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

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**Abstract**

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.

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**Note:** This work is partly presented at Advances in Cancer Prevention