

**Human epididymis protein 4 (HE4) plays a key role in ovarian cancer cells proliferation and motility**

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The Human Epididymis Protein 4 (HE4) is a novel biomarker for epithelial ovarian cancer (EOC). We previously ascertained the serum HE4 level was significantly elevated in the majority of all ovarian cancers but not in benign diseases or health control, therefore, it is useful for application in clinical diagnosis, even for the malignant ovarian carcinoma patients at early stage. Although the molecular mechanism of the HE4 protein is unknown, the *HE4* (*WFDC2*) gene is amplified at high levels in ovarian cancers. We therefore performed experiments to explore preliminary the functions of HE4 in ovarian cancer cells. Here, we reported that HE4 was specially overexpressed in human ovarian cancer SKOV3 cells. And, we showed that HE4 secreted by ovarian cancer cells enhances cell adhesion and motility. At the molecular level, HE4 promotes epidermal growth factor receptor activation, increases the expression of cell adhesion molecules on the cell surface. Moreover, stable transfection of cells with plasmid expressing HE4-pcDNA3.1 promoted cell migration and adhesion. Correspondingly, HE4 enhanced migration of cells was also inhibited by HE4-shDNA expression. Interestingly, following down-regulation of HE4, the phosphorylations of JNK and ERK were dramatically decreased. This study suggested that expression of HE4 was associated with cancer cell proliferation and migration through MAPK signaling pathway. Taken together, our results provide the first evidence of the cellular and molecular mechanisms that may underlie the motility-promoting role of HE4 in EOC. In addition, these results underscore the important functional implications of HE4 processing in ovarian cancer progression. Therefore, it might be taken into consideration in future studies that examine the role of HE4 as a target for gene-based therapy.