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OVA66 increases ovarian cancer cell growth, invasion, and survival via regulation of IGF-1R-MAPK signaling

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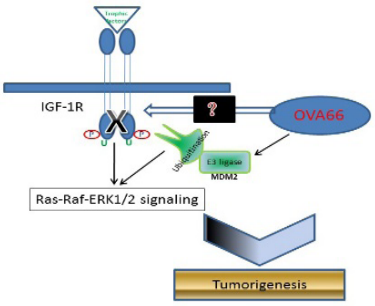
Ovarian cancer-associated antigen 66 (OVA66), also known as CML66 (GenBank Accession No. AF283301) was first identified in an ovarian carcinoma cDNA expression library and was shown to play a role in tumorigenesis. Here, we find that OVA66 influences tumorigenesis by regulating the type I insulin-like growth factor receptor (IGF-1R) signaling pathway. Stable knockdown of OVA66 in cancer cells attenuated phosphorylation of IGF-1R and ERK1/2-Hsp27; similarly, a higher level of p-IGF-1R and ERK1/2-Hsp27 signaling were also detected after OVA66 overexpression in HO8910 cells. In vivo knockdown of OVA66 both reduced tumor burden in nude mice and decreased phosphorylation of IGF-1R, ERK1/2, and hsp27. We blocked IGF-1R function both by siRNA and with the chemical inhibitor linsitinib (OSI-906). By either method, tumorigenesis was inhibited regardless of OVA66 expression; thus, mechanistically, IGF-1R likely lies downstream of OVA66 in cancer cells. We also found that OVA66 regulates expression of MDM2; this attenuates ubiquitination of IGF-1R in response to IGF-1 stimulation and promotes active ERK1/2 signaling. Thus, we propose that combined overexpression of OVA66 and MDM2 promotes oncogenesis by enhancing activation of the IGF-1R-ERK1/2 signaling pathway.



Recent Publications

1. Wang H, Wang Y, Qian L, Wang X, Gu H, Dong X, Huang S, Jin M, Ge H, Xu C, Zhang Y (2016) RNF216 contributes to proliferation and migration of colorectal cancer via suppressing BECN1-dependent autophagy. Oncotarget May 18
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Biography

Hailiang Ge, male, is professor of Department of Microbiology and Immunology, Shanghai Jiao Tong University School of Medicine. He graduated from Shanghai Second Medical University in 1977 majoring in medicine. Then he obtained the Master Degree in Nuclear Medicine of Ruijin Hospital, Shanghai Second Medical University in 1985 and got the Doctor Degree in Immunology of Shanghai Second Medical University in 1991. He worked on research as a postdoctoral fellow in the Department of Microbiology and Immunology, University of California, San Francisco, U.S.A. from 1992 to 1995. In 1998 and 2002, he studied in School of Medicine, University of Michigan and School of Medicine, University of Pittsburgh, U.S.A. as a visiting professor respectively.

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