Methylation profile of genes in precursor lesions of cervical cancer

Caroline Domingues Rogeri (Barretos Cancer Hospital, Brazil), Rhafaela Lima Causin (Barretos Cancer Hospital, Brazil), Ana Carolina de Carvalho (Barretos Cancer Hospital, Brazil), Lidia Maria Rebolho Batista Arantes (Barretos Cancer Hospital, Brazil), Maíra Degiovani Stein (Barretos Cancer Hospital, Brazil), Júlio Possati (Barretos Cancer Hospital, Brazil), Úrsula Moraes Leme (Barretos Cancer Hospital, Brazil), Larissa de Mello Kuil (Barretos Cancer Hospital, Brazil), Rui Manuel Reis (Barretos Cancer Hospital, Brazil/ICVS, University of Minho, Portugal), Cristovam Scapulatempo-Neto (A.C, Camargo Cancer Center, Brazil), Luiza Lina Villa (HPV – National Institute of Science and Technology, Brazil), Adhemar Longatto-Filho (Barretos Cancer Hospital, Brazil/ICVS, University of Minho, Portugal/Laboratory of Medical Investigation (LIM) Faculty of Medicine, University of São Paulo, Brazil/HPV – National Institute of Science and Technology, Brazil), Henrique César Santejo Silveira (Barretos Cancer Hospital), José Humberto Tavares Guerreiro Fregnani (Barretos Cancer Hospital, Brazil)

BACKGROUND: There are numerous and well documented evidences in the literature demonstrating that cervical cytology is limited as an isolated method for cervical screening. Thus, there is a need to incorporate molecular tests to improve the accuracy of precursor lesions detection, as seems to be the assessment of epigenetic changes. Methylation of tumor suppressor genes has been reported as an early event in carcinogenesis and tumor progression. Therefore, methylation profiling of these genes could help in detecting high-grade cervical precursor lesions. **OBJECTIVES**: The aim of this study was to evaluate the methylation status of genes in Pap smear. **METHODS**: It was randomly selected 20 liquidbased cervical cytologies from women with normal uterine cervix and 20 from women with confirmed histopathology diagnosis of cervical intraepithelial neoplasia grade 2 or 3 (CIN23). The following genes were analyzed in all samples: APC, C13ORF18, CADM1, CDH1, DAPK1, EPB41L3, HIC1, HsamiR1242, JAM3, LMX1A, MAL, NKX61, PAX1 and TERT. The promoter regions were analyzed by quantitative methylationspecific PCR (qMSP). Two different promoter regions were evaluated in CADM1 and MAL. The area under the ROC curve (AUC) was calculated to each gene in order to estimate accuracy of CIN23 detection. **RESULTS:** The following AUCs were observed for CIN23 diagnosis: APC (0.714), C13ORF18 (0.711), CADM1 M12 (0.738), CADM1 M18 (0.825), CDH1 (1.000), DAPK1 (0.740), EPB41L3 (0.895), HIC1 (0.943), HsamiR1242 (1.000), JAM3 (0.815), LMX1A (0.936), MAL M1 (0.970), MAL M2 (0.845), NKX61 (0.780), PAX1 (0.740) and TERT (0.990). All AUCs were significantly higher than 0.500 ($P<0.05$). Genes with AUC greater than 0.9 are currently being evaluated in a larger sample (n=350). Gene methylation analysis seems to be a promising tool for cervical câncer screening, as the detection rate of CIN2 or CIN3 was impressively high. However, the best panel of gene methylation to detect precursor lesions is unknow so far, being necessary more studies to make it clearer. Moreover, population based trials are needed to define the role of gene methylation in câncer prevention.

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