Researcher investigates protein interactions involved in cancer cell growth

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(Medical Xpress)—Matthew Hartman, Ph.D., a chemist, is searching for a single molecule out of a trillion. Talk about stacked odds. Still, it is possible. Though the process is complex, Hartman has the patience, technical know-how and expertise to get the job done.

Hartman's research is focused on two hot topics in the arena of cancer research: developing drugs that inhibit key cancer proteins and developing better ways to target cancer tumors. He studies how proteins interact with each other on the molecular level.

As an organic chemist with a background in molecular biology, Hartman is equipped to tackle these challenging cancer topics. He brings to the table valuable insight and inventive ways to approach these complex issues thanks to his diverse training, knowledge and expertise. His talent is understanding the language of experts in the chemical and life sciences, as well as in medicine.

Hartman is housed in the Department of Chemistry in the Virginia Commonwealth University College of Humanities and Sciences, but spends much of his time in his lab at the Massey Cancer Center Goodwin Laboratory, on the medical campus.

Below, Hartman discusses his research, the benefits of having a diverse background as a researcher and the importance of scientific integrity.

What is the goal of your research?

Hartman: In cancer, problems often arise when two proteins interact in a way that they shouldn't and set off a potentially damaging chain reaction of events. So researchers are searching for the right molecule to fit in between the proteins – to halt their interaction and to stop the cancer from growing and spreading. This has been one of the ongoing challenges in developing new cancer drugs.

The typical protein model works like a lock and key. It is hard to find molecules that block that interaction and prevent the proteins from fitting perfectly together. There are different ways of going at this problem, but our approach is similar to one of those arcade games, where players use a mechanical arm or crane to grab fuzzy toys out of a bin.

We first create an enormous pool of diverse molecules and then lower our "crane," in this case, the protein that we want the right molecule to bind to.

We pull the "crane" out, and hopefully, if we've done things correctly, the molecule that has the right shape will bind to and will be captured into the molecular crane. Of course, we don't actually have a crane, but that's the principle – we make trillions of compounds and though it is very rare, our hope is that there is something in there that will have the right function to block the interacting protein. By making more compounds, we increase our chances of finding something that is very hard to find. It's kind of like a needle in a haystack, but we have some very careful ways of finding the needle among the hay. So if the molecule is one out of a trillion, we can find it.

Part of me has always liked probability. You never know what you're going to find! You can't predict the properties of all the molecules you

have created, but by creating a powerful system of sorting through all of the possibilities you can find something rare.

How do your other ongoing projects relate to cancer research and drug delivery?

Hartman: Another longstanding challenge in cancer treatment is delivering drugs only to the cancer tumor. People fighting cancer are not only ill from the disease, but ill from the chemotherapy. [We] are trying to develop ways that involve light to direct the drug to the site of where the tumor is.

The concept is the drug which goes throughout the body does not enter any cell in the dark. Even though it has potential to go into any cell and destroy it, it can't in the dark. We've developed chemistry for that. When we shine light, the drug then becomes activated in that region … the idea is that you illuminate the site of the tumor but nothing else.

You have a diverse training and academic background. How has this benefited your research and collaboration?

Hartman: I earned my Ph.D in chemistry, but my post-doctoral work was in molecular biology. When I initially began my post-doctoral work – which again, was in a completely different field – it was very humbling for the first six months. It was difficult transitioning from my Ph.D. where I had become an expert in my specific area to a new field entirely. I was suddenly in a new lab and exposed to new techniques that I had never seen before. But once I mastered those techniques, I was able to think about things in a different way. I had a different outlook and perspective from my non-chemist colleagues.

My diverse training has helped me learn how to talk to a wide variety of collaborators – from other chemists to medical folks. In contrast, if you were to get the average cell biologist and chemist in a room together, they probably would not be able to communicate very well.

As a research mentor, what do you hope your students walk away with from their time in your lab?

Hartman: For one thing, a firm understanding and commitment to scientific integrity. There's a lot of science published in respected journals under the guise that it is real, when actually, it's shoddy and unreproducible. Some researchers get a novel result, and they share it widely in a publication before reviewing it thoroughly. In some cases the original study is done hastily. The paper comes out and a year later a retraction is issued in the journal indicating the study was not reproducible.

So one of the things I strive for in my research is to teach students to ask hard questions about their own work. When my students present to me new data, I often ask a bunch of questions to see if the data is really true because it is easy to misinterpret. We try to dot every "I" and cross every "T," because we could be wrong. We could be short-sighted.

Together, we think of as many experiments as we can that corroborate our conclusions, and we put those in the paper. In some cases, we have gone down the path thinking that everything is great, and then we've done another experiment that totally contradicts our data. But that is just part of science and we can't be afraid of that. In fact, you have to embrace that, because in the end, results need to be accurate, correct and solid. That does mean it takes longer sometimes. Scientific research is competitive and every researcher wants to be the first to present his or her data, but at the same time, the work needs to be right.

What advice do you have for rising researchers?

Hartman: Don't be afraid to try something new or enroll in a class that's outside your comfort zone. And don't be afraid to interact with people in very different fields.

I intentionally try to provide my students with a wide variety of opportunities – the chance to step into a lot of things. I emphasize to my students that a diverse academic training is important and beneficial. Interacting with people outside your field helps you explain your research to others – it's a key skill, especially as we all work to educate the public about the importance of science.

There are a lot of different things going on in my lab, so students can specialize in different areas, but at the same time, they are exposed to a range of things. Additionally, in our weekly group meetings for graduate students, I choose scientific papers that focus on a variety of topics because I want them to know what's going on in other fields. This can really help the students increase their breadth of knowledge.

When my students leave the lab, they have a mixed background. Are they an organic chemist or a molecular biologist? Neither really – they are sort of a hybrid – they are likely not the world's best organic chemist because it's not the only work they've done. But they come out as this mixture of many things, and I think that is better than being very specialized. It provides them the future opportunity to interact with a number of experts and also encourages them to try new things.

By definition, a new idea is bringing together two or more things that have never been brought together before. If you have a breadth of knowledge to draw from, it's much more likely that you will come up with a creative idea because you know those things that others may not. You can connect the dots and bring them together.

I have friends who are business consultants, and they do a lot of creative thinking. We do not talk about science, but they know a lot about how to solve problems. Being exposed to folks who work in other fields helps spark ideas, and I can incorporate some of these creative ideas into my work.

Having a broad background helps ideas flourish.

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