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Message From the Editor

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Finding ways to alter cancer's 'ecosystem' in our favor.

Often in science, big advances are made not through a sensational discovery, but by fundamentally changing the way we think about a problem. This happened in the field of cancer biology over a century ago when the surgeon Stephen Paget noted that the growth and spread of tumors depended in large part on the "soil," or the surrounding environment.

We now know that blood vessels, nutrients, and growth factors are all supplied to the tumor by surrounding cells and tissues that may not be cancerous, but are co-opted by cancer cells to change their behavior and create more permissive conditions for cancer cell growth and spread. "Bad Neighbors" highlights the details of the tumor microenvironment and, more importantly, addresses the two major opportunities that may result from further study. First, it can provide new targets for therapy, and second, it can allow for diagnostic tests that tell doctors what type of therapy might be most effective for a given patient.

The relationship between a tumor and the surrounding environment is complex, with each influencing the other. While the host may attempt to fight the tumor with inflammation and fibrosis (scarring), these physiological responses may actually aid the tumor. One of the biggest advances in microenvironment-based therapy has been anti angiogenic treatment that has improved survival in colon, lung, breast, and brain cancers. Other possible targets being looked at include certain growth factors and hypoxia (low oxygen levels that might bring about drug resistance and more aggressive behavior), as well as factors that induce cells to leave their primary site and spread to distant organs.

The tumor and surrounding tissue form a type of "ecosystem." And just as in other ecosystems in nature—think of the famous isolated ecosystem of the Galapagos Islands—over time, a very complex set of organisms emerge based on the environmental conditions. A tumor also undergoes evolution, except in a much faster time frame. The tumor and normal tissue around it eventually form a unique set of characteristics that differ from anyone else's tumor, and this is increasingly being used as the basis for personalized medicine.

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This evolution also creates the chance for tumors to become resistant to therapy—just as organisms evolve to adapt to their environment, so do tumor cells as they are exposed to different therapies and challenging growing conditions. Moreover, tumor cells can adapt to grow independent of the microenvironment and eventually spread to other organs, or even “re-seed” the primary tumor with slightly modified cells that now have “addresses” on their surfaces that home them to specific sites.

As for oxygen-deprived tumors, research has shown that in patients who received chemotherapy prior to surgery for breast cancer, the tumors that lacked oxygen were more resistant to chemotherapy. Based on this information and many other studies that have reached similar conclusions, investigators are using various creative approaches to modify the complex reaction to low oxygen (the hypoxia pathway) and trick cells into thinking they are not in a hypoxic state and thereby reverse the negative consequences.

So the study of the tumor “microecosystem” will open up ways to disable tumors with a combination of tailored treatments that reflect their evolutionary state. The tumor microenvironment is an old concept, but lots of new details of the inner workings of this system open up myriad possibilities that you will certainly be hearing more about in the future.