Targeted therapy plus chemotherapy may pack 1-2 punch against melanoma

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By targeting and disabling a protein frequently found in melanoma tumors, doctors may be able to make the cancer more vulnerable to chemotherapy, according to a new study by researchers in the Duke Comprehensive Cancer Center.

“We tested a compound that can weaken the tumor by targeting a protein expressed on the surface of a melanoma cell. When chemotherapy was applied to the tumor in this weakened state it was much more effective compared to conventional therapy alone,” said Douglas Tyler, M.D., a surgeon at Duke and the Durham Veterans Affairs Medical Center, and senior investigator on this study. “These results are extremely significant because they may help us better treat patients with this deadly condition.”

Although this study was done in laboratory rats, a clinical trial applying the same concept to humans has already begun at four comprehensive cancer centers nationwide, including Duke.

The researchers published their findings from the animal study in the May 15, 2008 issue of the journal *Cancer Research*. Funding for this study came from the United States Department of Veterans Affairs, the Duke Institute for Genome Sciences & Policy, the Duke Comprehensive Cancer Center and Adherex Technologies, the company developing the compound that was tested in combination with chemotherapy.

After being implanted with melanoma tumors, rats were given a drug

known as ADH-1, which makes it difficult for cells to bind properly to one another. The animals were then given one of two types of common chemotherapy drugs, melphalan and temozolomide.

“We found that the response to ADH-1 in combination with melphalan was more dramatic than the response to the drug in combination with temozolomide," Tyler said. "The reason may be that the melphalan was infused directly into the affected area while temozolomide is given systemically.”

The researchers saw a 30-fold reduction in tumor size following treatment with ADH-1 and melphalan chemotherapy compared to chemotherapy alone. Tumor size shrunk about twofold in response to ADH-1 and temozolomide, Tyler said.

“We saw a complete regression of the tumors in the animal model when we used the regional melphalan chemotherapy in combination with ADH-1, which is far better than anything we have seen before with the chemotherapy alone,” Tyler said. “Furthermore, the addition of ADH-1 produced no additional side effects, which is an important consideration in cancer treatment.”

Regional infusion of chemotherapy for melanoma is given under surgical conditions, through the artery and vein in the affected limbs. Melanoma often affects people on their extremities, with a common scenario being a mole that appears on the foot and then spreads up the leg.

“These results clearly demonstrate the effectiveness of combination therapies,” said Christina Augustine, Ph.D., a researcher in Duke’s Department of Surgery and lead investigator on the study. “Used alone the ADH-1 really didn’t confer any significant benefit but in combination with the melphalan chemotherapy, we saw a powerful one-two-punch effect.”

The incidence of malignant melanoma is increasing at a rate faster than any other cancer, with 60,000 new cases expected to be diagnosed this year in the United States. Melanoma that has spread beyond the primary site is rarely curable, and treatment options are limited; even when it is treated, the response rates are typically poor and most people die within six to nine months.

Source: Duke University