How a Tumor Gets its Spots

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The research story

Among the great challenges facing the treatment of cancer is the diversity of cell types within a tumor. Each of these cell types may have different responses to drug treatment, making it necessary to consider using a combination of drugs that target different cell types within the tumor. We focus on the diversity of cell subtypes in colon cancer, which is among the leading causes of cancer-related deaths in the world. Most colon tumors have mutations that aberrantly turn on a critical cell signaling pathway known as Wnt, leading to deregulated, increased cell proliferation rates, among other cancer characteristics. We study Wnt in human colon cancer cells by injecting them into mice and following the activities of Wnt signaling as the injected cells form a vascularized tumor. Even when the cells used to develop these tumors are genetically identical, we observe that fields of cells self-organize via signals to one another to establish a variety of cell subtypes that differ in how they process nutrients.

The image

We observe a striking pattern of heterogeneity in which groups of cells that utilize the resource-intensive process called glycolysis, are encircled by cells using a more resource-efficient mode of energy production called oxidative phosphorylation. Using animal tumors and mathematical simulations, we find that this pattern of cell clusters or "spots" is in part regulated by Wnt signaling. Model simulations suggest that drugs targeting Wnt signaling and glycolysis could serve to effectively treat colon cancer patients by taking advantage of this relationship between Wnt and metabolism.

Reference

[1] Lee M, Chen GT, Puttock E, Wang K, Edwards RA, Waterman ML, Lowengrub J, Wang K, Waterman ML, Lowengrub J, Mathematical modeling links Wnt signaling to emergent patterns of metabolism in colon cancer, Mol. Syst. Biol. 13: 912, 2017.

F. Matthäus et al. (eds.), *The Art of Theoretical Biology*, https://doi.org/10.1007/978-3-030-33471-0_19