Scientists reveal how different cancer cells 'team up' to help incurable childhood brain tumor spread

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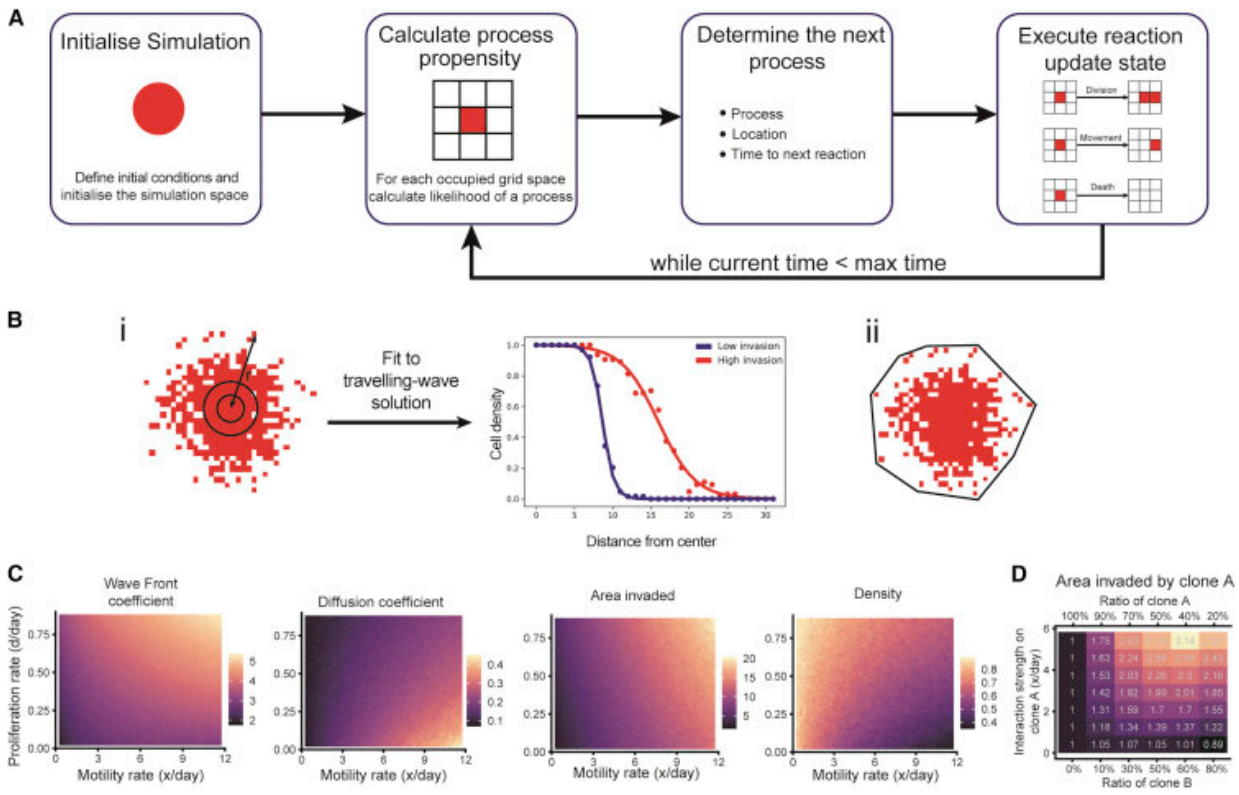

Simulating cellular invasion (A) Illustration of simulation flow. (B) Summary statistics used to measure invasion: (i) traveling-wave solution to reaction-diffusion equations fit to the spatial configuration of cells, (ii) convex hull area. (C) Measurements of pure population invasion, detailing the effect of proliferation and motility rates on the phenotype observed. (D) Highlighting the effect of introducing interactions on the phenotype observed. As the positive interaction strength increases, the area invaded relative to the pure culture also

increases in a co-culture. Credit: *Cell Reports* (2022). DOI: 10.1016/j.celrep.2022.111283

Scientists have shed light on how different types of cancer cells in an aggressive childhood brain cancer interact and work together to spread.

Using mathematical modeling, the team provides a framework for detecting, measuring and mapping interactions between different types of cells in diffuse intrinsic pontine glioma (DIPG)—a brain tumor starting in a type of cell known as 'immature glial progenitor cells' before spreading to other parts of the brain.

Researchers at The Institute of Cancer Research, London, led the study, published in *Cell Reports*.

They hope targeting and blocking interactions that allow cells to work together to invade surrounding areas could become a new treatment strategy, which is urgently needed in this currently incurable childhood cancer.

Cells within tumors cooperate

DIPG tumors are made up of more than one subtype of cancer cell. In 2018, the team of scientists at The Institute of Cancer Research (ICR) found the first evidence that different subtypes of cells within a tumor can cooperate—rather than solely compete for resources, as was the common belief.

Their new findings show for the first time that some subtypes have a positive effect on others in terms of how the cells spread—opening up new avenues for testing and developing treatments for this childhood

cancer.

The study explored the interaction between two different subtypes of cancer cells—labeled VI-E6 and VI-D10—obtained from donated tissue from patient biopsies, when grown together in the lab. The VI-E6 subtype was able to spread further when grown in a co-culture with VI-D10.

Cooperation more than doubled the spread

Using deep learning to process images from experiments in the lab, scientists were able to identify interactions where one cell subtype cooperated and helped the other grow and spread—and differentiate between these interactions and those where one subtype spread more than the other due to other unrelated factors, such as space restrictions.

Previous models exploring cooperation between cancer cells focused on growth, but this innovative study is the first to measure interactions that affect the way tumor cells spread and invade surrounding areas.

Researchers demonstrated that cells behaved differently when cultured together in the lab, rather than in separate environments. Culturing two different subtypes together more than doubled the spread of the tumor.

When they grew the two different cell subtypes together, researchers found cancer cells were able to spread and invade a greater area. While one subtype traveled and spread more quickly, the speed of the other decreased—highlighting commensal interactions, where one subtype gains benefit without harming or benefitting the other, as well as exploitative interactions, where the fitness of one subtype is enhanced while reducing the fitness of the exploited subtype.

Towards more and better personalized treatment options

The findings demonstrate that interactions between DIPG cell subtypes play a key role in helping tumors invade the local environment and spread—adding to our understanding of how this childhood cancer progresses.

In this way, researchers provide a framework which could be applied to more cancer types. By providing a method of identifying and measuring these cell interactions, the effect of treatments can also be explored.

Researchers are increasingly aware of the importance differences between cancer cells within a single tumor can have on treatment outcomes. Their hope is that identifying and measuring interactions between cancer cell subtypes could lead to better and more personalized treatment options.

The study was co-led by Professor Chris Jones and Professor Andrea Sottoriva, former Team Leader at the Centre for Evolution and Cancer at the ICR.

Attacking tumors by 'disrupting positive interactions'

Study co-leader Professor Chris Jones, Professor of Childhood Brain Tumor Biology at The Institute of Cancer Research, London, said,

"This childhood cancer is incredibly difficult to treat. Nearly all children with DIPG die within two years, and new treatments are urgently needed.|

"We are beginning to decipher how different types of cells in DIPG

interact and work with each other to fuel the disease.|

"By combining deep learning and advanced mathematical modeling with experimental data, we provide a framework for detecting, measuring and mapping these interactions—which we hope will lead to new ways of testing and developing treatments that attack tumors by disrupting positive interactions and promoting negative interactions between cell subtypes."

Study author Dr. Haider Tari, who was part of the Evolutionary Genomics and Modeling Team at The Institute of Cancer Research, London, said, "If one subtype cooperates with a different subtype in a way that drives the tumor's growth and spread, it would be crucial to target and block this cooperation—with the goal of stopping cancer in its tracks."

"This innovative study provides a way to identify whether cells are interacting and by how much, and the framework could be applied to a number of different cancer types."

Dr. Laura Danielson, Children's and Young People's Research Lead at Cancer Research UK, said, "This study demonstrates the power of mathematical modeling to better understand how cancer cells interact and spread."

"More work needs to be done to understand how we could potentially target these interactions, but discovery research like this brings hope for development of more effective treatments for children and young people affected by cancer."

More information: Haider Tari et al, Quantification of spatial subclonal interactions enhancing the invasive phenotype of pediatric glioma, *Cell Reports* (2022). DOI: 10.1016/j.celrep.2022.111283

Provided by Institute of Cancer Research