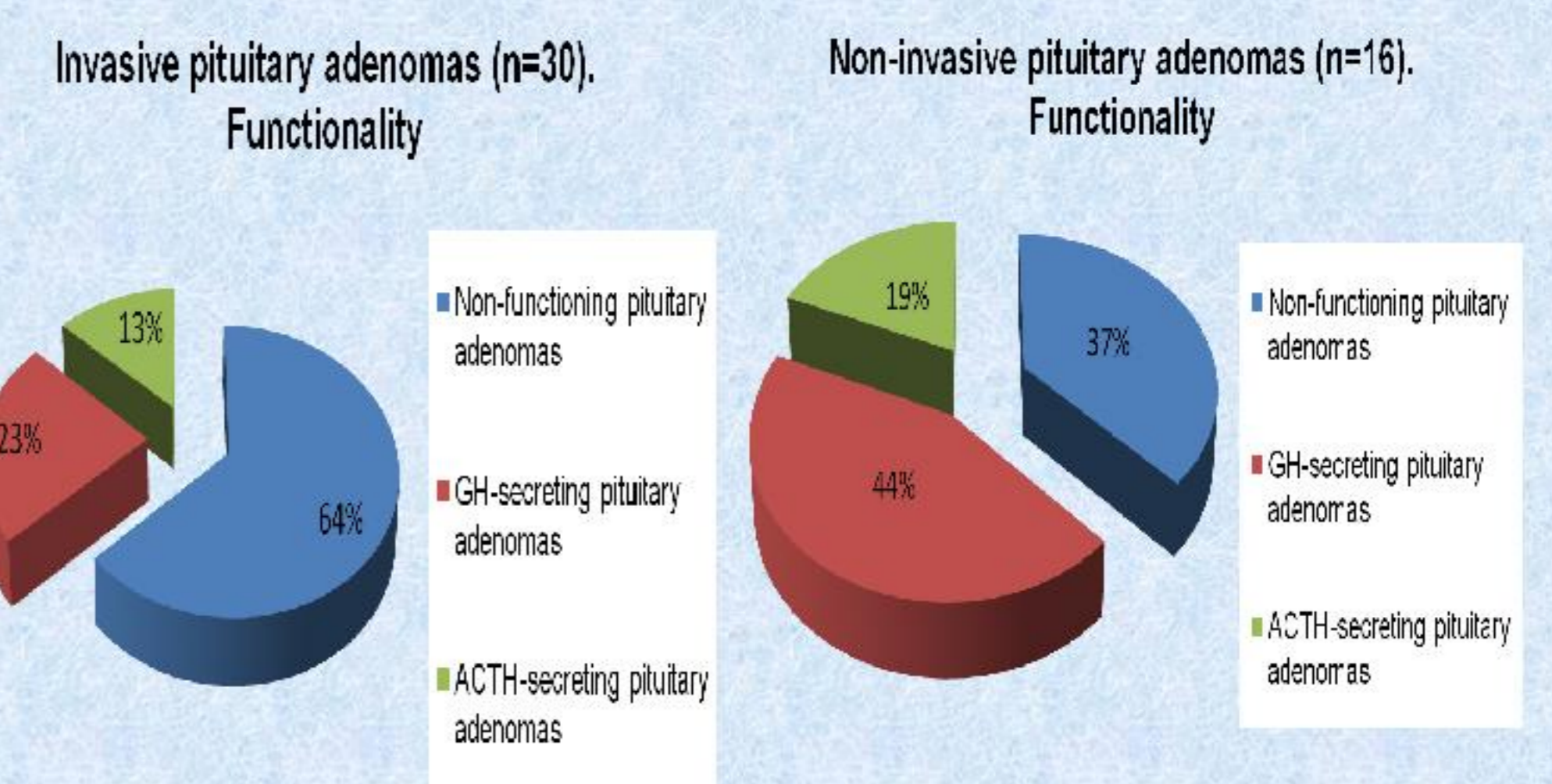
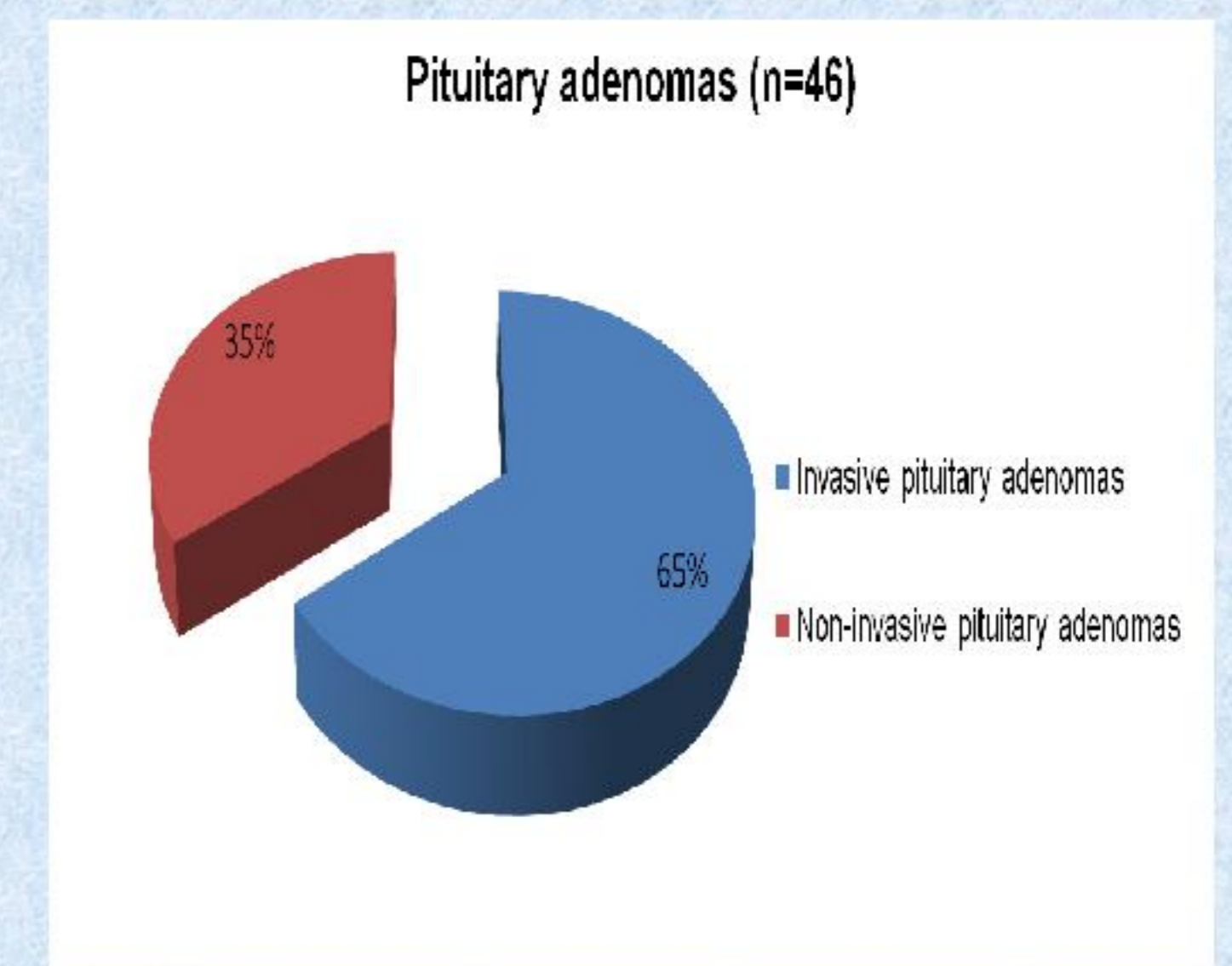
## Design and Methods

### Subjects:

In this retrospective descriptive study, we analyzed 46 pituitary adenomas randomly selected from patients who were surgically intervened at the Hospital University Virgen del Rocío, Seville (Spain) between 2000 and 2012. The inclusion criteria was the availability of frozen adenoma tissue to perform molecular analysis of gene expression as well as presurgical evaluation data. Adenomas were diagnosed with immunohistochemical analysis according to the WHO 2004 classification. Nonfunctioning pituitary adenoma was defined as the lack of a hormone-related syndrome regardless of the presence or not of a biologically active. Invasion was defined as radiological signs (MRI) of cavernous or sphenoid sinus invasion. The presence of tumor remnants after surgery was determined by MRI the day after surgery

### Methods:

Total RNA was isolated from frozen adenoma tissue using a Rneasy kit (Qiagen) and retrotranscribed using cDNA reverse Transcription Kit (Qiagen). Real time quantitative PCR were performed in a 7500 Real Time PCR system (Applied Biosystems). The expression level (copy number) of membrane receptors important for pituitary function were analyzed including somatostatin receptors (SSTR1-SSTR5), dopamine receptors (DR1-DR5) including the long isoform of dopamine D2 receptor 2, GHRHR, GHSRS1, GHSRS1b. Proliferation genes (ki67 and PTTG1) and 3 housekeeping genes (glyceraldehyde-3-phosphate dehydrogenase, beta-actin and HPRT) were also measured. Standard curves were used to estimate the normalized copy. Since the three endogenous genes were highly correlated (spearman rank correlation), all the results were normalized to beta-actin



## Results

No differences in age, sex, functionality were observed between Invasive and non-invasive pituitary adenomas. A higher presence of tumor remnants, need for surgical re-intervention and radiotherapy was found in invasive adenomas.

Increased expression of PTTG1 (Figure 1), SSTR3 (Figure 2) and the long isoform of DR2 was found in invasive adenomas (Figure 3).

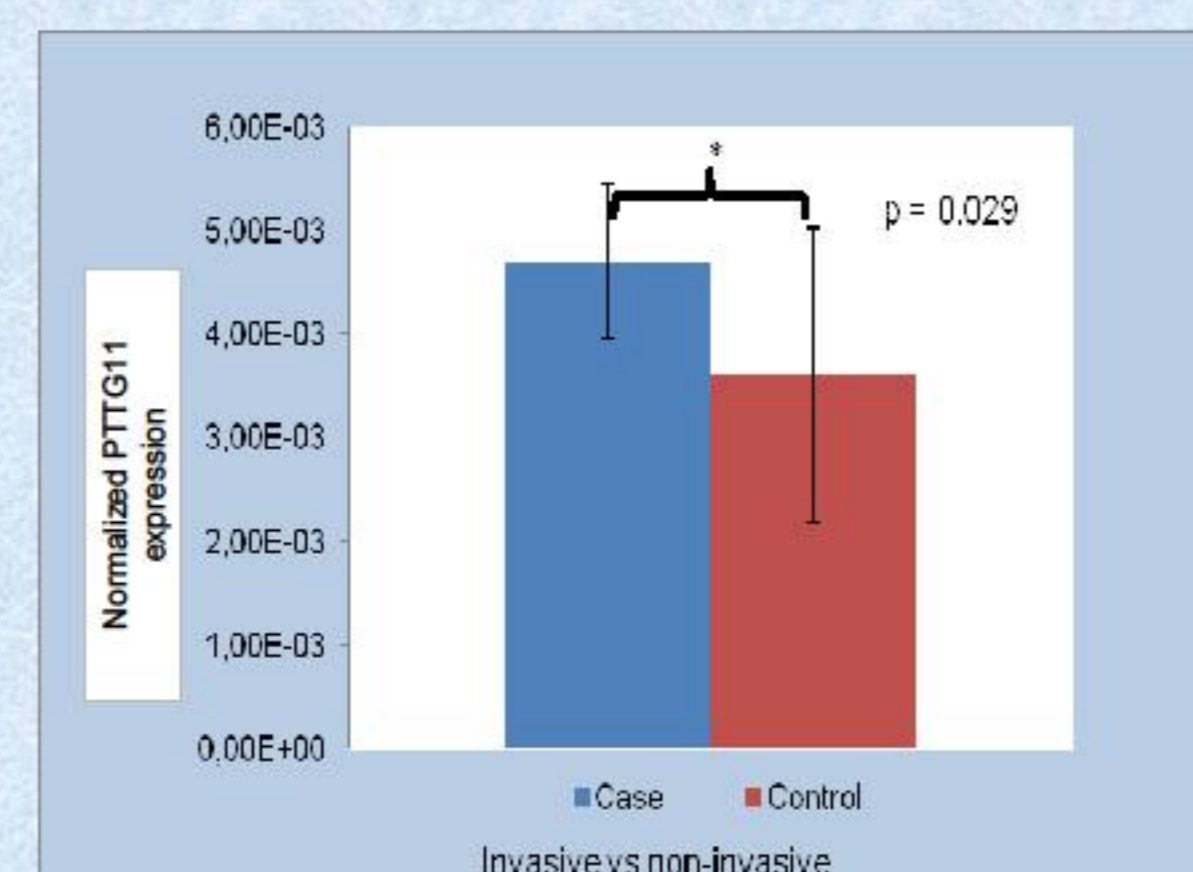


Figure 1

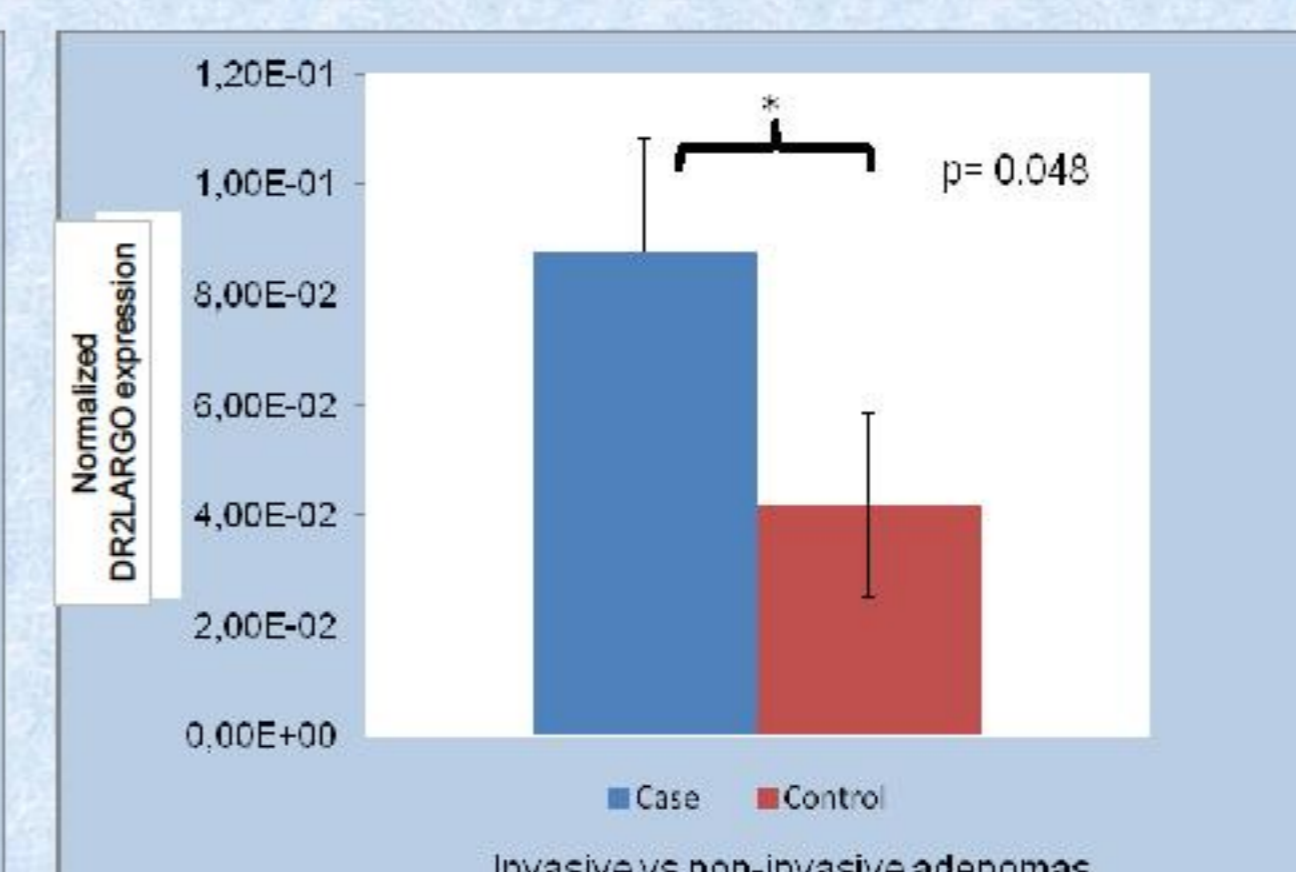


Figure 2

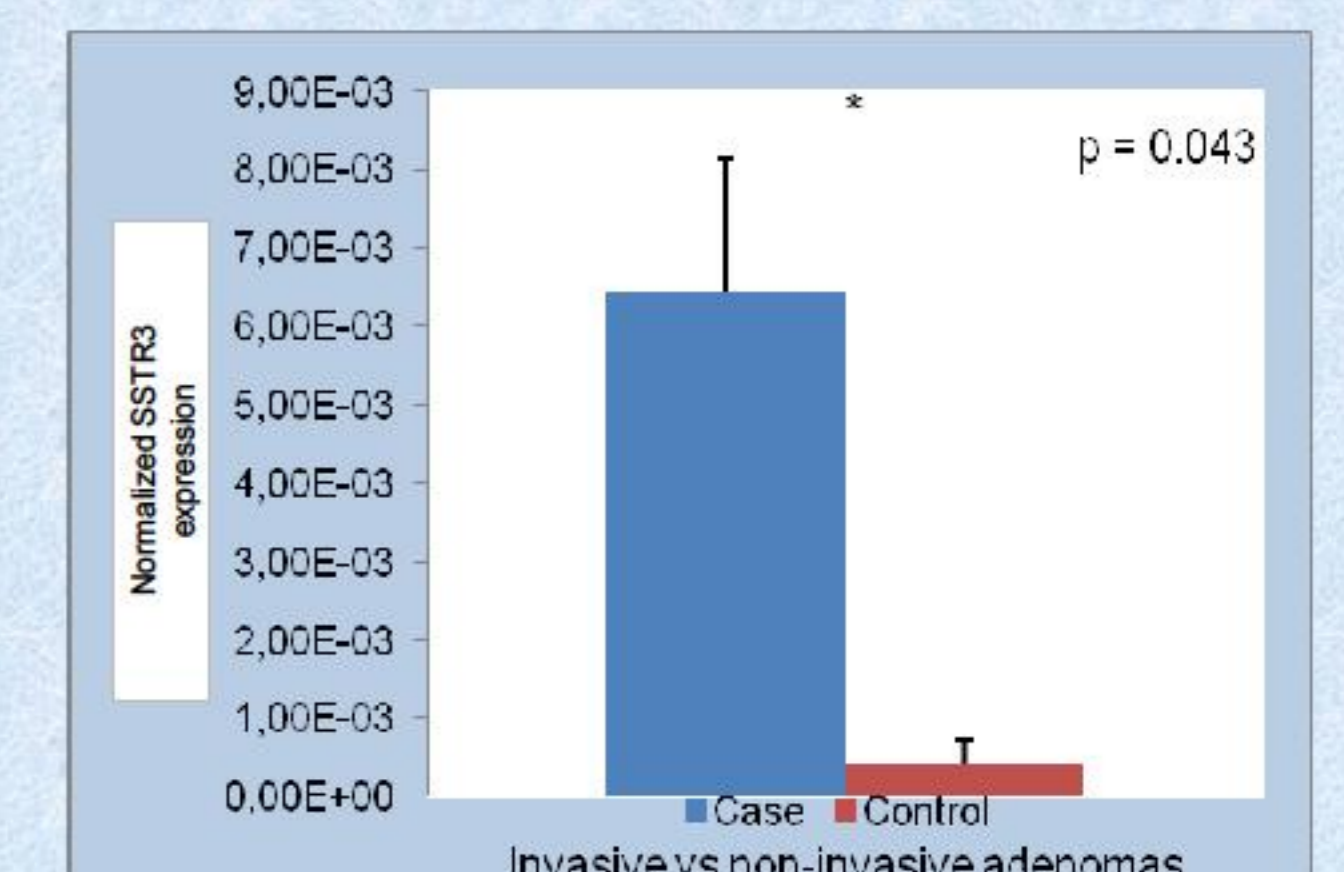


Figure 3

## Conclusions

- Invasive and non-invasive pituitary adenomas display differences in clinical features and molecular parameters
- Invasive pituitary adenomas exhibit higher presence of tumor remnants after surgery, surgical re-intervention and radiotherapy.
- Higher expression of PTTG1, SSTR1 and long isoform of DPR2 is found in invasive adenomas.

