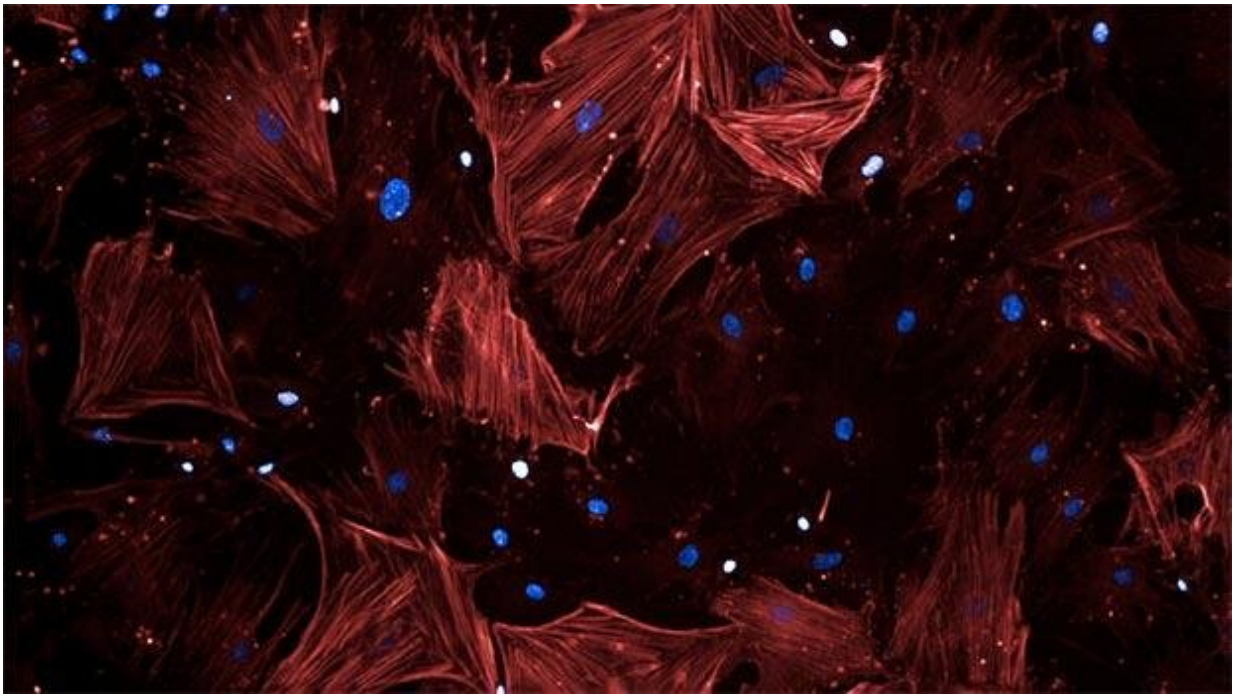
Targeting cancers' surroundings to prevent or limit metastasis

January 27 2020, by Harry Jenkins



Cancer-associated fibroblasts stained to reveal their DNA (blue) and structural proteins (red). Credit: Dr Alice Santi, Cancer Research UK Beatson Institute

Cancer depends on blood. Just like the rest of the body, tumors need blood vessels to supply them with nutrients and oxygen to grow. But cancer uses these vessels in another way as well—to spread to other parts of the body.

When cancer spreads—a process known as metastasis—it does so by a few cells breaking away from the main tumor and traveling through the blood stream or the network of vessels used to drain toxins from the body, the lymphatic system. If the conditions are right, circulating cancer cells get caught in a small blood vessel, escape, and grow into another tumor somewhere else in the body.

This makes the cancer much harder to treat. And it's something that scientists are working to stop.

Researchers at the Beatson Institute in Glasgow are looking to see if targeting the cells that surround the tumor, rather than the tumor itself, could be a potential way of preventing cancer spread.

"The spread of cancer cells to other parts of the body is the primary cause of cancer death. And understanding this process is fundamental to learning how to prevent it." says Dr. Alice Santi, a postdoctoral researcher working on this project.

Studying cancer's surroundings

Cancer cells don't exist in isolation.

Most tumors are embedded in a network of cells that provide structural or connective support for an organ, otherwise known as the stroma.

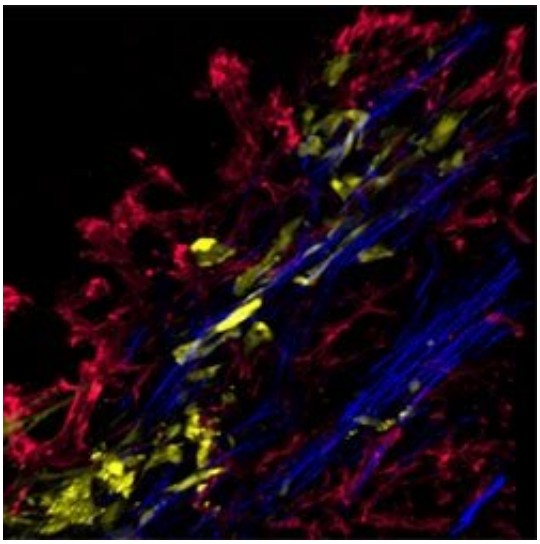


Image of blood vessels (red), cancer-associated fibroblasts (yellow), and the extracellular matrix (blue). Credit: Dr Alice Santi, Cancer Research UK Beatson Institute

This support system is made up of a variety of different cells, including cells called fibroblasts. These handy units produce all the molecules that make up the environment our cells live in, otherwise known as the extracellular matrix.

But these cells aren't always good. In the presence of cancer cells, normal fibroblasts can be co-opted to become cancer-associated fibroblasts (CAFs).

These newly activated cells have been shown to play a crucial role in cancer progression, including metastasis. One way they do this is by changing the properties of the area surrounding the tumor, as well as the behavior of both healthy and cancerous cells.

It's these cells that researchers are hoping to target. But first, they need to know more about this vital support system and how it can change to

promote tumor growth and metastasis.

Interrupting the conversation

Santi is focusing on how these fibroblasts communicate with the cells that line blood vessels.

"CAFs can modify the behavior of these cells to support metastasis," says Santi. She says that cancer cells need to enter the blood stream to spread, which requires them to interact with the cells lining blood vessels. And CAFs help to get blood vessels ready for that interaction.

"CAFs can provide the blood vessel cells with new functions by transferring them proteins they normally wouldn't have."

She hopes that understanding the communication between CAFs and blood vessels could uncover a way to stop it all together, blocking cancer spread.

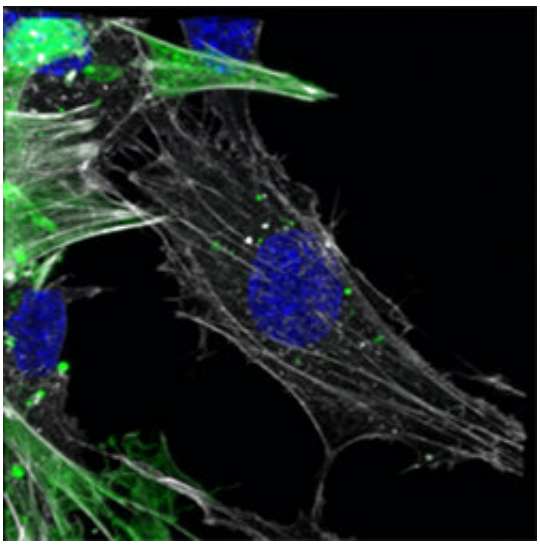


Image showing fibroblasts (green) with a blood vessel cell (white). The green dots in the blood vessel cell are proteins that originally came from the fibroblast,

prepping the blood vessel to support cancer spread. Credit: Dr Alice Santi, Cancer Research UK Beatson Institute

Growing cells together

But before they can de-code this cellular chatter, Santi needs a good way to grow all the different types of cells together, a method known as co-culturing. This has proved to be a challenge.

"The problem with co-culture systems—where you have different cell types on the same place—is that you want to grow the cells together, but then want to analyze the behavior of each cell type again, and there's a problem in separating them. We're working on an experimental model to try and address this," explains Santi.

Santi and the rest of her research group, led by Professor Sara Zanivan, hope to develop this experimental model to improve the way they can study the way CAFs communicate and interact with other cells.

Their research focuses on the potential of exploiting CAFs to primarily treat breast and ovarian cancers, as they tend to grow in a rich stroma that contains a lot of CAFs.

"Because of their ability to remodel the environment where tumors grow, I think of CAFs as architects," says Santi. "My research shows that one of the tools they use is the transfer of their own proteins. And thanks to the co-culture system, I now know what these proteins are. The next step is to see if blocking this transfer can indeed prevent metastasis."

Provided by Cancer Research UK