

Fighting a cunning cancer opponent

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(Medical Xpress)—It was a classic eureka moment. In 2006 Mary Bebawy was listening to a lecture outside her area of research when suddenly the intellectual penny dropped. "My mind went elsewhere. I didn't hear the rest of the lecture," says the University of Technology, Sydney (UTS) cancer researcher and pharmaceutical scientist.

"Elsewhere" in this case was to a possible explanation of how cancer cells rapidly become resistant to the arsenal of anti-cancer drugs tossed at them. It was as if they shared secrets with one another, she imagined.

Seven years on that unexpected insight has proven correct. After teaming up with the scientist who sparked her eureka moment – Sydney University vascular [immunologist](#) Georges Grau – Associate Professor Bebawy has found that drug-resistant cancer cells really do communicate with other cells, healthy or otherwise. And they do so in a surprising way.

"We discovered that a resistant cancer cell can shed tiny [vesicles](#), or micro particles, from its surface," Professor Bebawy explains, adding that inside these micro particles is genetic material and large molecules called proteins which confer [drug resistance](#). In a nutshell, the proteins pump drugs out of a treated cell.

"The [micro particles](#) dock onto a drug-sensitive cancer cell and within two hours they release their contents into the cell. As early as four hours later that cell is multi-drug resistant cancer cell," Professor Bebawy says.

But it gets worse. In April, Professor Bebawy presented new findings to a specialist science conference in Boston. Not only can [resistant cancer cells](#) transfer resistance to drug-sensitive cells, they can also mop up and sequester [cancer drugs](#) from the [blood stream](#), rendering them useless. "The patients have roughly 50 per cent less drug in their body," she says.

The implications are clear. Cancer cells are survivors. "I'm in awe of the inherent capacity of cells to survive. It's an evolutionarily conserved pathway. It's quite remarkable," says Professor Bebawy who now has National Health & Medical Research Council funding.

While cancer cells are cunning opponents, if Professor Bebawy and her team of 10 UTS doctoral students can tease out all their tricks it should be possible to design drugs able to circumvent them or tests that can detect developing drug resistance. The latter would help clinicians keep up with the adaptive cancer cells.

Working with collaborators such as Professor Grau and cancer specialists at Royal Prince Alfred and Concord hospitals, the UTS team is developing a blood test for identifying the resistance proteins in patients with Myeloma, a bone marrow disease. Currently, the only way to do this is with highly invasive biopsies from the bone marrow.

It's early stages for clinical applications of the micro particle work but Professor Bebawy – who has seen cancer in her own family – is confident they're gaining the upper hand, based on a growing body of scientific evidence detailing the devious survival skills of [cancer](#) cells.

So, today it's obvious [cancer cells](#) can communicate drug resistance to other cells. But as with any new field of research that wasn't the case in 2006. Just finding funding to explore this blue-sky hypothesis was tough.

Eventually, the NSW Cancer Council took a chance. "In 2009 they gave

me \$120,000 per year for three years," Professor Bebawy says. "It allowed me to employ a research assistant and do the experiments. The fact they believed in me, I'm forever grateful."

That initial support enabled professors Bebawy and Grau and their colleagues to publish their first paper on the micro particle mechanism in the journal Leukemia in 2009. That too was challenging.

"It's a new area so initially it was very difficult to get the work published. It was really out there," Professor Bebawy says. "Finally, the work is acknowledged. It's a huge team effort."

A team effort that was based on one eureka moment in the mind of one scientist. "That's why I encourage students to read outside their area to attend unrelated seminars," she says. "You may get an idea".

Provided by University of Technology, Sydney

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