Spotlight

By Caroline Seydel

A Better Protein Kinase Inhibitor

Wilhelm *et al*.
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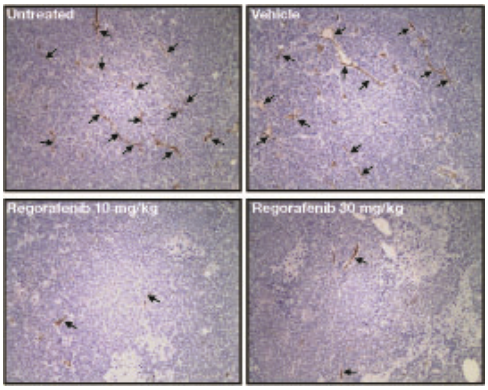
A newly described protein kinase inhibitor, regorafenib, shows great promise for slowing tumor cell proliferation and limiting the formation of new tumor blood vessels. Inspired by the earlier success of a previous kinase inhibitor from the urea class as an anticancer treatment, Wilhelm *et al.* sought to develop additional members of this class for possible treatments. They found a promising candidat with regorafenib, which potently inhibits several key kinases that contribute to tumor growth.

To characterize regorafenib, the authors looked at its kinase inhibition profile *in vitro* and in cellular assays using epithelial cells and tumor. Regorafenib strongly blocked certain angiogenic and oncogenic kinases. They then investigated whether regorafenib could halt tumor cell proliferation. In the vascular and tumor cell lines tested, which are stimulated by kinases known to be targets of regorafenib, the drug did dampen cell growth significantly.

In mice bearing human tumors, regorafenib reduced the total tumor blood volume, possibly by decreasing the number of blood vessels. The drug slowed the growth of a wide range of tumors, including lung, melanoma, pancreatic and ovarian tumors, and seemed well-tolerated by the mice. Because regorafenib blocks both VEGFR2 and TIE2, it could be a great improvement over other agents that may not block TIE2, as inhibiting both seems to have a synergistic effect. Thus, regorafenib could represent a great advance over earlier multikinase inhibitors.



Regorafenib reduced the growth of blood vessels in tumor xenograft tissue.