Genetically engineered MSCs kill metastatic lung cancer cells in mice

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Researchers in London have demonstrated the ability of adult stem cells from bone marrow (mesenchymal stem cells, or MSCs) to deliver a cancer-killing protein to tumors.

The genetically engineered stem cells are able to home to the cancer cells, both in culture and in mouse models, and deliver TNF-related apoptosis-inducing ligand (TRAIL), destroying the tumor cells while sparing normal cells.

The research will be presented on Tuesday, May 19, at the American Thoracic Society's 105th International Conference in San Diego.

"Present oncological therapies are limited by host toxicity," said Michael Loebinger, M.D., M.A, who, along with S. M. Janes, M.D., Ph.D., conducted the research at the Centre for Respiratory Research at the University College of London. "They are also limited by cancer resistance and may not destroy cancer stem cells."

With these experiments, the investigators combined two disparate areas of research that they believed held promise for treating cancer. Studies had shown that MSCs can be used as vectors to deliver anti-tumor therapy, while other studies found that TRAIL killed cancer cells, but not normal cells.

For their experiments, Drs. Loebinger and Janes identified those cells likely to be resistant to therapies (cancer cells that have characteristics of

stem cells) and found that they were just as likely to be destroyed as tumor cells by this novel therapy.

In culture, the stem cells caused lung, squamous, breast and cervical cancer cells to die (all p

In mice, the researchers showed that the stem cells could reduce the growth of subcutaneous breast tumors by approximately 80 percent (pmetastases and could eliminate lung metastases in 38 percent of mice compared to control mice, all of which still had metastases (p=0.03).

It is the first study to intravenously introduce MSCs that have been genetically modified to deliver TRAIL. Drs. Loebinger and Janes chose the breast cancer cells for both models because in their in vitro experiments, the MSCs "demonstrated a particularly strong homing to breast cancer cells."

"Breast cancer tumors are a good model of metastases," added Dr. Loebinger, "but our plan is to test the engineered stem cells with other models, including lung cancer."

While not fully understood, Dr. Loebinger added, the homing of the engineered cells appears to be a characteristic of MSCs themselves.

The authors conclude that, "this is the first study to demonstrate a significant reduction in tumor burden with inducible TRAIL-expressing MSCs in a well-controlled and specifically directed therapy."

They believe that human trials of TRAIL-expressing MSCs could begin in two or three years.

Source: American Thoracic Society (news : web)