**Abstract Title: Methylation status analysis of promoter regions of MALM1 and MALM2 genes as screening high-risk human papillomavirus positive patients**

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**BACKGROUND:** On early detection of cervical cancer, it is known that the analysis of cytological and morphological is limited as an isolated method for the screening of cervical cancer. Thus the analysis of others markers are needed especially to improve the positive predictive value for population-based screening of cervical neoplasia. Promoter methylation of tumor suppressor genes has been reported to be an early event in carcinogenesis. Gene promoter methylation analysis of several cervical cancer-specific genes has been suggested as an alternative diagnostic tool for early detection of cervical neoplasia by QMSP. **HYPOTHESIS:** Thus, we proposed to evaluate the methylation status of genes MAL M1 and MAL M2 to triage HPV-positive women for CIN2 +. First, in training set was used, containing 40 samples cervical cytology samples from women who were submitted the colposcopy in Barretos Cancer Hospital, being 20 samples from women CIN2+ (case group), and 20 without CIN (control group). Second, was analised the gene MAL M1 by quantitative methylation-specific PCR (qMSP) containing 450 samples cervical cytology samples from women who were submitted the colposcopy in Barretos Cancer Hospital, being 150 samples from women CIN2+ (case group), 150 samples from women CIN1 and 150 without CIN (control group). **METHODS:** It was randomly selected 150 liquid based cervical cytologies from women with normal uterine cervix, 150 from womwen with confirmed histopathology diagnosis of cervical intraepithelial neoplasia grade 1 (CIN1) and 150 from women with confirmed histopathology diagnosis CIN2/3. Two different promoter regions were evaluated in CADM1 and MAL.The promoter regions were analyzed by quantitative methylationspecific PCR (qMSP). The area under the ROC curve (AUC) was calculated to each gene in order to estimate accuracy of CIN2+ detection. **RESULTS:** The MAL gene methylation status in regions M1 and M2 were verified 95% and 75% of methylated samples in CIN 2+ group and 30% and 10% methylated samples in control group, respectively. Therefore it was made The area under the ROC curve in order to determine the gene with the possibility of provide an alternative screening of precursor lesions of cervical cancer in brasilian population. The region promoter gene MAL M1 was selected because, showed an 0.92 AUC. Thereat, to analysis in complete population of MAL M1 gene methylation status were found 53% of methylated samples in CIN 2+ group and 47% of unmethylated samples this group. In CIN1 group was evidenced 60,7% of methylated samples and 39,3% of unmethylated samples in CIN1 and the control group showed 30,4% of methylated samples and 69,6% of unmethylated samples. We performed also the analysis to sensibility and specificity to gene MAL M1, it showed 52,9 sensibility and 69,6 specifity. Finally, we can demonstrate that CIN 2+ group showed higher percentage of methylated samples in comparison with CIN1 group and control group. In conclusion, this open the possibility of provide an alternative triage using gene promoter methylation analysis.