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Q&A Barbara Dunn

Controversy and intellect

Barbara Dunn is a programme director in the Division of Cancer Prevention at the National Cancer Institute (NCI). She tells Nature Outlook *about the challenges of stopping the disease before it starts.*

How did you get into cancer research?

I actually started out in basic research and had no special interest in medicine until later. I have loved genetics ever since I was 13 or 14 years old and read a book called You and Heredity. I got my PhD in *Drosophila* genetics from the University of Wisconsin. Then I did a couple of postdocs in virology and chromatin [the combination of DNA, RNA and proteins that forms chromosomes], which is what was hot in the early 1980s, here at the NCI.

It wasn't until I was 37 that I decided to go to medical school. I went to Georgetown University, did my internal medicine residency there, and came back to NCI for a clinical oncology fellowship.

What keeps you excited about cancer research?

I love the controversies. I've worked mainly in breast cancer, and I remember back when they were designing the Breast Cancer Prevention Trial, which eventually showed that tamoxifen cuts the incidence of breast cancer in high-risk women by nearly half. But there was a lot of pressure from many of the patient advocacy groups not to do the trial at all. They said: "Don't give healthy women a drug."

Other controversies include whether there is a link between cell phones and brain cancer: overall, the data do not support an association, but it's very hard to study. For instance, people don't remember how often and how long they were on their cell phone and whether they use the ear on the same side of the head as the brain tumour. And radiation levels have changed with cell phone technology over the years.

These types of issues fascinate me because they engage my intellect and require me to draw on the wealth of knowledge I've amassed over my career. They're also interesting because they're in the realm of public health, so they affect people directly.

Several large trials testing vitamins for cancer prevention have been disappointing. What have we learned from them?

When you're delivering substances, such as vitamins, that are derived from natural products, it is important to consider that people have different quantities in their body. The amount of vitamins that people have varies widely depending on many factors, such as where the food they ate was grown. The current thinking regarding vitamins is that you need just the right amount — deficiency is bad, but so is an excess. Although some of the major trials did measure endogenous vitamin levels, we still don't know what specific form of a vitamin is best, or understand how a person will react to these substances when given in pill form. We are now focused on understanding how specific genes affect nutrients and molecular targets, which may help us understand who might benefit — or be harmed — from targeted dietary changes.

Does the NCI have any cancer prevention trials underway?

We're in flux now. A cancer prevention trial with a defined clinical endpoint has to be large and last for a long time, and that costs a lot of money. So for now, we're putting a lot of our effort into smaller biomarker-based trials. The idea is to use a biomarker as a surrogate endpoint for cancer, and then measure the biomarker in patients before and after treatment to see if the treatment is working. The problem is, we don't have any biomarkers that have been validated as reliable surrogates for clinical endpoints. Some people think that the protein Ki-67, which is associated with cell proliferation, could be a great biomarker, but we need a large trial to test it.

Has genomics had an impact on research into cancer prevention?

The Cancer Genome Atlas (TGCA) is collecting tissue samples from many different types of cancer to record the genetic changes compared with normal tissue. One of the main goals is to create new therapies based on this knowledge. For preventive medicine, we're not there yet. We need to collect samples from people with premalignant lesions that might look the same pathologically but are different genetically. In fact, our division is developing an initiative, as yet unnamed, that would be like a premalignant version of TCGA and would compare normal tissue with abnormal tissue that we think might turn cancerous. We already know some of the molecular markers, but these haven't been organized on a massive level.

What would we learn from a 'premalignant version of TCGA'?

Ultimately, the information from such a project could help us distinguish between what we call indolent and interval cancers. Indolent cancers are the slow-growing cancers that we pick up on conventional screening tests like mammograms and PSA tests. The dilemma is that many of these cancers never do any harm, so how aggressively should we treat them? Interval cancers are aggressive cancers that show up between routine screenings and are often missed. These are the cancers that eventually kill. We need to understand the differences between the two on a molecular level. That's the challenge we're facing right now. ■

Interview by **Julie Corliss**, *a freelance science writer in Rockville, Maryland.*