



Unlocking the Secrets of Circulating Tumor Cells to Prevent Breast Cancer Metastasis

Most breast cancer-related deaths occur as a result of metastasis – a process where the tumor cells break away from the original tumor and form a new tumor in another part of the body such as the bones, liver, lungs or brain. The process of metastasis involves multiple steps. Fortunately, most tumor cells do not survive the journey, but those that do are very robust, which is why metastasis is a difficult process to control. With support from a Komen research grant, Dr. Shyamala Maheswaran and a team of Harvard researchers including scientists, clinicians and engineers have uncovered some of the secrets of circulating tumor cells (CTCs) that may be used to predict disease progression and metastasis in breast cancer patients.



Dr. Shyamala Maheswaran (right) with co-authors, Dr. Min Yu (left) and Dr. Daniel Haber

Circulating tumor cells break away from the primary tumor and enter the circulation. Some may invade distant tissue and form a new tumor. Understanding which CTCs are capable of forming new tumors is the central focus of Dr. Maheswaran's research.

Scientists believe that CTCs – tumor cells that have broken away from the tumor and entered the circulation – may hold the key to understanding, treating, and even preventing metastasis. These cells are rare, estimated at one CTC in a billion blood cells which makes them very difficult to isolate and study.

In an article published in the journal *Science*, Dr. Maheswaran and her colleagues show that CTCs not only share similar characteristics with the original breast cancer, but they also undergo changes in response to cancer treatment. By tracking these changes, the researchers gained important information about tumor response to therapy and disease progression. In this study,

the researchers collected CTCs from the blood of breast cancer patients using technology capable of isolating single CTCs from other cells in the blood. This method allowed them to identify specific types of CTCs that were then analyzed for clues about which CTCs were likely to metastasize and form a new tumor.

Because monitoring patient response during the course of treatment is vital to successful cancer therapy, the researchers also wanted to know whether CTCs could be used to measure response to treatment. To do this, they measured changes in the number and types of CTCs in breast cancer patients before and after treatment. In the first study of its kind, they found that patients who responded well to treatment had fewer CTCs than patients whose cancer progressed or metastasized. They also observed changes in CTC characteristics depending on response to treatment. In patients whose cancer improved, the CTCs resembled the original tumor cells. Conversely, if the patient's cancer progressed, the CTCs were more “sticky” and formed clusters. The researchers believe that the clusters of CTCs could indicate a high risk for metastasis. While the study is in its early phases, these results suggest that CTCs could be a reliable way to track tumor progression and may be good targets for drugs that would prevent metastasis.

“The most striking finding was that the tumor cells were able to evolve quickly and we need to keep that in mind when we treat patients.”- Dr. Maheswaran

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