



THE **STORIES**

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Mary Bebawy

Understanding How
Cancer Cells Communicate

There are few amongst us whose lives have not been touched in some way by the challenge of cancer. In fact, with more and more people projected to live well into their 80s, current estimates are that one in every two (men) or three (women) will develop cancer before they turn 85; a sobering statistic, without doubt. But just as remarkable is that, whilst a diagnosis of cancer 40 years ago was virtually a death sentence, today more than 50 per cent of all cancer patients survive for at least a decade, and for certain types of cancer, survival rates are higher.

Despite these gains, little is understood about cancer recurrence and cancer cell behaviour. However, one Australian woman is helping to change that. For over 20 years, Mary Bebawy has researched the way cancer cells communicate and essentially clone themselves in a fight for survival, in the process unlocking some of the disease's most potent secrets and opening up a whole new field of scientific investigation.

"I've always been interested in cancer research. It's a disease... it's so complex.... There's so much to be done and it affects every family at some time. There's an arsenal of therapeutic drugs available to kill off cancer cells, so why is it that cancer cells tend to reoccur?"

A cell biologist, Bebawy decided to launch her assault on the disease by looking at the mechanisms driving cancer cell survival. She started by examining drug resistance. At that time, it was known that some cells were resistant to drugs and others weren't, but what wasn't clear was why or how the number of resistant cells seemed to be able to increase and hence survive the chemo-therapeutics, as though their resistance was being acquired after they'd been exposed to the drugs.

"We started focussing on multi-drug resistance and it's an area I am committed to because it is the basis of anticancer treatment failure."

In 2009, Mary Bebawy and her team at the University of Sydney found that, whilst certain cells were susceptible (responsive) to cancer drugs, others were resistant – and those resistant cells were programmed to seek out the susceptible cells and transfer their genetic material into drug-sensitive cells, virtually cloning themselves and their resistance into the non-resistant cells. She presented her new ideas at various conferences. It took time for

the scientific community to get their heads around her important discovery, as it challenged previous thinking about how and why chemotherapy sometimes failed or patients relapsed, but the research spoke for itself.

A graduate of the University of New South Wales in the mid-90s, Bebawy did her Honours degree in cancer research at St George hospital where she was exposed to expert practitioners, researchers and surgeons. In particular, her supervising professor at the time made sure that his team attended and presented at conferences irrespective of what level they were at.

“To have that exposure as an Honours student where one is in a room with the leading researchers in the field, it builds your confidence and reinforces what you’re learning and it’s just so important.”

These early experiences ignited a passion for the field, and she decided to do her PhD in the Pharmacy faculty at the University of Sydney, looking at mechanisms that were driving cancer cell survival. During her studies, Mary kept asking the same questions:

“If there is an arsenal of therapeutic drugs that are available, why is it that patients start to relapse and why do people die from this disease? Why haven’t we cured this disease, why do we relapse? Why do some people survive 20, 30 years with cancer and others pass away in just a few months? And why do some people relapse and others don’t?”

And it is in that area of relapse and drug-resistance that Bebawy’s discoveries are having the most significant impact. In 2009, she and her team discovered that resistance could be acquired.

“We found they do adapt. Cancer cells transfer survival proteins amongst each other. Essentially the resistant cells shed tiny vesicles packed with functional nucleic acids and proteins which then dock onto the drug-responsive cell and re-template the protein and nucleic acid landscape in the recipient cell to reflect that of the donor cell, making it resistant to the drugs.

“That was our first major finding. We discovered that the cells ‘talk’ to one another in this way and we were the first to discover that this is how resistance can be disseminated throughout a cancer cell population within

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a matter of only a few hours. The area took off from there and we've been publishing prolifically ever since. We are at the international forefront of this area given that we discovered the phenomenon and we're now looking at other cancer traits such as increased metastatic capacity and various other things."

Now an Associate Professor at the University of Technology Sydney (UTS), Bebawy is convinced that what she's learned at conferences throughout her career has been a crucial factor in her development, and sees conferences as opportunities for further education beyond higher education.

"I go to conferences primarily to learn. It's the only way in which I can further my knowledge because it is in these conferences and the works presented there that I hear new things. Many of the conferences I attend require that works not yet be published, and it is here that you are exposed to the very latest technologies, the latest methodologies, latest knowledge etc."

She says that there is no way you can acquire that knowledge via the internet or by sifting through a book.

"You just can't access it because it hasn't been published yet – so you have to go to these conferences to be one step ahead in your thinking and in the development of your thoughts."

Certainly, Bebawy admits, it's possible for knowledge to filter through via other mediums, and for ideas and insights to occur regardless of conference attendance, but she says it's a question of how long it might otherwise have taken and the lives that might have been impacted in the meantime.

"I can't really say whether my ideas and discoveries would have occurred without conferences, because I'm exposed to all sorts of knowledge, but I just really feel that conferences have played a significant part in my learning. Yes, perhaps I could have read it in some paper or something eventually but that may have impacted on the timeliness of things because, as I said before, at conferences you're getting the latest research before publication, and without that initial information from the conference I probably wouldn't have come across that idea or research so quickly."

Equally, some of the greatest benefits from what she hears at conferences can take years to become relevant or realised.

“In research we’re hearing things from here, there and everywhere, so it’s hard to recall specific examples of things I’ve actually learned at conferences, but what I do find all the time, is that I can go to a conference one year, and I can hear someone talking about a certain thing (like their methods, or maybe a finding they’ve looked at in another model), and you don’t think that much about it because at the time it might not be all that relevant or important to what you’re doing, but then a couple of years later as your research progresses, that moment comes back.”

“You think about it. You remember. You can picture where you were. And you go back to the abstract or program from the conference, you read the abstract, you then start looking up that individual’s papers to see what else they’ve done since and that’s the way that I have found conferences have really helped me. It’s not immediate, it’s actually usually a couple of years later – that’s where my most important application of that knowledge has come into play because it wasn’t immediately recognised as being relevant when I’d heard it before.”

Other benefits can also come about years later in terms of collaborations, research findings and invitations.

“Sometimes, years later, you might also be invited to something because someone’s heard the extent of your work and what you’re doing at a previous conference and they then want you to participate or perhaps to be part of an organising committee for the next conference. This is how collaborations often arise.”

Now a highly respected and sought-after PhD supervisor, Bebawy was encouraged by her supervisor at St George hospital to attend conferences, and now insists her own students do the same.

“I travelled to Adelaide for my first ever conference and had to give a short presentation, which was quite intimidating, but to have that exposure and to be in that forum where you’ve got top people sitting there builds your confidence and reinforces what you’re learning and I just think it’s so

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important. I make sure now that when I travel, my students are with me. With my current teaching load I can only really attend about 2 conferences a year, but I usually go to them with an entourage of students.”

So convinced of their value, Bebawy’s students attend conferences both nationally and internationally, and if not on scholarships, Bebawy often funds students from her own research budget.

One of the most important ideals she tries to convey to her students is the need to read and learn outside their own area of interest and to attend what they think might be unrelated seminars.

“Research is dynamic, and it changes depending on what you’re finding at the time, and it could be that you’re finding something so new that no-one’s really looked at it in the field, and as a result you need to look elsewhere. This is a great way for collaborations to arise.”

Bebawy recently developed one such important collaboration in the area of tissue bio-mechanics after listening to a physics researcher from Perth talk about a new technique he was using.

“I was in the audience and I spoke to Prof Vincent Wallace very briefly afterwards and then about a year later he came to Sydney and literally was knocking on my door wanting to explore what we had spoken about. I sent a student over to him mid last year, and he brought people into the project from London, and an electrical engineer, and we’ve got a publication coming out soon and are applying for further funding together. This is an example of how you can meet an individual in a scientific forum and there’s a domino effect, you know, you co-supervise a student, you publish a paper, you bring in other international researchers in the field and great outcomes such as grants and publications result.”

Mary says that apart from the insights academics and researchers can gain at conferences, clinicians, too, can glean important first-hand knowledge that can be used to help their own patients more efficiently.

“Industry is always strongly represented, and clinicians working with patients are there ... Those sort of people can also then be exposed to new ideas that have not yet been published, and which contribute to disease

state management in the long term.”

According to Bebawy, it is the act of physically engaging with the conference environment that helps stimulate higher thought and generate new ideas. She says she is not a fan of the recent push towards use of webinars, believing participants need to be actively present at a conference to get the real benefits.

“You need to dissociate from your usual environment and allow yourself to be positioned in the conference environment; allowing yourself to be physically present.”

“Conferences can go for three or four days and you need to get away; otherwise, there’s no way you can actually absorb and ... recall what it is you’ve listened to down the track.”

She believes the use of webinars and teleconferencing at conferences is at times akin to other shallow approaches to learning, such as listening to lectures at home rather than sitting in a lecture theatre with the expert.

“You’ve got a deep approach to learning and a shallow approach to learning, and with a shallow approach you’re skimming the surface. The possibility of recall then is significantly compromised, whereas with a deeper approach to learning – when you’re sitting there with the speaker and you engage with the speakers – you immerse yourself and the learning is personal. You’re engaging with the content and the speakers; with whomever it is you want to talk to ... and it’s only then that important concepts are reinforced; in that deeper learning.”

She maintains that, although you can still learn from reading and researching, recall of that information is slower and more difficult.

“I’m a visual learner, and when there is physical engagement and visual cues like those associated with actually attending a conference, you can remember things more easily and recall relevant information more quickly.”

Similarly, she says that some of the best conferences pay attention to creating environments where attendees can casually speak to people, for example, at conference dinners or informal events.

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As far as shaping the level of public engagement and discussion on scientific issues goes, Mary feels public forums are a great way to get important findings and advances into the public sphere.

“Members of the general public aren’t usually present at conferences, but I’ve participated in public forums that were open to the general public that had media present, and when people have picked up on things and said ‘Wow... what is this research?’, the media have become involved and the messages start to get out. The Sydney Morning Herald has done a few stories on our work, so at public forums or larger conferences with the media present there is the potential for public discussion to be influenced.”

Another consideration in terms of the importance of conferences to Mary’s progress is the role they play in helping her obtain ongoing funding. In 2009 the Cancer Council supported Mary’s research by way of a \$120 000 per year grant over three years, and since then their projects have attracted other funding, thanks largely to the contribution they’ve made to this area of research, and because of their willingness to share their achievements with others at conferences and public forums.

“This is all an important part of international recognition and contribution to the field.”

Their work has recently gone translational, which is where basic scientific findings and laboratory experiments are ‘translated’ firstly into clinical trials.

“We’ve just published an article in NEOPLASIA showing how we can monitor the number of these vesicles being shed in multiple myeloma patients and then link those levels to how patients are handling or responding to chemotherapy. There were times we could pick up patient relapse weeks in advance of ... traditional tests – so it’s a hot area and yes, it’s very exciting.”

Finally, on a scale of 1 to 10 in terms of the importance of conferences to knowledge creation and diffusion and the flow of important information, Mary has no hesitation in ranking conferences a clear 10.

“Conferences are essential on many levels and they help show you’re engaged with the scientific community and that your research is significant and topical. We’re getting recognised at conferences and we’re getting invitations from top conferences now, which is a huge privilege.”

But those most truly privileged are the thousands of scientists, researchers and practitioners being exposed to Mary and her team’s findings at such conferences, and the millions whose lives or those of loved ones may be saved as a result of her dogged determination to unlock the secrets of this disease.