

Gene known to protect against cancer can also promote tumor growth: study

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Can a gene simultaneously protect against cancer and favor its growth? Researchers at the Spanish National Cancer Research Centre have discovered a gene with this double-edged property and suspect there may be many more that share it. In the words of Oscar Fernandez Capetillo, head of the group responsible for the study, this gene "can be both Dr. Jekyll and Mr. Hyde, in that it can either protect us against the appearance of tumors or promote tumor growth".

The study, appears this week in the <u>Journal of Experimental Medicine</u>, with Andrés J. López-Contreras and Paula Gutiérrez Martínez as first authors, focuses on the activity of Chk1, a gene known for its tumour suppressing effect. It is what Fernández-Capetillo calls "a genome guardian, a gene that keeps our genome free of mutations and, therefore, protects against the development of tumours".

The team wished to ascertain whether the tumour-protective effect of Chk1 was magnified in organisms with a larger quantity of the protein it codes for, so they created a mouse with three copies of the gene instead of the normal two. They then extracted and cultured the animal's cells and turned them cancerous with the aid of other genes. What they observed confounded all expectations: the cells became malignant more easily when carrying an extra copy of Chk1.

The reason for this paradox is that Chk1 has a beneficial effect on healthy cells, but also benefits tumour cells once they have established themselves in the body.



The dual role of Chk1

"Initially, Chk1 prevents the <u>appearance</u> of tumours, by limiting the spontaneous mutations that take place in our cells", remarks Fernández Capetillo. "This is the Dr. Jekyll side. However, advanced tumours exhibit extensive damage to their DNA and it is here that Chk1 comes to the tumour's aid by reducing the damage built up in its genome", he continues.

Chk1 works by protecting against replicative stress, a kind of damage that occurs in cells' genetic material as they divide. Some tumours indeed suffer continuous lesions in their genome due to their high division rates.

"The presence of 'genome guardians' like Chk1 may favour the growth of this kind of tumour by lessening its lesion load", explains López-Contreras.

"This study sheds light on why Chk1 is overexpressed in many tumours, when we would intuitively suppose that what favours the development of cancer is the loss of protective genes," the scientist concludes.

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