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Angiogenic activities of YKL-40 in cancer development: A potential biomarker and target for cancer diagnosis and therapy

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Accumulating evidence has shown that elevated serum levels of a secreted glycoprotein YKL-40 are associated with a worse prognosis from a variety of advanced human cancers, including breast cancer, colorectal cancer, ovarian cancer, and brain tumor. Furthermore, these increased levels correlate with poorer survival of cancer patients, suggesting that serum levels of YKL-40 might be a prognostic biomarker. Yet the role of YKL-40 activity in these cancers is poorly understood. To explore a functional role of YKL-40 in tumor development, we engineered cancer cells with YKL-40 cDNA to express ectopic YKL-40. Over-expression of YKL-40 in these cancer cells led to larger tumor formation with an extensive angiogenic phenotype than did control cancer cells in mice. Affinity purified recombinant YKL-40 protein promoted vascular endothelial cell angiogenesis *in vitro*, the effects of which are similar to the activities observed using cancer cell conditioned medium after transfection with YKL-40. Immunohistochemical analysis of human breast cancer revealed a correlation between YKL-40 expression and blood vessel density. YKL-40 levels were positively correlated with tumor grade and Her2/*ne*u, but negatively correlated with estrogen and progesterone receptor. In complementary approaches, we found that blockade of YKL-40 by YKL40 siRNA gene knockdown and a YKL-40 neutralizing antibody restrained tumor growth, angiogenesis, and progression. Taken together, these findings have shed light on the mechanisms by which YKL-40 promotes tumor angiogenesis and progression; thus pointing to a valuable cancer diagnostic and prognostic biomarker as well as a target for cancer therapy.

Biography

Dr. Rong Shao has been working on identification of key molecules that mediate tumor angiogenesis and metastasis since he received a postdoctoral training at the Dept of Pharmacology and Cancer Biology, Duke University in 2004. He is a scientist and assistant professor at Pioneer Valley Sciences Institute, University of Massachusetts Amherst, MA. He has published more than 20 papers in prestigious journals. He also serves as an editorial board member of two peer-reviewed journals and a reviewer of more than ten journals. Recently, Dr. Shao's research work has received a number of federal funding agencies including NIH (NCI) and DoD.