Yebin XI et al., Madridge J Cancer Stud Res. 2016
http://dx.doi.org/10.18689/2640-5180.a1.003

madridge CONFERENCES

International
Cancer Study & Therapy Conference

April 4-6, 2016 Baltimore, USA

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 over expression 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 over expression of OVA66 and MDM2 promotes oncogenesis by enhancing activation of the IGF-1R-ERK1/2 signaling pathway.

Biography:

Mr. Yebin Xi is from Department of Immunology and Microbiology, Shanghai Jiaotong University School of Medicine. He graduated from Shanghai Second Medical University in 2001 majoring in medicine.