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Vacuolar ATPase 'a2' subunit is a tumor associated antigen candidate for diagnosis and treatment of ovarian cancer

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The identification of novel targets for early diagnosis and development of alternate therapies is vital to patient outcome in ovarian cancer (OVCA). Tumor associated vacuolar-H+-ATPases (V-ATPases) are multi-subunit proton-pumps that acidify the tumor microenvironment, thereby promoting tumor invasion, metastasis and drug-resistance. The subunit 'a' of its V0 domain is the major pH-sensing unit. Specifically, its 'a2' isoform (V0a2) is critical in metastasis through tumor-acidification and immuno-modulation. Initial evidence suggests that this is an ideal molecule for early diagnosis/treatment of OVCA. We investigated the expression of V0a2 in the clinical tissues from low-grade, high-grade and endometrioid OVCA. Immuno-histochemistry revealed that V0a2 was expressed in both low and high-grade serous-adenocarcinoma with weak staining in normal ovarian tissues. Among different pathological grades, V0a2 expression was significantly higher ($p<0.05$) in high-grade compared to low-grade serous-adenocarcinoma. The V0a2 expression correlated with Ki67 and CA-125 cancer cell antigen staining, confirming its expression on cancer cells. In these tissues, immuno-fluorescence analysis showed V0a2 localization on the plasma-membrane of cancer cells with no surface expression on normal ovary. V0a2 DNA/RNA-seq studies are ongoing to identify its underlying gene expression and regulation in OVCA. We also examined the presence of V0a2 in infiltrated immune cells in these OVCA tissues. V0a2 was expressed on CD68-positive tumor-associated macrophages (TAMs). In TAMs, V0a2 is known to regulate IL-1β expression leading to angiogenesis. Therefore, we conclude that V0a2 isoform is the plasma-membrane form of V-ATPase-'a' subunit and is a potential tumor associated antigen candidate to target for diagnosis and treatment of ovarian cancer.

Biography

Arpita Kulshrestha has completed her PhD in 2012 from National Institute of Pathology, New Delhi, India. Presently, she is pursuing her Post-doctoral training from Rosalind Franklin University of Medicine and Science. She has published more than 20 papers in peer reviewed journals along with several book chapters.

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