ISGE
GYNECOLOGICAL ENDOCRINOLOGY
THE 18TH WORLD CONGRESS
7-10 MARCH 2018 FLORENCE, ITALY

P314. Non-canonical activation of SHH signaling as a metastatic marker in vulvar cancer

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The vulvar squamous cell carcinoma (VSCC) corresponds to about 95% of vulvar tumors. It has a good prognosis when diagnosed at an early stage, and survival depends on the inguinal lymph nodes compromised. Surgical treatment, while effective, can be mutilating and results in serious psychosocial damage to patients. Although researches have evaluated molecular aspects involved in VSCCs prognosis, little is known about the mechanisms that determine their biological and clinical behavior. Many studies have been shown that deregulations in the Sonic Hedgehog signaling pathway (SHH) are related to several cancer types' development. For our best knowledge, there is no study about SHH signaling in VSCC. Our major aim was to assess the potential of the SHH signaling pathway components as biomarkers for diagnosis, prognosis or treatment prediction in vulvar cancer cells. We accessed the main SHH pathway genes, SHH, PTCH1, SMO, SUFU, GLI1, GLI2, GLI3, BMP4, BCL-2 and CCND1 in non-metastatic (SW954) and metastatic vulvar cancer cells (SW962) by qRT-PCR. Our results showed that the non-metastatic vulvar cells presented overexpression of PTCH1 and CCND1, while SHH, SUFU, GLI1, GLI2, BMP4, and BCL-2 showed down expression. There were no differences in SMO and GLI3 expression, comparing to normal cells. In metastatic cells, GLI1, GLI2, PTCH1, and CCND1 were overexpressed, however, SHH, BMP4, and BCL-2 were down expressed. SMO, SUFU, and GLI3 did not show differences, all of them comparing to normal cells too. Apparently, SHH signaling is activated by a non-canonical pathway in metastatic vulvar cells, by the fact that SHH ligand showed down-regulation, while GLIs factors (GLI1 and GLI2) showed overexpression. Our results were relevant because the SHH signaling may be used as a prognostic marker and as potential target-therapy to vulvar carcinoma. However, more studies are necessary to understand the role of SHH signaling pathway in VCSS.

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