

# Tumor cells engineer acidity to drive cell invasion

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Researchers at Moffitt Cancer Center and colleagues at Wayne State University School of Medicine investigated the acidity in solid tumors to determine if pH levels play a role in cancer cell invasion in surrounding tissues. They found that an acidic microenvironment can drive cancer cells to spread and propose that neutralizing pH would inhibit further invasion, providing a therapeutic opportunity to slow the progression of cancers.

Their study appeared in the Jan. 3 online release of *Cancer Research*, a publication of the American Association for [Cancer Research](#).

According to the study's corresponding author, Robert J. Gillies, Ph.D., chair of the Department of [Cancer Imaging](#) & Metabolism at Moffitt, acidity in solid tumors is the result of an increased fermentative metabolism combined with poor delivery of blood to tissues.

In this study, [tumor](#) invasion and pH were monitored in immunodeficient laboratory mice hosting a variety of tumors. "We monitored the test animals over time using microscopy and found that the highest regions of tumor invasion corresponded to areas with the lowest pH," Gillies explained. "Tumor invasion did not occur in regions with normal or near normal [pH levels](#). Furthermore, when we neutralized the acidity with oral sodium bicarbonate, the invasion was halted."

Researchers proposed that the acidic pH of the tumor [microenvironment](#) represents a "niche engineering" strategy on the part of tumor cells,

promoting invasion and growth of malignant tumors into surrounding [tissue](#). Niche engineering is a concept in ecology describes how plants and animals alter their environment to in ways that promote their own growth and survival over their competitors. "We have long regarded cancers cells as an invading species," said study co-author Robert Gatenby, M.D., chair of the Diagnostic Imaging Services and Integrated Mathematical Oncology departments at Moffitt.

A key to this process of adaptation and invasion is increased glucose metabolism in the tumor. "The vast majority of malignant tumors metabolize glucose at high rates," Gillies said. "We have proposed that there is a direct, causative link between increased glucose metabolism and the ability of [cancer cells](#) to invade and metastasize."

According to the research, elevated glucose metabolism is the cause of increased acidity in the tumor microenvironment. Most tumors develop an abnormal vascular network that tends to be poorly organized and leaky, disrupting blood flow and hampering the delivery of oxygen.

"This poorly organized vascular system has a two-fold effect on tumor acidity," explained Gatenby. "First, it subjects tumor regions to poor perfusion, which restricts oxygen and increases the rate of glucose fermentation. Second, the poor perfusion hampers the ability to eliminate the resulting acids, resulting in very low pH in surrounding tissues."

As tumor cells adapt to increasing acidity, niche engineering through normal cell death and new blood vessel formation occurs in the tumor and the immune response is suppressed.

"Tumor cells perform niche engineering by creating an acidic environment that is not toxic to the malignant cells but, through its negative effects on normal cells and tissues, promotes local invasion of

malignant cells," Gatenby said.

The researchers suggested that targeting this activity with buffers and other mechanisms aimed at increasing pH levels will likely provide a valuable alternative to traditional therapies focused entirely on killing tumor cells.

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