RESEARCH MATTERS

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Disease maps that point to possible cures: University of Toronto prof peers into inner workings of human cells

Sharon Oosthoek | April 6, 2017

(http://yourontarioresearch.ca/wp-content/uploads/2017/04/Andrew-Emili-and-colleagues.png)

University of Toronto molecular geneticist Andrew Emili (middle) chats with post-doctorate researcher Dr. Uros Kuzmanov (sitting) and Hongbo Guo, manager of Emili's mass spectrometry facility. They are researching biomarkers — signals that diagnose disease and show how advanced it is. (Courtesy: Andrew Emili)

Every second Thursday, we will be featuring an Ontario Research Chair (ORC) (http://cou.on.ca/key-issues/research/ontario-research-chairs/) from one of the province's universities. ORCs are university research professorships created to drive provincial research and develop excellence, to create world-class centres of research, and to enhance Ontario's competitiveness in Canada's knowledge-based economy. See previous profiles here (http://yourontarioresearch.ca/team-rm/2016-2017/).

Every cell in your body contains proteins—molecules that physically interact with each other, allowing cells to do what they are meant to do. Properly connected proteins in a heart muscle cell for example allow it to contract and stretch. In a skin cell, proteins interact to repair DNA damage from ultra violet radiation. In the liver, they come together to cleanse the blood of toxins.

It's no surprise then that most human disease can be traced back to proteins failing to interact in the way they were meant to, says University of Toronto molecular geneticist Andrew Emili (http://www.moleculargenetics.utoronto.ca/faculty/2014/10/1/andrew-emili). It also stands to reason that getting proteins to make the right connections could alleviate or even cure disease.

But here is the problem: While science has made progress in understanding which genes carry instructions for building which proteins, we don't have a clue which proteins work together and how. This means we are also in the dark about how faulty protein interactions lead to disease and how to treat it.

"It's like trying to put together IKEA furniture when you've lost the assembly instructions," says Emili. "You see bolts, you see holes and you know the relationship between the two, but not which ones go where."

Emili is the Ontario Research Chair in Biomarkers in Disease Management, funded by an endowment from the government of Ontario. He is working to create maps of healthy protein interactions so that he can spot faulty ones. These faulty protein maps can then be used as biomarkers, signals that indicate disease and reveal how advanced it is.

Such biomarkers hold promise for diagnosing disease early, perhaps even before symptoms appear, which means doctors can prescribe early treatment that nips it in the bud and reduces health care spending.

Such a long journey

Emili began his research into protein maps in 2000 by working with simpler life forms: yeast and E.coli bacteria. While yeast and E.coli look and act nothing like a human, all three have remarkably similar proteins that interact in comparable ways. This is because once evolution hits on a winning formula for protein interaction, it tends to conserve it across species.

There are of course differences. “Protein X may interact with three other proteins in yeast, but four in humans,” says Emili. But knowing what one organism’s protein map looks like gives him and his team a huge head start. They are now ready to work with human cells, or as Emili puts it, “we are moving up the food chain.”

They are still a long way from testing treatments on people, or even on human tissue. They must first peer into the inner workings of individual human cells, comparing the protein maps of healthy and diseased cells using techniques Emili and his team refined in their work with yeast and E.coli.

That includes mass spectrometry, a tool that can separate individual proteins from their connections. Once isolated, the protein’s mass can be calculated. Each protein has a unique mass which allows researchers to identify it.

Emili aims to begin by mapping protein interactions involved in cardiovascular disease—specifically in heart muscle cells—but will also study cancer and neurodegenerative disease. His long-term goal is to give other researchers the information they need to develop and test drugs that put proteins back into their correct position on the map so they can effectively interact with others.

It’s a grand vision, but none of this will happen overnight. Human biology at the molecular level is more complicated than it was to figure out how to land on the moon, says Emili. “That’s why this kind of basic research is so important—it illuminates discoveries that will eventually cure disease,” he says. “You need this kind of evidence before you can make policy decisions.”

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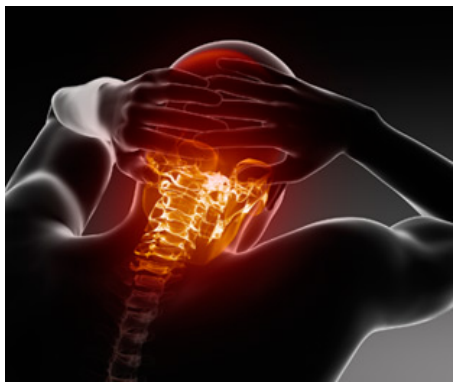

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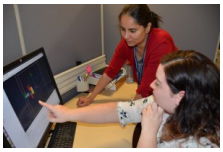

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