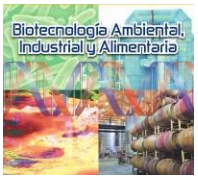
Poster



Molecular analysis of prolactinoma formation in Pten-deficient mice

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ABSTRACT

Pituitary tumors are abnormal masses developed in the pituitary gland. Although they are generally benign, between 40-50% of pituitary adenomas cannot be removed by surgery alone due to local invasion. Moreover, they are associated with hormonal dysregulation. Prolactinoma is the most common type (50-60%), followed by somatotropic cell adenoma (10-15%), corticotropic cell adenoma (5-10%) and finally thyrotropinoma (less than 1%) (Cano González et al., 2015).

Previous descriptive studies have suggested a possible role for the PI3K/AKT/mTOR signaling pathway in the formation of pituitary adenomas. In this study, we used genetic mouse models to assess the oncogenic capacity of this signaling pathway in the pituitary. For this purpose, conditional knockout mice have been generated in which the Pten gene is inactivated specially in the pituitary, indirectly causing the AKT overexpression. To accomplish this, a HesX1-Cre mouse line, whose expression is controlled by a pituitary-specific promoter and which is present in very early stages of embryonic development (Rizzoti, 2015) were crossed with mouse lines in which the Pten gene is floxed by two LoxP sequences.

We have analyzed the pituitary in Pten-deficient mice at three different ages: 12, 6 and 1 month of age, comparing genotype and sex. At young ages, Pten-deficient mice show pituitary hyperplasia. After 12 months of age, Pten-deficient mice develop pituitary tumors. However, this is only observed in mutant female mice, whereas male mice simply display pituitary hyperplasia. Data from immunohistochesmistry, immunofluorescence, and blood hormones show that Pten-deficient mice developed prolactinomas. These tumors show high rates of cell proliferation as well as alterations in the expression levels of several cell cycle inhibitors.

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