How cancer stem cells evade the immune system

WHEN Daniel D. Liu first encountered the world of research, he saw giants in white lab coats shaking flasks and squirting liquids into small vials. He was 4 years old, and his parents, both biochemists, would bring him to work and set him down with a book and instructions to keep quiet.

"I didn't really understand what was happening, but I guess that was my first impression of what adults do," said Liu, Class of 2018, who is majoring in molecular biology. It was no wonder that he went into the family business at a young age. During summer breaks in high school, he worked at the National Institutes of Health near his home in Potomac, Maryland.

At Princeton, Liu joined the laboratory of Yibin Kang, the Warner-Lambert/Parke-Davis Professor of Molecular Biology, where he focuses on breast cancer stem cells, which are a subset of cancer cells that can self-renew and cause tumors to spread or grow back after treatment.

In a study published earlier this year in *Nature Cell Biology*, Liu helped identify a molecule that protects cancer stem cells by shielding them from the immune system. When the immune system cannot attack the cancer cells, the cells can spread to surrounding tissues, a process known as metastasis and a leading cause of cancer-related deaths.

The team found that when cells produce a lot of this molecule — actually a short strand of genetic information called microRNA-199a — both healthy and cancerous cells take on stem cell-like properties such as a heightened ability to regenerate breast tissue and to create spherical clumps of cells called mammospheres.

This stem cell-like property is necessary for normal breast tissue functioning, but it is also fuel for cancer cells to survive and duplicate, helping them to escape from the suppressive effects of immune cells.

The findings may shed light on the puzzle of why immunotherapy, a cancer treatment that spurs the immune system to attack tumors, is highly successful against some types of cancer patients but does not work well for others.

"Everyone is really banking on immunotherapy as a breakthrough in cancer treatment, but it only works really well for some types of cancers," Kang said. "In breast cancer the response isn't great, and we don't really understand why."

As a result of this study, made possible through funding from the National Institutes of Health and the U.S. Department of Defense, Kang now thinks the lack of response to immunotherapy by some patients could, in part, be due to the microRNA's role in protecting the cancer stem cells.

Since the team now understands what guards the cancer cells, Liu said, "perhaps we can target this pathway so as to sensitize cancer stem cells to immunotherapy."

Liu's contributions to the lab go beyond bench experiments. Recently, he coded a user-friendly program that enables the team to sift through large patient data sets quickly, improving upon the lab's previous, manual approach. He also co-founded the *Princeton Undergraduate Research Journal* (see page 2) to help fellow students publish their work and learn firsthand about the peer-review process.

"Daniel not only does his own work but also makes life much easier for everyone in the lab," Kang said. "It's quite unusual for an undergraduate to make fundamental contributions to the lab that enable everyone to do research in a better way." **–By Yasemin Saplakoglu**

PHOTO BY WEIHONG XU

Undergraduate Daniel D. Liu co-authored a *Nature Cell Biology* study on the discovery of an RNA molecule that protects stem cells.