Endocrinol Diabetes Nutr. 2020;67(Espec Cong 2):2

Endocrinología, Diabetes y Nutrición

2 - INCREASED E2F1 MRNA AND MIR-17-5P EXPRESSION IS CORRELATED TO INVASIVENESS AND PROLIFERATION OF PITUITARY NEUROENDOCRINE TUMOURS

A. García-Martínez[1], S. Martínez-López[1], B. López-Muñoz[2], R. Cámara[3], C. Fajardo[4], C. Lamas[5], S. Silva-Ortega[6], I. Aranda[6] and A. Picó[2]

[1]Research Laboratory; [2]Endocrinology Department. Hospital General Universitario de Alicante-ISABIAL. Alicante. [3]Endocrinology Department. Hospital Universitario y Politécnico La Fe. Valencia. [4]Endocrinology Department. Hospital La Ribera. Alzira. [5]Endocrinology Department. Complejo Hospitalario Universitario de Albacete. [6]Pathology Department. Hospital General Universitario de Alicante-ISABIAL. Alicante.

Resumen

Introduction: *E2F1* regulates the expression of genes required for cell cycle progression and apoptosis. miR-17-5p regulates expression of *E2F1*. Both miR-17-5p and *E2F1* have been described deregulated in cancer but they have been scarcely studied in human pituitary neuroendocrine tumours (PitNETs).

Objectives: To evaluate the relationship of E2F1 and miR-17-5p with the invasiveness and proliferation of PitNETs.

Methods: In this cross-sectional descriptive study, we evaluated the expression of *E2F1*, c-MYC and two microRNAs of miR-17~92 cluster (miR-20a and miR-17-5p) by qRT-PCR in 60 human PitNET samples: 29 gonadotrophs (GT), 15 functioning somatotrophs (fST), 8 functioning corticotrophs (fCT) and 8 silent corticotrophs (sCT). Clinical, radiological and pathological data were recovered to determine the pre-operative behavior of the tumour. We defined invasiveness according to the Knosp classification and proliferation according to a molecular expression of Ki-67 ≥ 2.59.

Results: E2F1 was more expressed in invasive than in non-invasive tumours in the whole series (p = 0.004) and in STs (p = 0.01). In addition, it was overexpressed in the silent subtypes (GTs and sCTs; all macroadenomas) and normoexpressed in the functioning ones (fCTs and STs; some microadenomas). miR-17-5p was more expressed in proliferative than in non-proliferative tumours (p = 0,041) in the whole series but not by subtypes.

Conclusions: Our study suggests that PitNETs, E2F1 could be a good biomarker of invasiveness, and miR-17-5p of proliferation, helping the clinical management of these tumours. In contrast, MYC's role in PitNET behaviour could be subtype-dependent. It is difficult to establish a relationship between E2F1 expression and functionality, because all silent operated tumours were macroadenomas, while most STs and fCTs were microadenomas. Finally, the effect of E2F1 on the growth of PitNETs could be mediated by a complex interaction between MYC and miR-17-5p.