

FUNCTIONAL MAPPING OF NOVEL HISTONE POST-TRANSLATIONAL ALTERATIONS IN COLON CANCER

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Introduction: Epigenetic alterations are related to the process of tumorigenesis and resistance to oncological therapies. Although more than 60 types of histone post-translational modifications (HPTMs) have been described, the alterations that manifest simultaneously in tumor tissue have not been systematically studied in colorectal cancer (CRC). This project aims to develop a new screening methodology to delineate epigenetic alterations present in CRC and to obtain a set of biomarkers related to malignancy and tumor response.

Methods: Using state-of-the-art tandem mass spectrometry (MS-MS) techniques, a direct injection protocol will be performed to simultaneously identify the presence of >200 HPTMs-related peptides in a cohort of primary tumors and paired healthy CRC tissue. Patterning of spectra and statistical analyses will be performed with the automated processing algorithm EpiProfile 2.0.

Results: A histone extraction protocol optimized for human tumor samples was developed. Likewise, we managed to make MS/MS sample processing more flexible by implementing a multiplatform workflow (Thermo / Sciex), which will increase the screening and data analysis capacity. Through this process we managed to detect >200 peptides related to HPTMs in control samples, and we observed significant differences in certain HPTMs with pharmacological treatments in primary cultures.

Conclusions: These results will allow the identification of epigenetic biomarkers related to grade, stage and recurrence in the context of CRC.