# Hundreds of genes distinguish patients likely to survive advanced melanoma

November 9 2009

Although the chances of surviving advanced melanoma aren't very good with current therapies, some patients can live for years with cancer that has spread beyond the skin to other organs. Now it may be possible to identify which patients are more likely to survive by analyzing the activity of hundreds of genes involved in the immune response and gene proliferation, according to researchers at NYU Langone Medical Center.

In a new study to be published online this week in the Proceedings of the National Academy of Sciences, the researchers used a powerful technique called DNA-microarray technology to find 266 genes associated with shorter or longer survival among 38 patients whose melanomas had recurred after being surgically removed.

Although it is early days, such genetic information may help decide the best course of treatment for patients with advanced disease. "If we could actually understand what was happening in those patients, within the tumor itself, perhaps we'd be able to help them in terms of what therapy they might go on," said Nina Bhardwaj, MD, PhD, professor of medicine, pathology and dermatology at NYU Langone Medical Center and the study's senior author.

The collaborative study, led by graduate student Dusan Bogunovic, provides some tantalizing hints about the underlying mechanism of melanoma. "We found that patients who survived longer had gene activity consistent with an immune response," Dr. Bhardwaj said. "Patients who didn't survive as long didn't have an up-regulation of those

genes but tended to have higher levels of genes associated with cell proliferation, suggesting that if your cells are growing more actively, the tumor is going to grow faster."

This year melanoma is expected to strike 68,729 people in the United States, and some 8,650 people with the disease are expected to die, according to the American Cancer Society. Excessive exposure to sunlight, a fair complexion, a family history of melanoma, and numerous moles, among other factors, place people at higher risk. With early detection and prompt treatment, however, melanoma is highly curable.

To help predict survival, doctors routinely assign melanoma to one of four stages, based on tumor size and location. Currently, the thickness of a melanoma at the time of diagnosis, sometimes combined with a procedure called sentinel node biopsy, is used to assess whether a patient's tumor will recur and if additional treatment with immunotherapy is warranted after the cancer is removed. Patients with early stage melanoma, called stage I cancer, have the thinnest lesions and are therefore the least likely to have a recurrence of their original cancer.

The prognosis usually worsens as the tumor extends deeper into the skin. By Stage III, the melanoma has generally spread beyond the skin to lymph nodes draining the tumor, and five-year survival rates begin dipping below 69 percent.

By the time the melanoma has metastasized to lymph nodes or organs far away from the initial tumor site, considered Stage IV disease, patients rarely survive more than a year.

But the staging technique can be ambiguous. Stage III has been subdivided into three groups according to the extent of the tumor growth within the lymph nodes. The latter two subgroups, IIIb and IIIc, correspond to more advanced disease but have proven nearly

indistinguishable as indicators of long-term survival.

When Dr. Bhardwaj's team added genetic profile information to the traditional staging technique, survival predictions improved substantially. Given that the researchers had found a bevy of cell growth genes associated with a poorer prognosis, she said, they tested whether they could obtain similar results by staining a tumor specimen to get its mitotic index. The measure of of cell proliferation not only helped distinguish between Stages IIIb and IIIc, but also proved to be the single strongest predictor of patient survival.

The study also found that two other measures of immune response, including the infiltration of tumors by T cell specialists or by the immune system's larger collection of white blood cells, also improved predictions when added to the traditional staging system.

"It's exciting, because we finally have some parameters that might help distinguish between these two stages in terms of survival, and possibly address how these patients should be treated," Dr. Bhardwaj said. She cautioned, however, that the study must still be validated with a much larger, independent group of patients.

Source: New York University School of Medicine (news : web)