NEWSMAKERS

By Diana LaChance

Tattle-tales

Dr. Sara Cooper is looking for small metabolites that can snitch on big diseases

Dr. Sara Cooper may be the head of her own lab at the HudsonAlpha Institute of Biotechnology, but at home she goes by a different name: mom. In September 2010, Cooper and her husband (Dr. Greg Cooper, who also runs a lab at HudsonAlpha), welcomed their baby daughter to the world – just a few short weeks after she started work. "I don't think a lot of businesses would be open to having someone start, work a month, and then take off two months of maternity leave!" says Cooper. But to her, it signaled a level of commitment on the part of the Institute that ultimately cemented her decision to join HudsonAlpha as a highly recruited post-doctoral fellow from the University of Washington at Seattle. "It told me that they weren't just investing in me for a year, they're investing in me for a career," she says. "So even though I took off two months at the beginning, it's not going to make a difference over the course of my career."

That insight may seem obvious to most, but in the corporate world, it's relatively rare. "The majority of PhD students in biology are women, but not many are successful at reaching the upper-level positions. So only about 30 percent of new professors are women, and the number is even smaller for tenured professors," says Cooper. She points to the age-old dilemma of family versus career as the reason why. "I think it's partly because women tend to start PhD programs in their early 20s and finish in their 30s, by which time they feel they need to choose between having a family or a career." Some, like Cooper, try to do both. But it can be difficult, she says, especially since the timing of a pregnancy isn't always in a woman's control. "The whole family planning thing – as much as you want to be able

to plan it out, it's not going to happen sometimes!" says Cooper. That's how she ended up going on maternity leave shortly after arriving at the Institute.

But with that short break now long since behind her, Cooper's faculty career at HudsonAlpha is in full swing. As an expert in human genetics, Cooper is seeking to understand disease pathology and to identify important biomarkers that would allow for more rapid and accurate diagnosis. "We know that the food you eat and the exercise you get plays an important role in your health, but we also know there's a strong association with genetics. So that's a key question that a lot of geneticists are trying to understand," says Cooper. "Can we identify the genes that play a role in whether or not a person gets a particular disease, and can we combine that with what we know about the associated environmental factors to improve overall human health?" Take diabetes, for instance. "Diabetes is an environmentally correlated disease – people who are overweight tend to have it more," she says. "But we know insulin plays a role, so we can determine whether insulin injections can help control symptoms or if there are other, more effective treatments." To do that, Cooper is using metabolomics, wherein metabolites such as lipids, sugars and amino acids are measured and analyzed using mass spectrometry.

WEIGHTY SUBJECT

"Basically, metabolites have a certain weight, depending on their chemical composition," says Cooper, "so whereas genomics is the study of all the genes in the genome, metabolomics is the study of all the metabolites in a sample." She points to glucose as an example. "Glucose has six carbons, which have an atomic weight of 12 each; six oxygens, which have an atomic weight of 16 each; and six hydrogens, which have an atomic weight of 1 each." This information is nothing new, Cooper says. "Most of the things we're looking for, we know what the weights are." But by using mass spectrometry, she can look for discrepancies in those weights or unexpected differences in patterns. "The quantities of each metabolite, such as glucose, are correlated with outward phenotype that you might be able to see, so people with diabetes would have higher level in their blood or urine," she explains. "The phenotype I'm measuring is the glucose level but the outward phenotype is whether you have diabetes or not." The same concept applies to diagnosing cancer. "We know the metabolism of cancer cells is different from that of normal cells, that their only job is to grow and divide. But there's not a lot of really specific information about what type of metabolic changes we can expect to see for a particular cancer," she says. "So because we don't exactly know what to look for, we look at everything and then use statistical analysis to see what distinguishes one group of samples from the other."

Once that pattern is identified, says Cooper, "then we can see how much it changes between different people." Ultimately, the cancer can be diagnosed sooner by being able to detect those changes in urine or serum rather than waiting for the tumor to be detected and biopsied. "By the time someone goes in for a biopsy, they're already suspicious that something is wrong. And pancreatic cancer in particular is often diagnosed late, after it's metastasized," says Cooper. "So if we could find a way to diagnose it early and noninvasively, that would be great." That's why she is currently collaborating with Dr. James Mobley, director of Urological Research at the University of Alabama at Birmingham. "Jim has some pancreatic cancer tumor samples as well as some urine and serum samples," say Cooper. "The idea is to study them to see if there are molecular changes that enable us to distinguish between those who have pancreatic cancer and those who don't." And by using both urine and serum, she says, "we are able to measure different things in each of them and combine the information."

WHAT'S THE FREQUENCY?

Again, this approach is not new. "Researchers have looked at urine before," says Cooper. But because "changes localized to the pancreas get diluted as they move further away, they become less obvious in urine and serum samples because they're further from where the cancer is." Today, however, Cooper says that machines are getting more sensitive, "so it's becoming more likely that we'll be able to find the changes or molecules that could be at very low concentrations in individu-

als who may have a tumor." The changes that Cooper is looking for specifically have to do with the frequency that a certain pattern appears in a given sample. "Then we can see how much it changes between different people, for example, people who have pancreatic cancer and people who don't," she says. "Once we identify the pattern, then we might be able to determine what's going wrong in those cells and how we might treat or fix it." Cooper envisions it as one day being "some sort of a screen, so that you could take a urine sample and identify small molecule biomarkers that might tell you if the patient has pancreatic cancer or is more likely to have it." The doctor could then diagnose the patient at an earlier stage and then potentially be able to treat them so they would have a better prognosis. "An even bigger dream," she says, "is that the molecules we identify could lead to a drug that could effectively treat or cure pancreatic cancer, because there's really nothing now that can do that."

That could make a huge difference to the tens of thousands of Americans diagnosed with pancreatic cancer every year. But Cooper says it's essential to maintain a realistic perspective. "I think that's a difficult thing for the general public to understand, how long it can take to go from an idea to a drug, and then once you have the drug, through testing it to make sure it's safe. It can easily be 10 years or more to get to the point of being able to change how things work for the average patient." Still, Cooper herself is optimistic and can't help thinking about the possibilities of where her research will lead. "That's one of the things that distinguish people who are happy and successful in a career like this – you get excited about small things," she says. "The reason why most people get interested in biology and human disease in general is to help people and make their lives longer, better and healthier. We have lofty goals but we also get excited about working on a disease, even if we can't cure it immediately. That's because we know the more we understand, the closer we are to a cure or at least a better treatment."

And that's important to her not just as a scientist, but as a mother. "Having a baby, you think about the future and about educating children and making sure science is a part of their lives," she says. Especially girls' lives. "Statistics always say that girls in middle school start to turn away from math in particular," says Cooper. But her experience was a happy one. "As a kid math was always my thing, which I know sounds really nerdy, but I never felt like I was unique as a girl who liked math and science," she says. "I always felt like I had lots of friends and I didn't worry that much about it." That's why she feels fortunate that she's able to pass on that positive experience through her job. "Here, I am one of 12 faculty members and I run my own lab, so I have a chance to make more of an impact than I would as a young faculty member at an established university."

In return, she says, HudsonAlpha incorporates the faculty members into their missions of improving human health and participating in education outreach, which is something that isn't always emphasized in other places. As for whether her own daughter will one day be a scientist in her own right, Cooper is diplomatic. "I wouldn't say I hope my daughter grows up to be a scientist, but I hope she does what makes her happy," she says. Still, as she points out optimistically, "There are lots of different things you can do with biology besides being a scientist!" ■