'Spiders' that battle cancer

April 29 2014

It is rare that one can find a person whose life has not been impacted by cancer, whether it be in a loved one, friend or acquaintance. At MSU, scientists are contributing in major ways to science to combat the disease that kills 1,500 people each day in the U.S., according the American Cancer Society. Mary Cloninger, a prize-winning organic chemistry professor at MSU, explains molecules that look like spiders, how cells "talk" to each other, and her laboratory's work to better understand the malfunctions that cause cancer to grow.

What specifically is your research group doing in the battle against cancer?

One of the early steps in cancer is that similar cells clump together—they aggregate. In addition to aggregating, these cells are multiplying and basically becoming a tumor. In my research group, we study the processes that cause cancer cells to form clumps because these processes are important for tumor formation and for cancer metastasis.

I think that's something that many people don't realize: cancer cells don't invade us, they're not viruses or bacteria that we get from the environment. Cancer cells are our cells but something has gone haywire with them so they aggregate and then start to replicate themselves as if their reproducing or cell-dividing "off switches" were broken.

By studying the process in which cells aggregate and looking at ways we might be able to disrupt that process, we hope to find a way to deal with cancers at a very early stage. In addition, if we can figure out how to make cancer cells unclump—or disaggregate—that could have implications for late-stage cancers, too.

How are you trying to make cancer cells 'unclump'?

To study cancer cell behaviors, we make large molecules called dendrimers. The dendrimers have many arms that branch out from a core, kind of like a many-armed spider. At the outside edges of the arms (where your hands are), we can decorate the dendrimers with groups that bind well to proteins that surround cancer cells. When we send the dendrimers into the cellular environment, we evaluate whether the presence of the dendrimer can change the cell's behavior. Think of the dendrimer as a wrench that we're throwing into a cancer engine. By seeing what stops working and what keeps working, or works in different ways, we can learn a lot about how the cell processes work. The more we are able to learn about how the cell functions, the more likely it is that we will be able to restore healthy processes if and when things go wrong in diseases such as cancer.

Making these dendrimers is not an easy task. If I go back to the image of a spider with many arms, my students and I tailor the size of the spider's body, the number of arms that the spiders have, and the number and type of carbohydrates that we put where the spider's arms (feet?) should be. We spend a lot of time synthesizing compounds in flasks in the lab and then purifying and characterizing them to make sure that we know exactly what we have. Then we develop the protocols for how to study the dendrimers' effect on the cancer cells. Sometimes, for example, we make dendrimers that give off a green fluorescent glow so that we can track them while they're interacting with the cells. We all like to work with the green dendrimers!

How do cells communicate with one another and with

their surroundings?

Cells use the carbohydrates that coat their surfaces as one important way to communicate with their surroundings. Carbohydrates are big groups of simple sugars such as the lactose that you find in milk and the glucose that you need for energy pathways in your body. In food, carbohydrates make up starches and dietary fiber. On the surface of a healthy cell, carbohydrates are there to help the cells to perform many important tasks including mounting an immune response against invaders, differentiating during growth ("deciding" what kind of cell it is going to be), and initiating uptake of hormones and cell signaling proteins. Cancer cells have different carbohydrates on their surfaces than healthy cells, and the cancer cell carbohydrates can bind to proteins that enable them to aggregate and form tumors, for example.

Our dendrimers are designed to intercept the cancer cellular aggregation/tumor formation process. We have incorporated carbohydrates onto the dendrimers' surface that bind well to proteins that cause the cells to aggregate. When the dendrimers bind to the protein, then the protein isn't able to bind normally to the cells. The dendrimer diverts the main players in the cancer cell aggregation process (the cells and some of the proteins that surround them) from their normal purpose of tumor formation. Thoughtful design of the dendrimers allows us to make molecules that can either make cancer cells stickier or less sticky. This teaches us about possible ways that new therapeutic agents can be designed that may one day help doctors to fight tumor growth and cancer metastasis.

Provided by Montana State University