Differences in tumor cell metabolism affect growth, invasion and response

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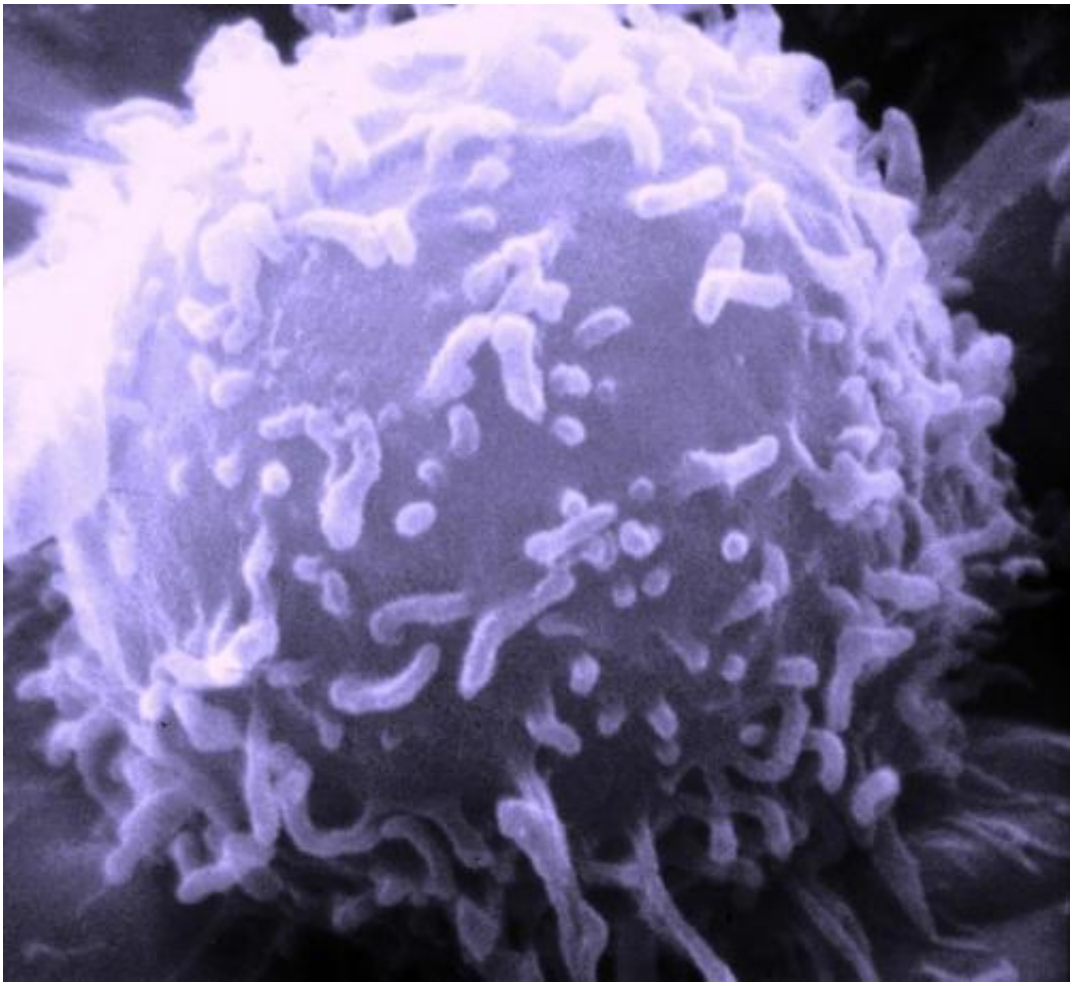

Electron microscopic image of a single human lymphocyte. Credit: Dr. Triche National Cancer Institute

Cells within a tumor are not the same; they may have different genetic mutations and different characteristics during growth and throughout treatment. These differences make treating tumors extremely difficult and often lead to tumor recurrence dominated by more aggressive tumor cells. Moffitt Cancer Center researchers are using mathematical modeling to characterize these differences within a tumor and hope that the results of their latest study will lead to better therapeutic treatments.

"Many tumors exhibit different metabolic behaviors compared to normal tissue; they consume more of the nutrient glucose and produce acid as a byproduct. This leads to an acidic environment that tumor cells are better adapted to live in and promotes the development of invasive cells." said Mark Robsertson-Tessi, Ph.D., an applied research scientist in the Integrated Mathematical Oncology (IMO) Department at Moffitt.

IMO researchers at Moffitt wanted to determine how differences in metabolic properties across the tumor affect cancer growth and treatment. They developed a mathematical model that examined the interactions between the metabolism of tumor cells and the surrounding normal tissue.

The researchers found that cells within the center of a tumor evolve to produce more acid and have a higher glucose metabolism than cells that are toward the outer edges of the tumor. This causes the central cells to become more aggressive. The aggressive cells will often move toward the outer edge of a tumor and become invasive.

The researchers wanted to determine how therapeutic treatments affect the metabolism and behavior of tumor cells. They discovered that treating the tumor when the heterogeneity was high could cause the less aggressive layer of cells toward the outside of the tumor to die and allow the central aggressive cells to become invasive faster.

Importantly, the researchers discovered a possible reason why one type of therapy, called antiangiogenic therapy, sometimes has failed in the clinic. Antiangiogenic therapy blocks the growth of blood vessels—a key nutrient source for the tumor. It was originally believed that this should starve a tumor of necessary nutrients and inhibit its growth. The team found that antiangiogeneic agents instead of starving the tumor actually selected for cells toward the center of the tumor leading to an even more aggressive and invasive tumor.

Mathematical models offer a unique perspective on how cancer develops that cannot be determined by simply studying genes or the surrounding tumor environment. "We strongly believe that only through the integration of mathematical and computational models with careful experimentation can we hope to bridge the gene-centric and microenvironment-centric views of cancer progression," said Alexander Anderson, Ph.D., Chair of the IMO at Moffitt.

More information: The article was published in the April 15 issue of *Cancer Research*. cancerres.aacrjournals.org/con … t/75/8/1567.full.pdf

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