

Getting to the roots of breast cancer

The lesson learned in eradicating dandelions from your yard could apply in treating breast cancer as well, said researchers from Baylor College of Medicine in Houston in a report that appears online today in the Journal of the National Cancer Institute.

“It’s not enough to kill the dandelion blossom and stalk that appear above ground,” said Dr. Michael Lewis, assistant professor of molecular and cellular biology and a faculty member in the Lester and Sue Smith Breast Cancer Center at BCM. “You have to kill the root beneath the soil as well.”

In a study involving women with breast cancer, he and colleagues at BCM showed that while conventional anti-cancer drugs can kill the bulk of breast cancer tumors, they leave behind many of the breast cancer stem cells from which tumor cells arise, setting the stage for the tumor to come back.

“What we found is that one reason chemotherapy frequently does not work is that you kill the bulk of the tumor but leave many of the stem cells behind,” said Lewis. “It appears that these cells, by their nature, are resistant to the effects of anti-cancer drugs.”

However, treatment with the drug lapatinib and anti-cancer drugs appears to kill both the tumor and the stem cells, reducing the threat of relapse in patients whose tumors carry a protein marker called HER2, Lewis said.

In their study, he and colleagues took biopsies from the tumors of patients before and after treatment.

The study had two parts. In the first, 31 patients whose tumors did not have the HER2 marker received conventional chemotherapy. In the second part of the study, 21 patients whose tumors carried the HER2 marker, received treatment with lapatinib and two other common breast cancer drugs. (The HER2 marker meant that the tumors would be susceptible to lapatinib.)

The researchers stained the samples to highlight the subset of tumor cells that contained the stem cells, which can be identified by the presence of certain markers on the cell surface. This enabled them to estimate the percentage of stem cells in the biopsy. In addition, stem cells in the laboratory can grow into colonies of cells that scientists call mammospheres. Because of this, they could also measure those to estimate what proportions of stem cells are present in a sample.

In the group that received conventional chemotherapy, the number of tumor cells decreased markedly. However, after the treatment, the proportion of cancer stem cells (identified by special markers and mammosphere formation) to differentiated tumor cells was greater than before treatment. In other words, there was a higher percentage of stem cells because the chemotherapy killed the regular tumor cells but left stem cells behind.

In the group that received lapatinib, the number of tumor cells again decreased dramatically. However, the percentage of breast cancer stem cells did not change or even went down slightly (although the change did not reach statistical significance). Consistent with this, the percentage of patients who received lapatinib had significant tumor shrinkage at greater rates than that seen in patients who received conventional therapy.

“The tumor shrank dramatically,” said Dr. Jenny Chang, associate professor of medicine at BCM and medical director of the BCM Breast Care Cancer Center. “But in contrast to treatment with conventional chemotherapy, the relative proportion of stem cells did not go up. This means the stem cells were killed off with the same frequency as the bulk of the tumor. This is the first time this has been demonstrated.”

Finding drugs that work specifically against stem cells is a course for the future, said Lewis. He plans to start by characterizing the markers specific to breast cancer stems cells, and inhibiting them one-by-one.

Source: Baylor College of Medicine

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