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Colorectal cancer (CRC) is the fourth most common cause of death from cancer worldwide. CRC is a multistep and progressive disease where genetic factors are important in the initiation, the development and the progression of the disease. Then, CRCs can arise from sequential steps including the acquisition of mutations in the adenomatous polyposis coli (*APC*), followed by the mutational activation of oncogene *KRAS* and the inactivation of the tumor suppressor gene, *TP53*. The occurrence of colorectal cancer is largely influenced by the environment, including food contaminants, lifestyle and nutrition. However, the influence of mutations on the response to environmental pollutants is poorly evaluated. Environmental carcinogenesis lacks robust models to explore the interaction between genes and environment and to determine whether genetic mutations associated with colon carcinogenesis generate a particular susceptibility to the harmful effects of pollutants.

Here, we outline the characterization of an innovative cellular model that consists in 6 human isogenic epithelial colon cell lines bearing mutations on master genes involved in CRC. Altogether, these cell lines recapitulate colon carcinogenesis from the healthy, preneoplastic, adenoma and carcinoma stages. We aim to perform a complete phenotypic and metabolic description of these cell lines, with a particular focus on their ability to express the battery of detoxification enzymes, to have a differential sensitivity to genotoxicity, oxidative stress and cell death stimuli, to display a flexible energy metabolism, to migrate and grow without anchorage.

We show that these models of human isogenic colonic cells of CRC could be a powerful and relevant tool to study the effects of environmental pollutants on the colorectal carcinogenesis from the early to the late and metastatic stages and to evaluate gene-environment interactions in food toxicology