Exploring the proteomic profiles of women with cervical intraepithelial lesions grade 3 co-infected by HIV and HPV16

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Introduction: Cervical cancer is the fourth most common cancer in women worldwide. In Brazil, and especially in the state of Amazonas, it is the most common type of cancer that affects women. This cancer is preceded by cervical intraepithelial neoplasias (CINs), including cervical intraepithelial neoplasia grade 3 (CIN3), which, if not detected and treated early, can progress to cancer. Persistent infection by some types of human papillomavirus (HPV) is directly related to the development of cervical intraepithelial lesions, also playing a central role in the etiology of carcinoma. The occurrence of co-infection between high-risk oncogenic HPV and the human immunodeficiency virus (HIV) in women with CIN3 can increase the chance of developing cervical cancer by six times. In this context, shotgun proteomics is an approach that can help understand relevant mechanisms regarding cancer development in patients CIN3 co-infected with HIV and HPV. So, this study aims to evaluate the protein profile of women with cervical intraepithelial lesions grade 3 positive for HIV and HPV16. **Material and Methods:** This study was approved by the ethics committee of FCECON under CAAE number: 39556220.2.0000.0004. Tissue samples were collected from the core of lesion of 9 patients, which were distributed into the different groups: 3 patients for the CIN3_HPV_HIV group; 3 patients for theCIN3_HPV group; and 3 patients for the CIN3 group. These samples were analyzed using the shotgun proteomics approach. Data analysis was performed using the PatternLab for proteomics V software, where proteins were identified by PSM and quantified by spectral count. Differential analysis was performed using the T-Fold module. For this, proteins present in at least two of the three patients in each of the study groups were considered. **Results:** The mean age of the patients was 32.4 years, ranging from 24 to 40 years. Differential analysis using the T-Fold module showed 95 differentially abundant proteins for the CIN3_HPV_HIV group; 20 for proteins for the CIN3_HPV group; and 10 proteins for the CIN3 group. The identified proteins are involved in processes such as: aerobic glycolysis, platelet degranulation, acute phase response and cytoplasmic ribosomal functions. When compared with patients without the presence of viral pathogens, the proteins haptoglobin, Peroxiredoxin-2, Parathymosin and Profilin-1 are 7, 6, 4 and 3 times more abundant in HIV and HPV positive patients, respectively. Besides, these proteins represent the most abundant in each of the enriched processes for HIV and HPV positive patients. In special, the Parathymosin protein belongs to the thymosyme family and previous studies have shown that in patients with cervical cancer who are positive for HPV, the interaction of Parathymosin with HPV E6/E7 proteins was observed. **Conclusion:** Thus, the analysis of the protein profile of women with cervical intraepithelial lesions grade 3 positive for HIV and HPV16 showed the presence of many acute phase proteins, as well as high abundance of the Parathymosin protein, which may be involved in the interaction of the pathogens in the carcinogenesis of cervical cancer.

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