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Review

VAV3 in human cancers: Mechanism and clinical implication

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ABSTRACT

Guanine nucleotide exchange factors (GEFs) are primarily involved in signal transmission between cell membrane receptors and intracellular mediators. Upon replacing GDP with GTP, GEFs can alter their conformation, resulting in their binding to downstream effectors, such as GTPases like Ras homologous (Rho). VAV GEF family are versatile proteins working as an adaptor mediator and GEF for Rho GTPase. They act as a phosphorylation-dependent molecular switches, fluctuating between active (tyrosine phosphorylated) and inactive (non-phosphorylated) conformation in cell signaling. Accumulating data showed that VAV3 is implicated in cancer progression. The higher levels of VAV3 in human cancers proposed that it may have an oncogenic role in cancer progression. Available studies demonstrated that VAV3 promoted cell proliferation, epithelial-mesenchymal transition (EMT), colony formation, cell cycle, survival, migration and invasion, and suppressed cell apoptosis. In addition, other studies indicated that VAV3 may have a prognostic value in cancer as well as it may act as a mediator in cancer chemoresistance. Here, we aimed to investigate the underlying molecular mechanism of VAV3 in cancer progression as well as to review its value as a prognostic biomarker and chemoresistance mediator in human cancers.

Abbreviations: ABL, Abelson murine leukemia viral oncogene homolog 1; AhR, dioxin receptor; AKT, protein kinase B; ALL, acute myeloid leukemia; AR, androgen receptor; Bax, B-cell lymphoma protein 2 (Bcl-2)-associated X; BC, breast cancer; Bcl-2, B-cell lymphoma protein 2; BCR, breakpoint cluster region protein; BM, bone marrow; BMI1, B lymphoma Mo-MLV insertion region 1 homolog; BTG2, B-cell translocation gene 2; ceRNA, competing endogenous RNA; CDC42, Cell division control protein 42 homolog; CH, [illegible]; CRC, colorectal cancer; CSH3, C-terminal SH3; DHT, dihydrotestosterone; DNMT3B, DNA methyltransferase 3B; EC, endometrial cancer; EGF, epidermal growth factor and EMT, epithelial-mesenchymal transition; EphA2, ephrin type-A receptor 2; ERα, estrogen receptor α; ERBB4, Erb-B2 Receptor Tyrosine Kinase 4; ERK, extracellular signal-regulated kinase; EZH2, enhancer of zeste homolog 2; F11R, F11 receptor; GC, gastric cancer; GAP, GTPase activating protein; GDP, guanosine diphosphate; GDI, guanine nucleotide-dissociation inhibitor; GTP, guanosine triphosphate; HER2, human epidermal growth factor receptor 2; lncRNA, long noncoding RNA; LSD1, lysine-specific demethylase 1; ME, meningioma; NSCLC, non-small-cell lung cancers; NKX3–2, NK3 Homeobox 2; NSCLC, non-small cell lung carcinoma; NF-κB, nuclear factor kappa B; ND, not determined; OC, ovarian cancer; OS, osteosarcoma; Pak-1, P21/Cdc42/Rac1 activating kinase-1; PRC, polycomb repression complex, osteosarcoma; PTX, paclitaxel; PCa, pancreatic cancer; PHLPP2, PH domain leucine-rich repeat protein phosphatase 2; PI3K, phosphoinositide 3-kinase; PTK, protein tyrosine kinase; Rac1, Ras-related C3 botulinum toxin substrate 1; RhoA, Ras homolog family member A; Rho, Ras homologous; PC, prostate cancer; PCNA, proliferating cell nuclear antigen; Rock, RhoA/Rho kinase; PRR, proline-rich region; SAT1, spermidine/spermine N1-acetyltransferase 1; sPLA2-IIA, secretory phospholipase A2 group IIa; TIMP, tissue inhibitor of metalloproteinase; WNK1, lysine deficient protein kinase 1; XIAP, X-linked inhibitor of apoptosis protein; ZF, zinc finger.

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