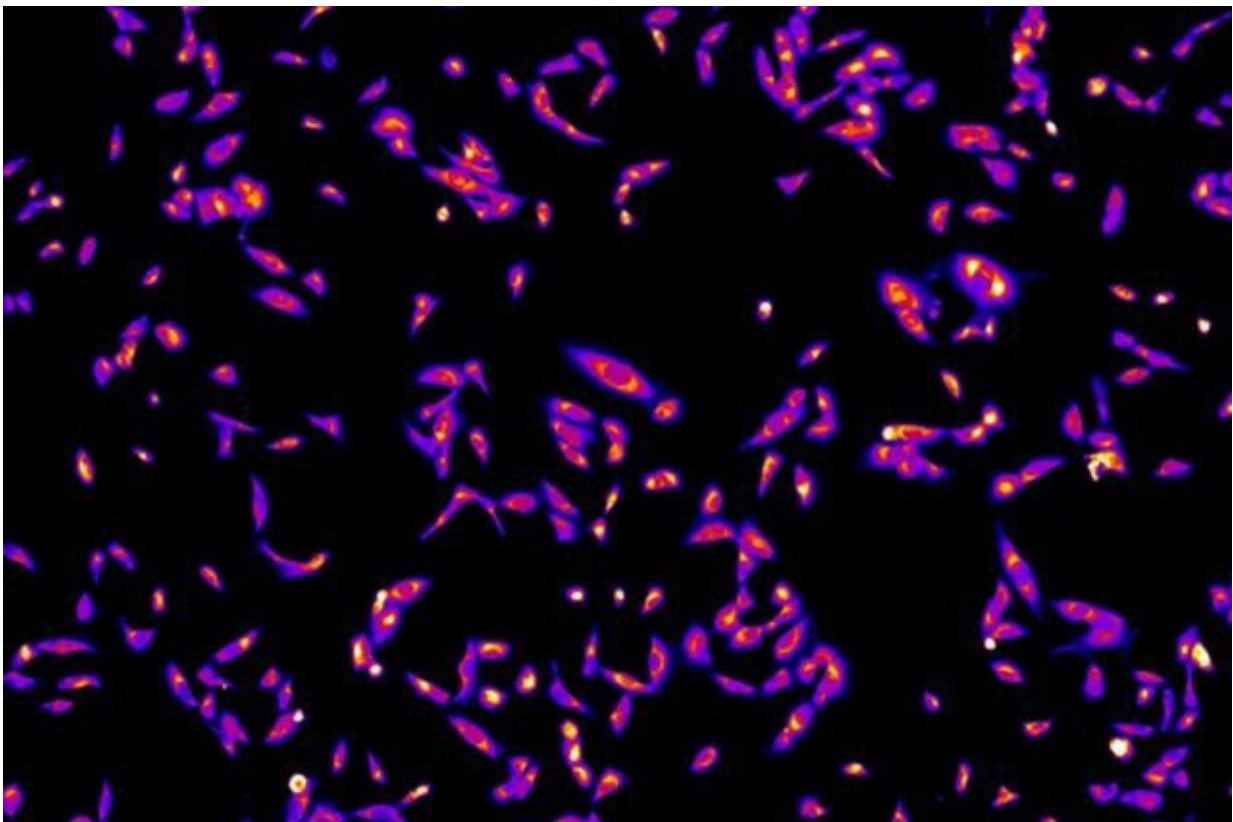


# Reducing breast cancer metastasis in animal models by modifying tumor electrical properties

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Breast tumor cells light up with a dye that indicates their electric potentials.  
Credit: Tufts University

In normal cells, electrical voltage patterns provide a blueprint for orderly

growth. But with cancer, the opposite happens. Marked by a breakdown in the normal electrical patterns generated by the cells, they lose their specialized functions, start expanding into a tumor and spreading into and disrupting the function of other tissues—metastasis. As of yet, there are no clinically available treatments that specifically target the process of metastasis, which remains the leading cause of death in cancer patients.

Now researchers at Tufts University have found that manipulating voltage patterns in [tumor cells](#) using ion [channel](#) blockers already FDA-approved as treatments for other diseases can in fact significantly reduce tumor cell invasion in a dish and metastasis in an animal model of breast cancer.

The discovery that drugs already approved for other conditions can slow or stop metastasis could lead to an expedited path to approval for the treatment of cancer.

"This is very much an unexplored, but highly opportunistic strategy for the treatment of cancer," said Madeleine Oudin, Tiampo Family Assistant Professor of biomedical engineering at Tufts University School of Engineering and corresponding author of the study. "Ion channels, which regulate the bioelectrical properties of [cells](#), are the second-most common target for existing pharmaceuticals, so we have a relatively large set of ready-to-use drugs that could be repurposed for cancer therapy."

To test their [therapeutic strategy](#), the Tufts research team focused on triple-negative breast cancer (TNBC), a subtype of the disease which accounts for approximately 15 percent of all breast cancer cases. The likelihood of metastasis for TNBC is greater than all other subtypes of breast cancer, and because TNBC is associated with a poor five-year prognosis, scientists are focusing efforts on counteracting it.

The researchers were able to show that manipulating the voltage properties of breast cancer cells can have a significant effect on their progression to metastasis, reducing the number of metastatic sites in mouse lungs by about 50 percent.

Cells in the body create a natural voltage across their membranes, caused by ion channels that actively push or passively allow positive and negative ions into and out of the cell. Mike Levin, Vannevar Bush Professor in the Department Biology, a collaborator on this study, has been working on dissecting the role of electrical properties in cellular behaviors for many years in model organisms. When Oudin joined Tufts, they received funding through the Tufts Collaborates program, which helps support collaborations between faculty in different schools to tackle new exciting areas of research.

While there are a variety of channels that drive the movement of positively charged sodium, calcium, and [potassium ions](#), as well as negatively charged chloride ions, potassium ion channels tend to dominate in generating the voltage across the cell membrane. When the Tufts researchers genetically over-expressed the potassium ion channels in tumor cells, the inside of the cells became more negatively charged, and the imbalance in voltage led to increased tumor growth and metastasis, both in plated cells and animal models.

The researchers' therapeutic strategy took the opposite approach—blocking the potassium [ion channels](#) led to a restoration of more normal voltages for the cells, decreased tumor cell invasion and significantly reducing metastasis.

Four FDA-approved potassium ion channel blockers were screened, and all had similar effectiveness in killing tumors cells. One drug, amiodarone, had the largest effect on normalizing cell voltages and was selected to see how well it would work in treating breast cancer in mice.

The researchers found that the drug, approved for use treating heart rhythm disorders, cut back on the tumors' ability to spread as cells broke off and move to other parts of the body.

By looking at the genes that were triggered by the [voltage](#) shift, they found a number of molecular pathways involved in the movement of cells. The effects of the ion channel blocking drug were consistent with limiting the cells movement, so they don't wander off and grow new tumors.

The Tufts team will continue to explore the effects of the ion channel blockers on [cancer](#) in animal models, in combination with existing standard of care treatments like chemotherapy. Since amiodarone and similar drugs are already approved for use in humans, phase I clinical trials in small groups of [cancer patients](#) could commence in the near future.

Provided by Tufts University

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