

IMMUNOHISTOCHEMICAL AND MOLECULAR SCREENING OF COLORECTAL TUMORS IN INDIVIDUALS WITH THE HEREDITARY AND SPORADIC PHENOTYPES

PATRÍCIA KOEHLER-SANTOS; IZETTI, P.; PITROSKI, C. P.; COSSIO, S. L.; CAMEY, S. A.; GIUGLIANI, T.; SILVA, V. D.; MEURER, L.; PROLLA, J. C.; ASHTON-PROLLA, P.

Introduction: Lynch syndrome is an autosomal dominant disorder caused by germline mutations in one of four mismatch repair (MMR) genes: hMLH1, hMSH2, hMSH6 and hPMS2. Objectives: Establishment of a screening protocol to predict MMR gene mutation status in colorectal cancer (CRC), and compare results in patients with the hereditary and sporadic phenotypes. Patients & Methods: We analysed 74 CRC tumors of patients seen at a university hospital in Southern Brazil (18 fulfilling Amsterdam I/II criteria, 33 with Bethesda Revised criteria, 23 with sporadic CRC) using Multiplex PCR for Microsatellite Instability (MSI), Immunohistochemistry (IHC) for protein expression and MS-MLPA for promoter hypermethylation of the four genes. Large genomic rearrangements were also investigated in the germline of these patients. Results: Loss of nuclear protein expression and methylation of the promoter region were observed in the 3 groups, but the MSI-high phenotype was observed only in the hereditary group. Regarding phenotype, the presence of 2 or more CRC cases in 1<sup>st</sup> ou 2<sup>nd</sup> degree relatives was significantly associated with loss of nuclear protein expression found by IHQ ( $p=0.044$ ). Conclusion: The investigation of CRC cancer patients for Lynch syndrome using a combination of MSI, IHC and methylation analysis is feasible in this setting and important to guide indication of mutation analysis of the most likely mutated gene.