



Cell research is an exercise in traffic control, William and Mary professor says

By Tamara Dietrich February 16, 2016

Microbiologist Lizabeth Allison likes to think of a cell as a city. The city is made up of cytoplasm, while the gated community within that city is the nucleus.

The workhorses of this city are transport proteins — receptors that haul cargo inside the gates of the nucleus. There, they bind with the genes stored inside the nucleus, turning them on or off as needed to keep the cell functioning normally.

Some proteins, such as thyroid hormone receptors, even exit the nucleus again to carry out other business in the cytoplasm, where metabolic action takes place.

A chancellor professor at the College of William and Mary in Williamsburg, Allison has been studying thyroid hormone receptors for 15 years now, figuring out their complex traffic patterns in and out of the nucleus.

"We're really interested in this idea of traffic control," said Allison.

What they've found is that the traffic flows quite well, actually — so long as the receptors are working right.

"If there are defects in the receptors, we call them mutations — changes in that protein," Allison said. "In some cases, this seems to affect their ability to get into the nucleus or to stay in the nucleus, to interact with the DNA."

When that happens, traffic can get gridlocked. Pile-ups can break out. Genes that should be turned on or expressed aren't. And the cell can start to divide or grow out of control.

All of this can lead to thyroid hormone disorders, or even certain types of cancer.

To be clear, Allison said, she and her students are conducting very basic research on cells, not on cancer treatment or thyroid disorders.

"In my lab, we're certainly not going to find a cure for a particular type of cancer," Allison said. "But our hope is we can (inform) researchers who really work on cancer treatment to have a better understanding of some of the changes that may occur in cancer cells. And then, perhaps, inform their ideas for treatment strategies."

Allison's research has received more than \$3 million in funding since 2001 from the National Institutes of Health and the National Science Foundation.

Early on, her lab discovered that thyroid hormone receptors were unusual in that they didn't just enter the nucleus and stay there, but will exit again — sometimes more than once, and in more than one pathway or channel.

"Thyroid hormone receptors are so different from the other receptors," said Dylan Zhang, a third-year graduate student who works in Allison's lab. "(They) do certain jobs when they're not even binding with anything else. That's fascinating."

The thyroid hormone itself is important because it influences nearly every cell in the body. For adults, it contributes to a healthy metabolism.

Now that they better understand how hormone receptors move in and out of the nucleus, Zhang said, they want to figure out how that movement can be manipulated by modifying the receptors.

"Will they get into the nucleus more, or are they going to be blocked out of the nucleus?" Zhang said.

They're also conducting live-cell imaging, tagging individual proteins with a colorful fluorescent protein so researchers can monitor their glowing traffic patterns around the cell and in and out of the nucleus.

And, Allison said, they're using their findings with thyroid hormone receptors to develop a general model of regulatory proteins.

"What are all the little factors involved in control?" Allison said. "There's signals, there's receptors, there are factors within the nucleus themselves. So we're just beginning to understand all of the parts of traffic control."

Some of the research by Allison and her students was published last month in the scientific journal "Molecular and Cellular Endocrinology."