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Straight talk with… Carolyn Bertozzi

Last month, Carolyn Bertozzi became the first woman to win the prestigious Massachusetts Institute of Technology (MIT)-Lemelson Prize, a $500,000 award that honors midcareer inventors. Bertozzi, a chemical biologist, works to understand how sugars mediate cell-to-cell communication. But she isn't content with just observing the process; her lab at the University of California–Berkeley has pioneered tools for labeling molecules inside living cells. Her biomedical inventions have contributed to the development of noninvasive methods for identifying disease tissue within the body—advances that could revolutionize both the diagnosis and the treatment of a host of diseases ranging from arthritis to cancer. **Roxanne Palmer** recently caught up with her by phone to discuss Bertozzi's sweet success with cell surface sugars.

First off, congratulations on winning the Lemelson-MIT prize. How did it feel to win that award?

It's pretty crazy, really overwhelming. Pretty surprising.

Can you describe what your research focuses on?

Basically, I'm a chemist who is interested in developing technologies to help advance biomedical research. My lab focuses on a type of chemistry we call 'bio-orthogonal chemistry'. This refers to the kinds of chemical reactions that neither interfere with nor interact with biological systems.

What inventions did the Lemelson prize recognize?

We have two applications of this bio-orthogonal chemistry that are reflected in some patents that have been licensed. One of those is a type of chemical reaction that can be performed in living animals. The other invention is an application of orthogonal chemistry for protein engineering.

Can you describe the importance of the first invention? What are the advantages of performing chemical reactions *in vivo*?

If you have a tumor that's excised by surgery, that tissue gets sent to a pathology lab. The pathologist will analyze it for a variety of different markers—the specific molecules that will tell the pathologist something about the stage of the tumor, its treatability or its metastatic potential.

It's much more difficult to do that *in vivo*, but it's useful for the purpose of detection or for monitoring the efficacy of a therapeutic regimen. For example, we know that some of the molecular signals unique to cancer come in the form of cell surface sugars and that there are changes in cell surface sugar structure associated with changes in malignancy. We're developing a way to target those cell surface sugars with reactive chemical groups that we can then use to target imaging probes.

What about the other application?

The protein engineering technology has now been spun out into a start-up company called Redwood Bioscience [which Bertozzi founded]. They're making protein-based therapeutics. Using this technology allows us to engineer them with very high precision.

What drew you to science?

I have to credit my father. He's a physicist on the faculty at MIT. When we were growing up, science was definitely the emphasis of the household. He used to bring home toys from his physics lab for us to play with: a huge magnet, or computer terminals—this was back when nobody had a computer.

What challenges remain in your research?

Plenty. The first bio-orthogonal reaction we invented was back in 2000. But we've discovered some liabilities of that early chemistry having to do with the flow kinetics and metabolic stability of the reagents. Then we shifted to a different kind of chemistry, and that was successful in zebrafish and [*Caenorhabditis*] *elegans*, but there were some problems with mammalian systems. So now we have a third generation of the chemistry. And I'm sure when we start taking this into clinical models relative to humans there'll be a need for further reaction optimization.

You were the first woman to win the Lemelson prize, correct?

So they say.

What do you feel like the climate is for women researchers nowadays?

I think it is uneven. Some environments offer a more productive climate for women than others. But I've noticed a significant improvement since I was a student 20–25 years ago. I've noticed a shift in the demographics of the PhD students. It's almost 50:50, and that's starting to percolate into the postdoctoral workforce. And, at Berkeley, we've definitely seen a shift in the demographics of the faculty with the most recent generation of hires.

So do you think the balance of representation will just naturally shift to 50:50?

It's hard to say what the endpoint number will be. The profession has become more attractive to women than it used to be. They feel like they can do the science they want to do, get funded to do it and get promoted and have some influence. They feel more entitled to these positions than a young student of my generation. We just kind of kept our heads down and really hoped for a couple of lucky breaks.

The problem we still have is representation in the faculty ranks. If you look at the numbers—especially in the physical sciences—it's pretty bad. That problem is totally solvable.

What can institutions do, in that respect?

It's simple—they should hire women. It's not rocket science!