Drug shows cancer stem cells not invulnerable

- 18:21 13 August 2009 by Ewen Callaway
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A promising new cancer drug targets and kills the pernicious tumour cells responsible for metastasis and relapse. It is far too early to test the drug, called salinomycin, in humans, but the findings offer hope that the so-called cancer stem cells will eventually prove vulnerable to treatment.

"It's been thought that these cells are responsible both for metastasis and for recurrence following anti-cancer therapy," says Piyush Gupta, a molecular biologist at the Broad Institute of MIT and Harvard in Cambridge, Massachusetts, who led the new study. "There's been a lot of evidence to suggest that cancer stem cells are resistant to a variety of cell-death-inducing agents."

Gupta's team found that salinomycin kills breast-cancer stem cells at least 100 times more effectively than another popular anti-cancer drug. And mice implanted with human breast-cancer cells and later treated with salinomycin showed fewer signs of metastases than mice given a standard cancer therapy.

**Hard to find**

One reason cancer stem cells have been hard to target with drugs is their rarity in tumours and in laboratory cancer-cell cultures. This makes it difficult to hunt for drugs that selectively kill the cells.

To sidestep this problem, Gupta and his colleague Tamer Onder, formerly of the Whitehead Institute for Biomedical Research, also in Cambridge, reprogrammed normal skin cells into cells with some of the properties of cancer stem cells. Like normal cancer stem cells, the reprogrammed cells proved impervious to chemotherapy.

Next, Gupta and Onder's team tested about 16,000 different drugs against the reprogrammed cells: 32 of those compounds killed the reprogrammed stem cells, but not normal skin cells. Of the 32, salinomycin proved one of the most effective and the easiest to obtain in large quantities, Gupta says.

Tests in laboratory-cultured human breast-cancer cells confirmed the drug's potency. Mice injected with human breast-cancer cells – a common model for the disease – developed fewer aggressive tumours when treated with salinomycin, compared with a commonly used anti-cancer drug called paclitaxel.

**Next steps**

Further experiments in animals are needed before even thinking of trying salinomycin in humans, Gupta says. The researchers tested the drug on genetically homogenous laboratory cultures, so it also remains to be seen whether it will have the same effect on tumour cells collected from living people.
Little is known about the drug's safety, or whether it would find its way through the bloodstream to human tumours.

Gupta says the significance of his team's result is proof that cancer stem cells aren't invincible to drugs. "They do have weaknesses and we've essentially shown an approach to find them systemically," he says.