Proyecto PID2020-113317RA-I00 financiado por MCIN/ AEI /10.13039/501100011033

Identificación del proyecto:

Caracterización sistemática de la comunicación de miARN dependiente de AGO2 en cáncer colorrectal

Descripción del proyecto:

Colorectal cancer (CRC) is the third most common cancer and the fourth most deadly. Thus, there is a clear demand for deepening our understanding of the disease and to improve therapeutic options.

Communication between the tumour, the microenvironment and the premetastatic niche is essential for tumour growth and survival, as well as for metastatic spread. Tumours communicate with their environment through the release of biomolecules, such as proteins, metabolites, and RNA. Tumour to microenvironment and metastatic niche communication through the release of RNA has recently gained increased attention, due to the potential of extracellular RNAs, especially of microRNAs (miRNAs), to serve as biomarkers of disease and potentially also to act as therapeutic tools. Most extracellular miRNAs are in complex with the protein AGO2. AGO2 loaded with RNA forms the RNAinduced silencing complex (RISC), which mediates miRNA-dependent regulation of gene expression inside cells. The contribution of AGO2-dependent intercellular miRNA transfer to tumour initiation, progression and metastasis has not been assessed in a systematic manner.

One example of tumour-mediated alterations in distant tissues is the rewiring of the circadian clock network and the resulting changes in temporal organization of physiologic processes in those tissues. Several miRNAs have been implicated in the functioning of the core clock machinery and uptake of miRNA from the circulation has been linked to regulation of core clock components. However, whether miRNAs are implicated in the communication between the tumour and the circadian clockwork in distal tissues is currently unknown.

Thus, the CARGO2CANCER proposal aims at a systematic analysis of AGO2-miRNA mediated communication between tumour cells and the environment in a colorectal tumour model and to determine whether CRC rewires the circadian clock network in distal tissues through AGO2-miRNA-dependent communication.

In order to do so, AGO2-miRNA transferred from the tumour to distal cells and tissues will be traced. In a second step, the impact of the transferred miRNAs on the physiology of the target tissues will be analysed and whether colorectal tumours rewire the circadian clock network in distal tissues will be determined.

The CARGO2CANCER project will reveal the extent of functional miRNA-mediated communication between tumour and environment in colorectal tumorigenesis and determine whether colorectal tumours systemically rewire the temporal organisation of tissue physiology.

Importantly, the technological approach that will be established in the CARGO2CANCER project could prove useful for determining the impact of miRNA-mediated communication in many other diseases. The data generated with this novel approach could lead to the identification of novel biomarkers and therapeutic targets for the treatment of CRC.

Financiación: AGENCIA ESTATAL DE INVESTIGACION

145.200,00€