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MicroRNA switches off tumour protection

The microRNA miR-21 suppresses the production of tumour suppressor Pdcd4, which protects cells from developing cancer. Researchers at the DKFZ have now found out that colorectal cancer cells in particular lack Pdcd4, while these cells have an oversupply of miR-21, which promotes the spread of malignant tumours in the intestine.

It was not so long ago that microRNAs were discovered. Only a couple of years ago, scientists found out how these tiny molecules – short transcripts of the hereditary substance, DNA – contribute to regulating life in a cell: They bind to other DNA transcripts that are necessary for protein production. The binding of microRNA leads to the blocking or even degradation of these protein-building instructions before they can even be used for protein production. In this way, the cell controls the type and amount of proteins produced.

If the cell's natural self-control is overactive, it can also cause damage by blocking the production of useful proteins. This is exactly what happens to the Pdcd4 protein in colorectal cancer cells, as reported in a recent study by the clinical cooperation unit "Molecular Oncology of Solid Tumours" at the German Cancer Research Centre (DKFZ). Pdcd is what is called a tumour suppressor. It protects cells from transforming into cancer cells. If the substance disappears from a cell, the risk of cancer increases. A research team headed by Dr. Heike Allgayer has found out that the microRNA miR-21 in colorectal cancer cells suppresses the production of Pdcd4.

Studying ten different types of colorectal cancer cells, the team found out that the more miR-21 was present in the cells, the less Pdcd4 they produced. When the scientists switched off part of the miR-21 present, Pdcd4 levels in the cells rose. At the same time, cancer-typical characteristics of the cells also became weaker when more tumour protection protein was present. Thus, invasive growth capacity was significantly reduced and the cells formed fewer metastases in natural tissue. If, however, the researchers treated the cells with additional miR-21, the effects were exactly the opposite.

The researchers were also able to identify the target for miR-21 on the building instruction of the Pdcd4 protein. To this end, the corresponding region of the Pdcd4 gene was inserted into an artificial gene construct, which was much more active the less miR-21 was present. Following a small genetic modification at the target, miR-21 no longer had any influence.

Literature:
Irfan Asangani, Kabeer Rasheed, Dessislava Nikolova, Joerg Leupold, Nancy Colburn, Stefan Post, Heike Allgayer: MicroRNA-21 (miR-21) post-transcriptionally downregulates tumor suppressor Pdcd4 and stimulates invasion, intravasation and metastasis in colorectal cancer. Oncogene 2007. DOI: 10.1038/sj.onc.1210856

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