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Investigador responsable

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Inflammation and Colon cancer: Implication of Stress signalling and Gut microbiota

Research on the role of the gut microbiome in colorectal cancer (CRC) is an emerging field of study. CRC, the second leading cause of cancer mortality in Western countries, represents one of the biggest problems for health systems worldwide, including ours. About 75% of CRC cases occur spontaneously, therefore, it is essential to identify which are the risk factors associated with CRC and understand what their role is in the development of tumours. The connection between inflammation and CRC is well established and the study of it will allow the development of new therapies for the treatment of cancer.

In this project, we propose to do a comprehensive analysis to understand the mechanism by which the microbiota stimulates the inflammatory immune response in the colon and how the host interacts with the intestinal microbiota during colitis and CRC. Signalling pathways such as the mitogen activated protein kinase p38MAPKs are implicated in the development of CRC. Furthermore, they regulate the immune response in inflammation and the response to pathogens, such as the commensal bacteria and fungus. Our working hypothesis is that, in the development of CRC, p38MAPKs perform different functions depending on the cell type by controlling the inflammatory response to the infection and the composition of the microbiome. All this will affect the transformation of intestinal epithelial cells and the progression of the tumour. This proposal will explain how all the functions of p38MAPKs are integrated during the development of colon cancer and will determine the effect that the inhibition of p38MAPKs may have on this pathology as a therapeutic tool.

The student will learn different biochemical, molecular and cellular biology techniques as well as cellular and animal models of colitis and colon cancer, following the protocols and recommendations of the Animal Ethics Committee. Histological study, analysis of the populations of the immune system, and analysis of proteins and RNA levels will be performed. Co-housing experiments will also be conducted to study the role of the

microbiota in tumor development. Biochemical and molecular and cellular biology techniques will be used (cell cultures, organoids, Western-blot, qPCR, immunohistochemistry, cytometry analysis, ELISA and gene silencing techniques (CRISPR/Cas) in cells.

The project will seek a comprehensive scientific training of the student, promoting their technical skills and also capacity for analysis and critical thinking. In addition, he/she will acquire essential transversal skills, such as scientific communication and dissemination skills; training in the ethics of animal experimentation; and education in equality and gender perspective.

The project will be carried out at the National Center for Biotechnology-CSIC, which is a Severo Ochoa center of excellence, which guarantees its quality and training potential. The student will participate in the activities offered by the CNB, such as international seminars and courses, achieving a top qualified scientific training.