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“Targeting imatinib-resistant, KIT-negative cells in human GISTs”

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Abstract:
Gastrointestinal stromal tumor (GIST) is a cancer that arises from nerve cells that control the movement of muscles in the intestine. Until the late 1990s, cancers like gastrointestinal stromal tumors were blanketed with chemotherapy without much success. Treatment changed to targeted therapy, leading the way to personalized treatment, when researchers discovered that the drug imatinib, developed to treat leukemia, could also be used to attack a protein called KIT that is found in gastrointestinal stromal tumors. In 50 percent of patients who are treated with imatinib, drug resistance develops leading to tumor recurrence and even death. It is critically important to identify new ways to treat this disease. Preliminary findings suggest that KIT-expressing human gastrointestinal stromal tumors contain a small population of cells that lack KIT, and are therefore resistant to imatinib treatment. Researchers propose to characterize these cells, study their properties, and use advanced screening technology to discover new therapies that can target these cells. These studies have the potential for rapid translational application because: 1) characterization of drug-resistant gastrointestinal stromal tumors cells may identify new methods for predicting patient outcomes; and 2) novel drugs identified in our studies may provide new approaches to treating patients with gastrointestinal stromal tumors whose cancer becomes resistant to current therapy.