ECE2015
Dublin, Ireland
16 - 20 May 2015

GP-18-08

Role of miR-375 in oncogenesis of pituitary adenomas

Laura Sánchez-Tejada[1], Ruth Sánchez-Ortiga[2], Pedro Riesgo[3], Javier Abarca[4], Carmen Fajardo[5], Irene Monjas[6], Rosa Cámara[7], Cristina Lamas[8], Antonio M. Picó Alfonso[2]

1 Research Unit of Endocrinology Department, Hospital General Universitario Alicante, Spain. 2 Endocrinology Department, Hospital General Universitario Alicante, Spain. 3 Neurosurgery Department, Hospital La Ribera, Spain. 4 Neurosurgery Department, Hospital General Universitario Alicante, Spain. 5 Endocrinology Department, Hospital La Ribera, Spain. 6 Otorhinolaryngology Department, Hospital General Universitario Alicante, Spain. 7 Endocrinology Department H.U. La Fé de Valencia, Spain. 8 Endocrinology Department H.G.U. Albacete, Spain.

Purpose

MicroRNAs (miRNAs) are a fundamental component of gene regulation mechanisms. Altered miRNA patterns of expression have been documented in different human cancers. In pituitary adenomas (PA), they may contribute to the behaviour of the distinct PA subtypes. miR-375 is a miRNA involved in reprograming cancer cell metabolism and which can target, among other genes, to insulin-like growth factor 1 receptor (IGF1R), a receptor tyrosine-kinase (RTK) whose altered signaling is critical in the development of many types of tumors. The **aim** of this study was to assess the miR-375 role on pathogenesis of different PA subtypes.

Methods

In this cross-sectional descriptive study, we evaluated miR-375 by qRT-PCR analysis on 60 human PA samples: 29 gonadotrophs (GT), 15 somatotrophs (ST), 8 functioning corticotroph (CT) and 8 silent corticotroph adenomas (SCA). 9 healthy pituitary from autopsies were used as calibrator reference. We graded aggressiveness according to invasiveness and Ki-67 gene expression: **high**: Hardy's grade IV and Ki-67 >2.59 fold change (FC); **medium:** Hardy's grade IV or Ki-67 >2.59 FC, and **low:** Hardy's grade <IV and Ki-67 <2.59 FC.

Results

In our whole sample, miR-375 was associated with sex (men: 3.00 (1.63-4.36) FC values vs women: 1.35 (0.47-1.92) FC values, p= 0.002) and was positively correlated with age (r= 0.466, p= 0.000). miR-375 expression levels (Figure 1) and patterns differed depending on PA subtype (p= 0.000) (Figure 2). Non functioning PA (GT and SCA) revealed overexpression compared with functioning PA (CT and ST) (81.3 % (26/37) vs 39.3 % (11/23) of tumours), entailing a risk of 6.7 (2.1-21.5) times higher (p= 0.001). miR-375 expression was also correlated with tumor maximum diameter (r= 0.303, p=0.022) and associated with their extension (intrasellar: 1.05 (0.47-1.47); extrasellar: 2.50 (1.47-4.39); invasive: 2.50 (1.07-3.88); p= 0.008) (Figure 3). In addition, 66.7% tumors with high or medium aggressiveness grades overexpressed miR-375 vs 28.6% with low grade, which entailed a risk 5.0 (1.6-16.0) times higher (p= 0.005) (Figure 4).

Figure 1

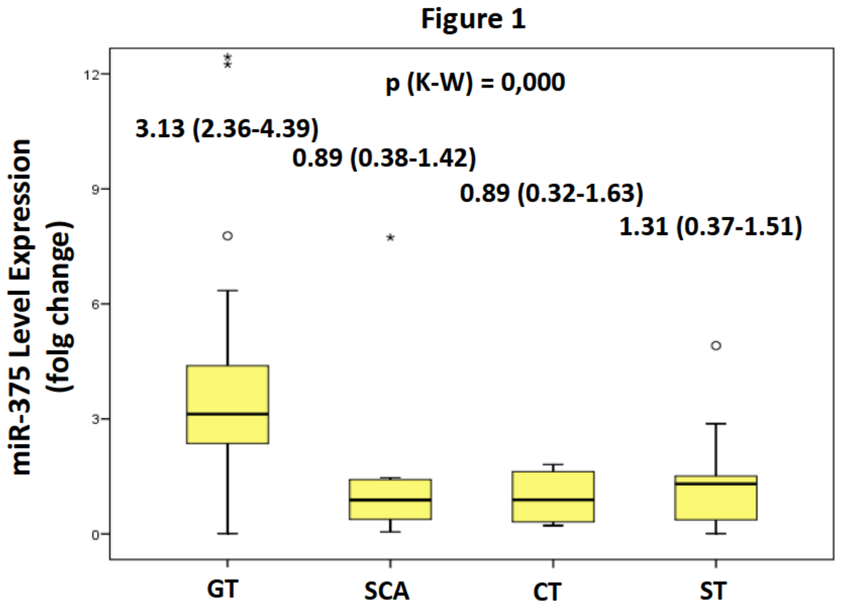


Figure 2

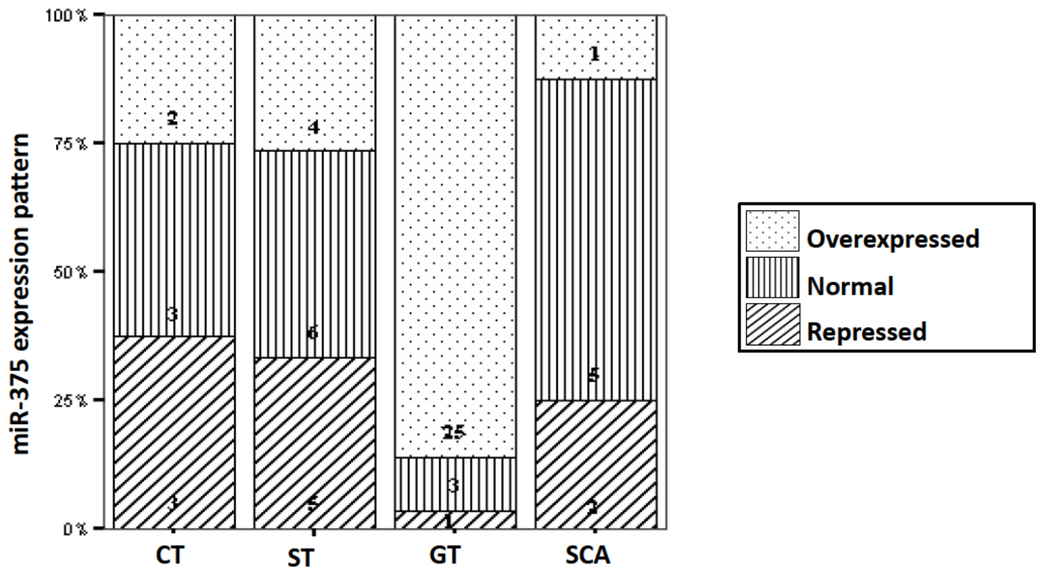


Figure 3

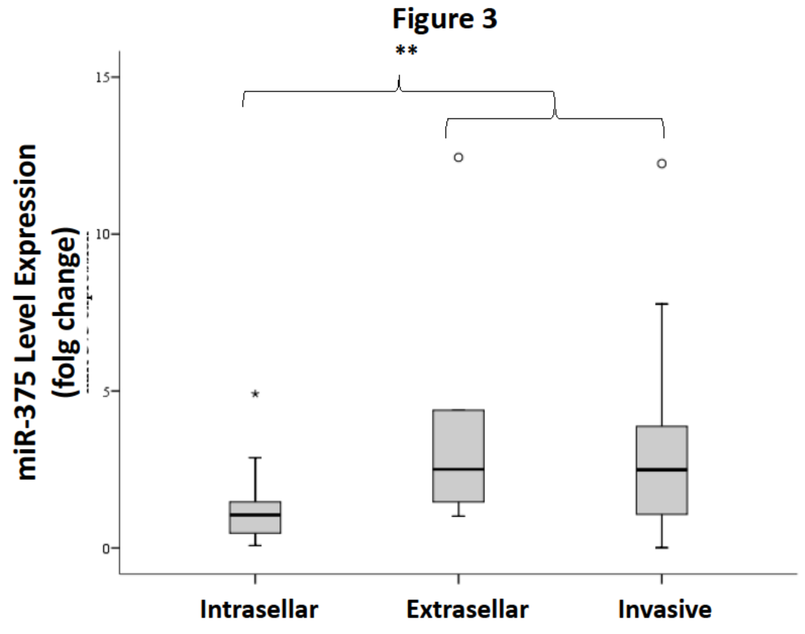
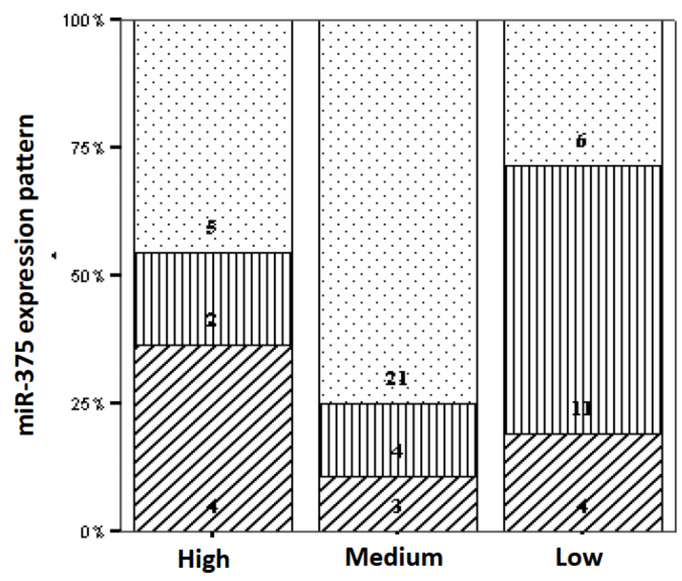


Figure 4



Conclusions

Our results revealed a different role for miR-375 in the pathogenesis of PA depending on subtype. This miRNA may be a marker of aggressiveness, but further studies are needed for endorse this utility.

Nothing to Disclose: AP, RS, LS, PR, JA, IM, RC, CL, CF. Sources of Research Support: by FISABIO Grant (FCVIHGUA-2012/C01)

Fundación para el Fomento de la Investigación Sanitaria y Biomédica de la Comunitat Valenciana

DOI: 10.3252/pso.eu.17ece.2015

Poster presented at: ECE2015 16-20 May 2015 DUBLIN, IRELAND 17th EUROPEAN CONGRESS OF ENDOCRINOLOGY

PosterSessionOnline.com