New genes identified that regulate the spread of cancers

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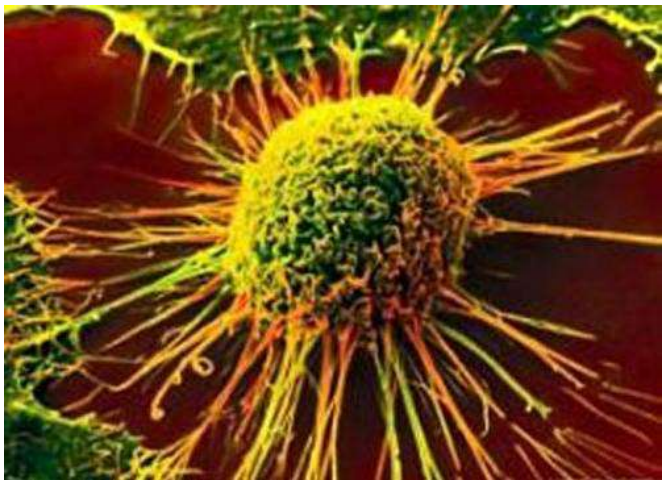

Research led by the Wellcome Trust Sanger Institute has discovered a new biological target for drugs to reduce the spread of tumours in cancer patients. Published in *Nature* today, the study with genetically modified mice found 23 genes that are involved in regulating the spread of cancers. The researchers showed that targeting one of these genes—Spns2—led to a three-quarters reduction in tumour spread.

The spread of tumours—metastasis—to other sites in the body is the leading cause of death for cancer patients. Up to 90 per cent of cancer deaths are due to this, however the process that regulates the spread of tumours is very poorly understood.

To find out what genes in the body could influence metastasis, the researchers looked at how tumours spread in genetically engineered mice that were missing specific single genes. They screened 810 unique genes and identified 23 genes that either increased or decreased the spread of skin tumour cells to the lungs. Many of these genes also caused an alteration in the immune system, such as changing the bodies' ability to fight infection.

Removal of the Spns2 gene caused the largest change, reducing spread of tumours to the lungs by approximately four times. The researchers then looked at the effect of this gene on the spread of other cancers, from colon, lung and breast, and showed that taking out Spns2 also reduced the metastasis of these cancers.

Dr David Adams from the Wellcome Trust Sanger Institute, said: "Loss of the Spns2 gene causes the greatest reduction in the formation of tumour colonies and represents a novel therapeutic target. We found that mice lacking Spns2 have a different ratio of immune system cells than normal, which seems to prime the immune system to remove cancer. Drugs that target this could help reduce or prevent the spread of tumours through the body."

Before this study, the Spns2 gene was known to affect the immune system, but was not implicated in tumour spread. It codes for a protein that transports a lipid, S1P, which signals to the immune system. Without this transporter protein, the signaling doesn't work properly and results in changes in the proportion of different immune cells in the body.

Dr Anneliese Speak from the Sanger Institute, said: "This work supports the emerging area of immunotherapy, where the bodies' own immune system is harnessed to fight cancer. Drugs could be designed to bind to the S1P transporter, preventing it from working and causing advantageous changes to the immune system. Investigation of further targets in the Spns2 pathway, or other targets identified in this study could help develop potential therapies."

Dr Justine Alford, Cancer Research UK's senior science information officer, said: "This study in mice gives a new insight into the genes that play a role in cancer spreading and may highlight a potential way

to treat cancer in the future. Cancer that has spread is tough to treat, so research such as this is vital in the search for ways to tackle this process."

More information: Louise van der Weyden et al, Genome-wide in vivo screen identifies novel host regulators of metastatic colonization, *Nature* (2017). DOI: 10.1038/nature20792

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