CELL METABOLISM AND CANCER

We have known for nearly a century that the metabolism of cancer cells can differ markedly from healthy cells. For example, cancer cells consume far more glucose to generate energy and to produce materials that support cell division. Until recently, these features were considered just another way cancer cells differ from healthy cells. But it is now becoming clear that these metabolic changes may be one of their driving forces. This insight will open the way to new approaches that treat cancer by disrupting cancer-cell-selective metabolic pathways, resulting in more effective and less toxic drugs as well as more precise ways to diagnose cancer.

The pathways that make up cellular metabolism are complex. Large networks of enzymes work together to convert food into energy and necessary chemical compounds. Cancer cells often abandon the efficient energy-producing pathways used by most cells and shift to alternative strategies that yield less energy but generate more materials needed to build new cells. Although this shift provides a growth advantage to cancer cells, it also represents a vulnerability because rapidly dividing cells can become dependent on these alternative pathways; interfering with them might be a powerful way to thwart tumor growth.

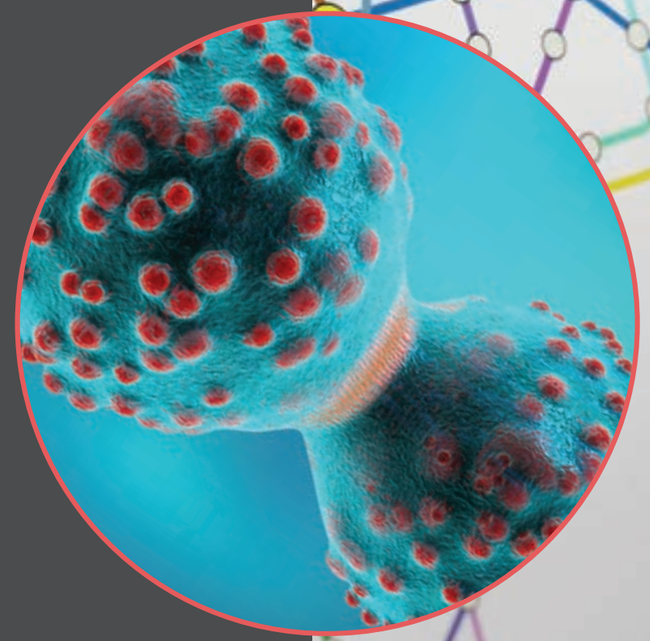
Some genes whose general involvement in cancer were identified long ago are now recognized to influence the way cells take up nutrients, convert food to energy and generate vital biological compounds. On the other hand, previously unsuspected genes and pathways are, in reality, acutely involved in tumor growth and survival. Identifying these culprits is important because they could lead to new targets for therapeutic intervention.

A first example of the importance of metabolism in cancer is the several metabolic genes discovered in CCR, that, when mutated, increase the risk of kidney cancer. Now it is known that mutations in metabolic genes contribute to a wide range of cancers, including cancers of the brain, prostate, pancreas and lung.

With new technologies that can detect thousands of different metabolites in tissue samples, it is now possible to identify the wide array of chemicals generated by cellular metabolism. These tools uncover how metabolic pathways are disrupted in cancer cells and how subtle changes contribute to tumor growth. Current studies aim to track how metabolism changes as cancer progresses and metastasizes, or as a tumor responds to anti-cancer therapies, especially when acquiring resistance.

Comprehensive elucidation of the metabolic landscape in cancer cells has the potential to guide the development of drugs that target metabolic pathways to deprive cancer cells of the biochemical resources on which they have come to depend. It is also possible that existing drugs that modify metabolism, such as those used to lower cholesterol or treat diabetes, will be useful in treating or preventing cancer.

A clinical goal is to comprehensively catalogue cancer-causing metabolites inside a patient's body and use the information to make treatment decisions. Using sensitive new clinical imaging technology, such as methods developed at the NIH Clinical Center, CCR investigators are beginning to do precisely that. With a deeper understanding of the relationship between cancer and metabolism, this type of imaging might one day be used to rapidly determine how aggressive a patient's tumor is, or to monitor how someone's cancer is responding to treatment.



Caption: A three-dimensional illustration of a cancer cell in the process of mitosis.

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