Mir-326 is an important mediator in colorectal cancer progression

Serrano-Huertas S *(1)*, Blanco C *(1)*, Salinas-Muñoz L *(1)*, Crespo-Toro L *(1)*, Giménez-Moyano S *(1)*, Rodríguez M *(1)*, Ramos ME *(1)*, García-Bermejo ML *(1)*, Conde E *(1)*

(1) Instituto Ramón y Cajal de Investigación Sanitaria (IRYCIS)

Colorectal Cancer (CRC) is the third most common cancer worldwide and the incidence is increasing. For this reason, it is necessary to identify precise biomarkers for early diagnosis, an adequate prognosis, and able to predict CRC development in at-risk populations. It has been evidenced that microRNAs are involved in multiple processes in the development and progression of cancer. In addition, microRNAs are secreted into the extracellular medium and can be easily detected in serum, urine, and/or faeces, among others. miR-326 is implicated in different types of cancer, acting mostly as a tumour suppressor. It has been associated with inhibition of cell proliferation, migration, and invasion in thyroid, cervical, and endometrial cancers. However, the specific role of miR-326 in CRC remains uncertain.

In particular, in our research group miR-326 has been identified and validated as a biomarker associated with tumour progression and has been proposed as a possible tool for better stratification of patients allowing a more accurate prognosis and a possible future therapeutic target for CRC. The aim of the present study is to investigate the role of miR-326 in colorectal cancer.

Thus, microRNA localization by in situ hybridization was studied in biopsies of primary colon tumour, finding that miR-326 is expressed in tumour epithelium, stroma and inflammatory infiltrate. In addition, cell cultures of intestinal epithelial cells, CACO-2 and HT29, were established to study microRNA expression, and miR-326 expression was transiently modulated in both cell cultures. miR-326 is involved in cell proliferation, overexpression of this microRNA inhibits cell proliferation in CACO-2 cells. Furthermore, increasing miR-326 maintains an epithelial cell phenotype maintaining the expression of epithelial genes such as E-cadherin in CACO-2 cells. Furthermore, miR-326 controls cell adhesion to fibronectin through ITGA5 in CACO-2 cells, pointing out ITGA5 as a possible direct target of this microRNA. Moreover, overexpression of miR-326 decreases inflammatory cytokines including IL-2, IL-1, IFN-γ, and some other molecules involved in inflammatory processes as TNFa, TGFb or PDL1. These pro-inflammatory mediators trigger several cell signalling cascades, displaying pro- and antitumoral effects in a context-dependent manner.

Therefore, this work demonstrates that the loss of expression of miR-326 leads to, the loss of epithelial markers in colorectal cancer cells and the increase of inflammatory genes, indicating that EMT and inflammation regulation could be miR-326 dependent mechanisms contributing to the progression of CRC.

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