Molecular glue sticks it to cancer

June 22 2011

University of Toronto Mississauga researchers have developed a "molecular glue" that sticks cancer-promoting proteins to a cell's membrane -- shutting off a cancer cell's growth.

Imagine dropping dish soap into a sink full of greasy water. What happens? As soon as the soap hits the water, the grease recoils—and retreats to the edges of the sink.

Now, what if the sink was a cancer cell, the globs of grease were cancer-promoting proteins and the dish soap was a potential drug? According to new research from the University of Toronto Mississauga, such a drug could force the proteins to the cell's membrane (a.k.a., the edge of the sink)—and make the cancer cell more vulnerable to chemotherapy.

"This is a totally new approach to cancer therapy," says Professor Patrick Gunning of the Department of Chemical and Physical Sciences. "Everything prior to this has targeted functionally relevant binding sites. Our approach inhibits the mobility of cancer-promoting proteins within cells—essentially, it's like molecularly targeted glue."

The "glue" is shaped like a dumbbell: at one end is an anchor that sticks to the membrane, and at the other is a molecule that binds to the cancer-promoting proteins. The anchor is a cholesterol molecule that is well known to chemists for sticking to cell membranes. The protein recognition molecule is fairly picky about what it will bind to, reducing the risk of drug-related side effects.

Gunning says that by sticking the target proteins to the cell membrane, the glue-like substance interferes with how they cause cancer cells to multiply out of control. However, on a normal cell, the new therapy should have little effect.

"We are really excited about the potential for this type of drug," says Gunning, who developed the concept along with Professor Claudiu Gradinaru at U of T Mississauga and Professor James Turkson at the University of Central Florida. "This is ready to move to preclinical studies, and this treatment could slow or stop the explosive growth of cancerous tumours. And for patients, this might reduce the need for really powerful chemotherapy, which can be very hard to tolerate."

The study appears on the cover of the latest issue of the journal *Angewandte Chemie*.

Provided by University of Toronto