Proteomic characterization of young women with grade cervical intraepithelial lesions grade 3

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Introduction: Cervical cancer (CC) is the fourth most common cancer in women worldwide. In Brazil, especially the state of Amazonas, this corresponds to the first type of cancer that most affects women. This cancer has a slow and progressive growth, being mainly preceded by cervical intraepithelial neoplasia grade 3 (CIN 3). Human papillomavirus (HPV) infection is the main risk factor for its genesis. An important fact about CC is that women under 45 years of age may have a poor prognosis linked to this disease. This fact may be associated with risky sexual behavior and greater exposure to infection with oncogenic types of HPV. In this context, Shotgun proteomics is an approach that can help understand the molecular heterogeneity present in different biological conditions, as well as relevant mechanisms regarding the development of cancer. **Objective:** So, this study aims to compare the protein profile of women with grade cervical intraepithelial lesions grade 3(CIN 3) aged <40 years and >40 years. **Material and Methods:** This study was approved by the Research Ethics Committee (CEP) of the Amazonas State Oncology Control Foundation (FCECON) with CAAE n. 71342417.4.0000.0004. For the analyses, we collected cervix\'s tissues (adjacent margin and the lesion) from 5 patients aged <40 years and 5 patients >40 diagnosed with cervical intraepithelial neoplasia grade 3. These samples were prepared and analyzed using a shotgun proteomics approach. Data analysis was performed using the PatternLab for proteomics V software, where proteins were identified and quantified, being the differential analysis was carried out using the Venn diagram module. **Results and discussion:** The average age of patients <40 years was 30 years. For patients >40, the average age was 52 years. Differential analysis identified 441 and 337 proteins in the lesion and margin of patients <40, respectively. In comparation with patients >40, we found 78 and 74 proteins in the lesion and margin differentially abundant. Besides that, it was observed that 5 protein (CCDC6, STOM, TST, STX12, SDHB) and 1 protein (DBI) were exclusive to the lesion and margin of patients <40, respectively. And only two (SERPINB1 and GGCT) proteins were exclusive to the lesion of patients >40. The CCDC6 protein, identified exclusively in lesions of women <40, is associated with the process of apoptosis and cell invasion in thyroid, lung and stomach cancer. This data is interesting, as it shows that the molecular response of women <40 years old tends to already have proteins involved in carcinogenesis processes, when compared to women >40 years old. **Conclusion:** This study demonstrated a panel of exclusive proteins in the cervical intraepithelial neoplasia grade 3 of younger women, including CCDC6, which has already been observed in other types of cancer and is associated with the stromal invasion process. Therefore, these data can help in the development of tools that can predict the risk of residual disease or recurrence more accurately, in order to increase their chances of survival in this group under 40 years.

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