



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

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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 $Ki-67 \geq 2.59$.

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.