MicroRNA-145 Upregulation in High-risk Genotype HPV Infected Atypical Squamous Cells of Undetermined Significance (ASCUS) Liquid Based Cytology Samples

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Abstract
Cervical cancer (CC) persists as a global health burden caused by persistent high-risk human papillomavirus (HR-HPV) infection. Among the HR-HPV infected cervical lesions, around 5 to 10% of them progress to cancer over several years. Recently MicroRNAs (miRNAs) have garnered much attention for their involvement in carcinogenic processes. Among them, MicroRNA-145 (miR-145) has been extensively studied as a tumor suppressor that is frequently downregulated in gynecological malignancy, including cervical cancer. Studies have shown that miR-145 expression is inversely correlated with disease progression, with the lowest expression observed in invasive carcinomas, then in HSIL or LSIL, or normal cervical tissue. Ectopic restoration of miRNA-145 in HPV positive cells reduces HPV viral genome amplification and late gene expression.
This study assessed the miR-145 expression level in HR-HPV positive ASCUS cervical samples (Bethesda) and HPV and PAP both negative cervical samples (the Control) using qRT-PCR. The sample's miR-145 expression level was normalized against its miR-16 expression level, an endogenous reference gene for microRNA. The normalized miR-145 expression results of the HR-HPV ASCUS samples were then compared with the "Control" samples. This study tested 4 HR-HPV ASCUS samples and 5 "Control". The qRT-PCR results indicated that miR-145 level was significantly upregulated in the HR-HPV ASCUS samples by an average of 2.5-fold (P= 0.0096) as compared to the "Controls". The upregulation of miRNA-145 in HR-HPV infected ASCUS cervical cells in this study coheres with other studies that miR-145 expression is higher in low-grade lesions as compared to normal cervical tissue which is interpreted as part of the host cell's intrinsic anti-viral and tumor-suppressive defense.
Further study on the miRNA-145 expression level with LSIL, HSIL, and invasive carcinomas, and with larger cohorts is warranted to assess the expression pattern, early upregulation followed by decline of miRNA-145, as a marker to predict progression to cervical cancer.

Keywords: Cervical cancer; High-risk HPV infection; MicroRNA; ASCUS; Liquid Based Cytology