Rong Shao, J Cancer Sci Ther 2017, 9:9(Suppl)
DOI: 10.4172/1948-5956-C1-111

A neutralizing anti-YKL-40 antibody blocks tumor angiogenesis through binding to an arginine (R) and lysine (K)-rich functional domain of YKL-40

Rong Shao
Shanghai Jiao Tong University School of Medicine, China

YKL-40, also known as chitinase-3-like-1 (CHI3L1), is strikingly elevated in serum levels of patients with a variety of advanced carcinomas, including breast cancer, colorectal cancer, ovarian cancer, leukemia, lymphoma, and glioblastoma. It thus has been suggested that serum levels of YKL-40 may serve as a cancer diagnostic and prognostic biomarker. However, little is known regarding its therapeutic value of whether and how blockade of YKL-40 can inhibit cancer progression. We recently developed a mouse-derived neutralizing antibody (mAY) against YKL-40 and found that mAY targeted to bind a positively charged arginine (R) and lysine (K)-rich domain (RK-domain) proximal to its C terminus and thus interfered its binding to heparin that is essential for YKL-40 angiogenic activity. The ability of mAY to block YKL-40 angiogenesis is identical to the R or K point mutations, where alanine (A) substituted for K or R in the RK-rich domain both in cultured vascular endothelial cells and animal models xenografted with breast cancer cells MDA-MD-231. These data suggest that mAY neutralizes YKL-40 via blockade of heparin binding of the KR-rich motif, the functional domain of YKL-40, revealing the molecular mechanisms underlying neutralization of YKL-40 activity. Our findings may help pave a new avenue to develop therapeutic agents targeting YKL-40 that is highly elevated in varied cancers and chronic inflammatory diseases.

Biography

Rong Shao is currently a Professor in Department of Pharmacology, School of Medicine, Shanghai Jiao Tong University, and an adjunct Professor of Department of Biology, University of Massachusetts, Amherst. He has published more than 40 papers in top-tier journals. He has also served as an editorial board of more than thirteen peer-reviewed journals and a Reviewer of 48 journals. His research work has been supported by several US federal funding agencies including NIH (NCI), DoD, DoE and Chinese National Science Foundation.

rongshao@sjtu.edu.cn

Notes: