Metastasizing Cancer Cells Face Harsh Conditions

BY DAMIAN McNAMARA
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TORONTO — “Survival of the fittest" might be the best way to explain the genetic and molecular machinery behind cancer metastasis. Researchers believe that overexpression of some genes in melanoma and other cancers allows them to survive the very harsh conditions that occur as they leave a primary tumor, travel to a distant site, and establish a new location for malignancy. “It is a similar theme to Darwin with natural selection, although it works out in a microenvironment," Dr. Yuwen Zhou said.

“When I do this research I think this is a big deal. We still do not have a cure for metastatic melanoma, and next year another 900 of my patients in Canada will die from melanoma," Dr. Zhou said.

Melanoma was the sixth most common solid cancer for men in Canada in 2005 and 2006. There were 3,900 new cases last year. Of 840 deaths in 2006 from melanoma, 90% involved metastatic disease, said Dr. Zhou, who is on the faculty in the department of dermatology and immunology at the University of British Columbia, Vancouver.

There are some reasons for optimism, however. Understanding the molecular machinery might permit earlier intervention through better diagnostic or prognostic tools, Dr. Zhou said at the annual conference of the Canadian Dermatology Association.

Serum protein testing, for example, might lead to more accurate estimates of the prognosis. The melanoma-inhibiting activity (MIA) protein is detected in high amounts in 100% of patients with metastatic melanoma so far. “About 20% of patients with metastatic melanoma will have signs of this protein in their serum. If they are negative for MIA protein, not one of them developed metastasis over the past year," he said.

Genetic insights also may lead to new therapeutic targets. "Selective gene silencing may work to cause metastatic cells to die," Dr. Zhou said.

So how do invasive tumors develop? Metastasis occurs when genetically unstable cancer cells adapt to a tissue microenvironment from the primary cancer site to a faraway organ or site. Metastasis is a common event in many cancers, particularly melanoma. The ability to metastasize makes melanomas resistant to standard therapies, and most recur even after apparent cure of the primary lesion.

The vast majority of the most aberrantly upregulated genes in cancer patients are able to work in concert to modify the microenvironment to the patient’s advantage. Before these breakthrough cells become "little tumor slugs," they have to overcome survival barriers, stimulate host defenses, undergo epithelial-mesenchymal transition, alter cell adherence, and increased genomic instability.

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