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Telomere function and Sirtuins 1 & 6 in colorectal Cancer

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Introduction: Telomere dysfunction is a frequent event in Colorectal Cancer (CRC). The role of telomeres and telomerase in colorectal cancer (CRC) is well established as the major driving force in generating chromosomal instability. However, their potential as prognostic markers remains unclear. On the other hand, it has been reported that Sirtuins 1 & 6 (NAD+-dependent histone deacetylases, HDAC), (SIRT 1 & 6) regulate cell senescence, DNA damage repair, apoptosis, and can control longevity. In fact, SIRT 1 & 6 have been related to telemere function. Objectives: The aim of this study consists of analyzing the possible relationship between telomere status and SIRT 1 & 6 in CRC, as well as, studying its usefulness as biomarkers to establish the prognosis in CRC. Materials and Methods: A total of 200 cases were considered in this study. Telomere function parameters, such as telomere length and telomerase activity, as well as the relative expression of *SIRT1* and *SIRT6* in samples of colorectal tumor tissue and non-tumor tissue (control), have been investigated. We also analyzed adipose (omental and subcutaneous) tissues from patients. The telomere length was determined by TRF (Telomere Restriction Fragment) and quantitative PCR (qRT-PCR). The relative expression of *SIRT1* and *SIRT6* was assessed by qRT-PCR. The body mass index of the patients included in the protocols was also available. Statistical analyses and survival studies were established with the package SPSS 22. Results: The critically shortened tumor telomeres were associated with a favorable clinical prognosis in CRC (P = 0.05, Kaplan-Meier method, Log-rank test) and correlated with the higher expression levels of *SIRT1* (P = 0.05, U de Mann-Withney test). Reduced expression of *SIRT1* (RQ ? 0.5) was detected in tumors that confer a more adverse clinical evolution (P = 0.04, Kaplan-Meier method, Log-rank test). Moreover, considering de body mass index of the patients included in this work, the telomeres of the non-tumor cells from obese or overweight patients were significantly longer than those of patients showing normal weight (P = 0.03, U de Mann Whitney test). In addition, in omental adipose tissue, telomere length was lower in obese patients with CRC than in obese patients without CRC, with a trend toward significant association (P = 0.05, U de Mann-Whitney test). Conclusions: Analyses of the telomeric length and *SIRT1* seem of interest in the investigation of the clinical evolution of subjects affected by CRC and in the establishment of the predisposition of obese individuals to the development of this tumor type. Telomere function and *SIRT1* levels could be considered as biomarkers in order to establish the prognosis of the CRC, as well as potential targets for the treatment of this tumor type.