Medical Xpress

Researchers demonstrate mathematical modeling limits aggressive tumor cell growth

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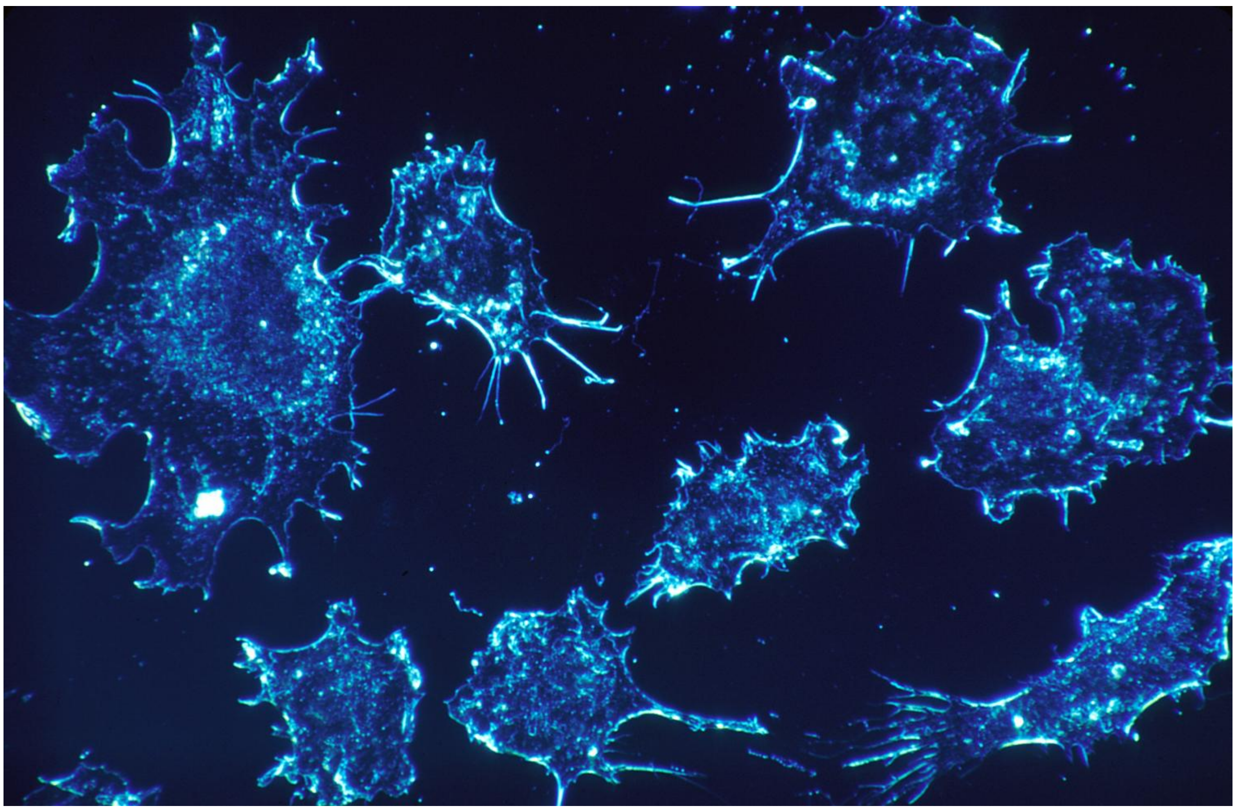

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Cancers can be viewed as complex dynamic systems because they have many interacting parts that can change over time and space. Perhaps the most well-known complex dynamic system is the weather and, similar to weather forecasting, researchers in the Integrated Mathematical

Oncology Department at the Moffitt Cancer Center are using mathematical methods to account for many variables in the search for new ways to understand and control cancer. Their recent study, which appears as the cover article in the May issue of *Cancer Research*, shows that mathematical models can be used to predict how different tumor cell populations interact with each other and respond to a changing environment. They found that, by using math models to understand the complex dynamics within cancers, they could use small changes in the environment to promote the growth of cells that are less aggressive and thereby decrease tumor growth.

A single tumor is composed of many different populations of cells. Using a combination of experimental and mathematical studies, the Moffitt researchers identified two different cell populations that co-exist in many different tumor types; an aggressive cell population that can invade the surrounding space and migrate to form metastases, and a non-invasive cell population that is prone to stay in one place and help produce blood vessels. They showed that in typical cancers growing in mice, the invasive cells are more numerous and have a survival advantage over non-invasive cells in a tumor.

But evolutionary principals dictate that the behaviors and actions of any organism (whether plants, animals or tumor cells) come with advantages and disadvantages. Even though the invasive cells have an advantage because of their ability to invade surrounding tissues, that invasive nature also has its drawbacks: increased susceptibility to changes in limited resources and their environment. The researchers used computer models to predict that small changes of the pH within the tumor could tip the balance, decreasing the survival advantage of the invasive cells in favor of the non-invasive cells.

Cell culture and mouse models of prostate cancer confirmed the mathematical model predictions. Researchers added sodium bicarbonate to the drinking water of mice to change the pH of their prostate tumors' environment. They found that non-invasive cells within the tumors developed a survival advantage over the invasive tumor cells. As a result, the mice had smaller tumors that were confined to the prostate - and fewer invasive metastatic tumors. Similar results were observed in a mouse model of breast cancer.

A well-recognized property of complex dynamic systems is the "butterfly effect," which proposes a butterfly flapping its wings in Japan could cause a tornado in Texas. This is often used to demonstrate that such systems, including cancer, are hopelessly complicated and cannot be controlled. Rather, the Moffitt investigators demonstrate the tendency of complex systems to magnify some small perturbation (i.e. the flapping butterfly wing) can actually be exploited. In fact, they show that, with sufficient understanding of the eco-evolutionary dynamics and input from mathematical models, cancers can be steered into a less invasive growth pattern with the application of small biological force.

More information: Arig Ibrahim-Hashim et al. Defining Cancer Subpopulations by Adaptive Strategies Rather Than Molecular Properties Provides Novel Insights into Intratumoral Evolution, *Cancer Research* (2017). DOI: 10.1158/0008-5472.CAN-16-2844

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