2018-09-24

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Jake Hogan  
Brigham Young University, jacob.s.hogan@gmail.com

Heiko Enderling  
Moffitt Cancer Center

Joel Brown  
University of Chicago; Moffitt Cancer Center

Robert A. Gatenby  
Moffitt Cancer Center

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Hogan, Jake; Enderling, Heiko; Brown, Joel; and Gatenby, Robert A., "Using Non Stem-Cells to Understand Early Tumor Growth" (2018). Library/Life Sciences Undergraduate Poster Competition 2018. 2.
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Using Non Stem-Cells To Understand Early Tumor Growth

Jake Hogan¹, Heiko Enderling¹, Joel Brown¹,², Robert A. Gatenby³
¹Integrated Mathematical Oncology, H. Lee Moffitt Cancer Center and Research Institute, ²University of Chicago, ³Radiology, H. Lee Moffitt Cancer Center and Research Institute

Introduction

Tumors of similar size and shape can exhibit different responses to the same treatment. Targeted therapy aims to better treat these tumors by classifying them according to genotypic traits. A better understanding of how tumor traits such as non-stem cells influence tumor growth could improve targeted therapy. We hypothesize that the production of non-stem cells may aid tumor growth in avascular tumors (tumors lacking blood vessels).

Patient Tumor Showing Three Distinct Layers¹

Methods

Mathematical Model

We used an ABM (Agent Based Model): a mathematical model where cells (or agents) interact according to a set of rules². Cells are represented as points on a 3-dimensional grid.

Cells in the tumor are either stem or non-stem cells. At each time step, viable cells (1) consume oxygen, (2) move, (3) and reproduce (if there's enough space). They are affected by 2 factors:

1. Oxygen levels- Oxygen is diffused from the blood vessels on the edges of the grid. Live cells consume oxygen at a constant rate.

2. Tumor Necrosis Factor alpha (TNFα) levels- TNFα is released at a constant rate by necrotic cells. High levels of TNFα cause necrosis in surrounding cells.

Results

Stem-Cell Tumor Growth Matches Patient Tumors

Figure 1- The results of this model match the three-layered growth shown in Image 1. Note the radial symmetry and large necrotic core.

Figure 2- This diagram corresponds to Figure 3. The release of TNFα increases the size of the necrotic core in stem-cell tumors.

Key Terms

Non-stem cells- cells that die out after a certain number of replications. Stem cells- cells that can replicate an infinite number of times. Tumor Necrosis Factor Alpha (TNFα)- chemical released by necrotic (dead) cells that can induce necrosis in surrounding cells.

Discussion

The 3-dimensional model supports our hypothesis that non-stem cells could help early growth stage tumors overcome the negative effects of TNFα. This is due to the lack of a necrotic core in non-stem cell tumors when compared to stem-cell tumors, which prevents non-stem cell tumors from going dormant due to TNFα. However, more simulations exploring different parameters are necessary.

This experiment invites further inquiry about the role of non-stem cells as an evolutionary advantage in larger, heterogeneous tumors as well as early growth stage tumors. Further research in this subject could potentially aid the development of targeted therapy in determining what genotypic traits are likely to cause cancer metastasis.

References:


Acknowledgement

This work is sponsored by the NCI as a part of the CSBC/PS-ON Summer Research Program in collaboration with the Moffitt Cancer Center PSOC, NIHNCI U54CA193489-01A1