

Secret weapon in the cancer fight

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The chemotherapy being used to treat acute leukemia is like hitting a pin with a sledgehammer. But scientists are developing more precise drugs that can attack cancer at the molecular level without killing normal cells.

"Understanding cancers at a molecular level is changing the way these diseases are treated. And at the forefront is acute leukemia," says Aaron Schimmer, staff physician at Toronto's Princess Margaret Hospital since 2003 and leader of an internationally recognized research program at the Ontario Cancer Institute.

Dr. Schimmer is taking an academic approach to developing new drugs. "We are moving new treatments from our lab bench to the patient," he says.

His lab has identified new molecules that target defects in cancer cells, which are used as tools to better understand the disease. "Some of these molecules are also leads for new anti-cancer drugs," he says.



One of the targets he has focused on is a protein called XIAP (X-linked inhibitor of apoptosis protein), which prevents cancer cells from dying.

By screening a million chemicals, Dr. Schimmer identified an inhibitor of XIAP that can kill cancer cells without damaging normal cells.

He and his 19-member team then used this molecule to show how blocking XIAP could be an effective strategy for the treatment of acute leukemia. His lab has teamed with Montreal-based Aegera Therapeutics Ltd. and begun clinical trials with an XIAP inhibitor in patients with refractory acute myeloid leukemia.

"It can take 10 years to develop new drugs and my patients can't wait that long for new therapies," says Dr. Schimmer.

To accelerate this process, he uses robotic equipment to sift through mountains of off-patent drugs used to treat other conditions.

"Some of these old drugs have unrecognized anti-cancer activity and could be advanced rapidly into clinical trials for leukemia and other cancers," he says.

"So far, we've found some very promising compounds. We've identified a drug related to the common anti-allergy medication Claritin with previously unrecognized ability to kill leukemia cells. The drug shows great promise.

But we don't know if we can achieve in people the dose required to produce anti-cancer activity." Over the next few years, clinical trials will include patients who have not responded to conventional therapy.

"This is an extremely exciting time to be a clinician-scientist and work on developing new cancer therapies," says Dr. Schimmer, who is also head of the University of Toronto's experimental hematology program.

He developed his interest in drug research during post-doctoral studies in San Diego, and returned to Canada with his wife, Ettie, and two children because it offered the best opportunities.

A lot of credit for drug discoveries should be given to patients and their families, he says. "They know the odds of benefiting personally are low. Yet they fight with such aggressiveness and are willing to participate in trials, knowing that even if it didn't help them, what we learn from these studies may help others."

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