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Two genes cooperate to cause aggressive leukemia

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Two genes, each one of which is known to cause cancer on its own, together can lead to aggressive leukaemia. This is the conclusion from new research carried out on gene-modified mice at the Sahlgrenska Academy at the University of Gothenburg, Sweden. The discovery has surprised scientists, and may lead to new treatments.

The two genes are often present in mutated form in acute leukaemias, but the mutations rarely occur together. Scientists have previously believed that the two mutated genes have exactly the same function: each one alone will lead to increased activity of a carcinogenic protein known as "RAS". This protein, in turn, causes blood cells to proliferate more rapidly.

"This is a surprising discovery that suggests that there is a mechanism behind the development of cancer that has not yet been recognised. It opens the way for new methods of fighting blood cancer cells with NF1 mutations", says Associate professor Martin Bergö, who leads the research at the Wallenberg Laboratory at the Sahlgrenska Academy.

One of the genes codes for the RAS protein, which is a known accelerator for cell proliferation in several forms of cancer. The other gene codes for a protein known as "NF1", which is known to reduce the activity of the RAS protein.

The research group at the Sahlgrenska Academy has previously used two different types of mouse models, one of them with the RAS-mutation

and the other with the NF1-mutation. Both mutations individually cause a slowly progressing leukaemia to develop in the mice. The research group has now combined the two animal models and shown that a very aggressive form of acute leukaemia develops in mice with mutations in both genes.

"The corresponding increase in the RAS signalling cannot explain the severe increase in disease aggressiveness, and this means that the NF1 protein may play a different role in the development of the leukaemia than we originally thought and may not involve the RAS protein at all. The discovery opens the possibility of developing new treatments for patients who have mutations in NF1", says Martin Bergö.

The research group is now collaborating with another research group at the Sahlgrenska Academy, investigating the role that the NF1 protein plays, and how these new results can lead to new treatment strategies.

Source: University of Gothenburg (news : web)