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Altered expression of a protein in high vs. low spreading cancer cells

Breast cancer cells start off growing in the breast and end up spreading to the lung, liver, bones and brain. This spreading to another organ is called metastasis and is the major cause of patient death due to breast cancer. Although many scientists generally understand how the tumor starts growing in the breast, they do not exactly understand how the cells are able to establish themselves in the lung, liver, bones and brain. This manuscript looks at two different cell lines, 67NR cells that have a low level of metastasis, or spreading to another organ, and 4T1 cells that easily metastasize. The 4T1 and 67NR breast cancer cell lines are established cell lines that were previously isolated from the breast tumors of mice and are the basis of our experiments. We injected these cells into mice, allowed the cells to grow into tumors, and then removed the tumors to see the differences between them. We found that 4T1 cells were able to metastasize to the lungs, liver, heart, kidney, spleen, bone and brain. When we injected the 67NR cells, they still formed tumors, but the cells were only able to metastasize to the lung. We isolated these tumors and discovered that 4T1 are more aggressive because they have decreased expression of an important protein called TNF-α.

TNF-α was first discovered in the blood of mice injected with a tuberculosis injection. Many people debate whether TNF-α promotes cancer cell growth or prevents it but our studies show that it prevents metastasis. We even went on to add pure TNF-α to the cells and saw that 67NR cells were more sensitive to it. This means that the entire pathway is shut down in 4T1 cells. This has great therapeutic importance because physicians can treat non-metastatic cells with TNF-α to kill them but they know they need another drug to kill highly metastatic cells. Studies like this are important because we have discovered that the shutdown of the TNF-α pathway is one of the reasons why 4T1 cells metastasize.

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