How does the shape of an immune cell change when it is killing cancer cells?

How could your research help fight cancer?

The goal of my research is to help develop more effective immunotherapy treatments for skin cancer. Immunotherapy is a new type of therapy in which a patient's own immune cells are used to kill cancer cells. I study how the shape of immune cells change when they are actively killing cancer cells in melanoma, a type of skin cancer.

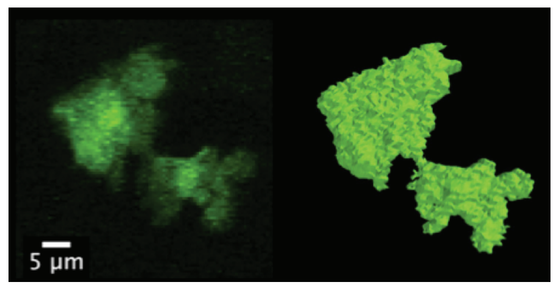
Alexandra Signoriello

I am a 5th year Ph.D. student in the graduate program in Computational Biology and Bioinformatics at Yale University. I work on a research project that incorporates knowledge from physics, computer science and cancer biology to understand how skin cancer grows. My advisers are Profs. Marcus Bosenberg and Corey O'Hern. Marcus is a dermatopathologist. His job is to diagnose skin cancer samples taken from patient tumors by looking at magnified images of the cells inside the tumor. He determines if the tumor is cancerous, based in part on the shape of the cells inside the tumor. Corey is a physicist who studies how particles of different shapes pack inside materials using computers. The goal of my project is to demonstrate that the shape of an immune cell changes when it is killing cancer cells.

I am working to develop automated ways to process and analyze images of immune cells inside mouse skin tumors. We use a specialized microscope to take images of cells inside of a tumor that is growing in a living mouse. I write computer programs to calculate the shapes of cells and measure how far each cell travels inside the tumor. In the figure, I show an image of an immune cell inside a skin cancer tumor (left) and the transformation into a computergenerated mesh (right). A mesh is a representation of a surface using points and lines to create a solid in three-dimensions with many flat faces. The mesh representation makes it possible to compute the volume, surface area, and shape of the cell. I can also track the position of the cells using many images taken at different time points. I can then measure how far each cell has traveled in the time between images.

The Bosenberg laboratory performs experiments on two populations of mice that have skin cancer. One population has a healthy immune system and is able to fight cancer, while the other population has a very weak immune system and is not able to fight cancer. By taking images of tumor growth in both populations, we can study the differences in immune cell shape as the immune cells are killing cancer cells.

Importantly, my current work has shown that immune cells become more flexible and mobile when they are killing cancer cells. These changes may allow them to squeeze between other cells so they can access cancer cells within the tumor. In the future, I will study whether the flexibility of the immune cells are different in big (lots of cancer cells) versus small (few cancer cells) tumors. To do this, I will use simulations, in which I imitate real processes using a computer. During simulations, I will pull the computer generated mesh in different directions and study how easily the mesh changes shape. This will tell us how rigid (not able to change shapes) or flexible (easily changes shapes) the immune cell is. I will compare the cells in the simulations to the real behavior of immune cells inside tumors.



(Left) A microscopy image of a macrophage, a type of white blood cell, within a mouse melanoma tumor. (Right) A computer-generated mesh of the macrophage on the left using a new image processing method that I developed. Note that the macrophage is highly non-spherical with a middle region that is extremely thin, which allows it to squeeze between neighboring cells in its search for cancer cells.

What sparked your interest in science?

I have always been fascinated by the simplicity and elegance of mathematics. In particular, I admire simple mathematical equations that can describe complex behavior in biology. For example, the Fibonacci sequence describes the spirals in sunflower seeds, the predator-prey set of differential equations can predict whether the Canadian lynx will have enough food to survive the winter, and the simple Vicsek model can explain schooling in fish and flocking in birds. My passion about science is rooted in the idea that complex patterns emerge from simple rules.