Immune system molecule promotes tumor resistance to anti-angiogenic therapy

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A team of scientists, led by Napoleone Ferrara, MD, has shown for the first time that a signaling protein involved in inflammation also promotes tumor resistance to anti-angiogenic therapy.

The findings by Ferrara – professor of pathology at the University of California, San Diego School of Medicine and senior deputy director for basic science at the UC San Diego Moores Cancer Center – and colleagues at Genentech, a biotechnology firm based in South San Francisco, are published in the August 4 Advance Online Publication of the journal *Nature Medicine*.

Angiogenesis is a physiological process in which new blood vessels form from existing vessels. It is fundamental to early development and wound healing, but some cancer tumors exploit angiogenesis to promote blood vessel growth and fuel a tumor's transition from a benign to a malignant state.

In the late 1980s, Ferrara led efforts to identify a key gene (VEGF) involved in angiogenesis and subsequent development of the first drugs to block VEGF-mediated growth in a variety of cancers, among them lung, kidney, brain and colorectal. Researchers discovered, however, that similar to other therapies, VEGF-targeting drugs may lose effectiveness as tumors develop resistance, allowing cancers to recur.

The latest research highlights the role of interleukin-17 or IL-17, one of a family of signaling molecules called cytokines that are involved in the

body's immune response. Ferrara and colleagues discovered that IL-17 signaling in tumor-infiltrating T cells, part of the body's adaptive immune response, encourages resistance to the VEGF-blockade in mouse models.

"Our work has the potential to have major translational and therapeutic relevance," said Ferrara. "By inhibiting the effects of IL-17 with monoclonal antibodies or other blockers, we can potentially improve the clinical efficacy of VEGF-targeting drugs."

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