NewsBlog:

A complement for cancer?

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A protein belonging to part of the immune system that researchers once hoped to harness to attack cancer cells actually spurs tumor growth, according to a study reported in *Nature Immunology.*

Researchers knocked out a receptor for one of a group of thirty proteins called **complement protein** part of the body's normal immune defense repertoire, and observed decreased tumor growth in a mou model.

"This elegant study puts complement in the row of factors that can enhance tumor growth," said Arko Gorter, an immunologist at Leiden University Medical Center in the Netherlands, who was not involve in the study.

Complement cascade is made up of about thirty proteins that cleave one another in a series of reactions that radiates from an initial binding site on a pathogen. Best known for its action against bacteria, complement proteins can kill a bacterium without the help of immune cells by burrowing int the bacterial membrane and creating a doughnut-shaped hole. Researchers had thought complement could be used to fight cancers as part of an antibody-based vaccine, as antibody binding is one of the factors that can set off a complement cascade.

However, some complement components, such as complement 5a (C5a), act as strong mediators of inflammation. Because in some cases inflammation can promote cancer growth, John Lambris at the University of Pennsylvania and colleagues decided to investigate whether C5a instigated tumor growth through an inflammatory pathway.

Lambris' team developed a knock-out mouse for the C5a receptor, which is expressed on a number of tissue types. They observed less tumor growth, as well as an increase in anti-tumor CD8+ T cells. The result suggested that the absence of the C5a receptor on suppressor cells blocks the activation of the cells, allowing the tumor fighting cells to attack the tumor.

But according to Gorter, this mechanism may not be the only way that complement excites tumor growth. Tumor microenvironments are complex, said Gorter: "A tumor consists of the real cancer cell the stroma, and a third component: the inflammatory cells," which can be active or suppressed. While it's clear that complement plays an important role in tumor growth, given the complexity of the tumo microenvironment, it's not completely clear how complement exerts its function, or what triggers it, said.

What remains to be seen, said Gorter, is "how general this mechanism is." Is the C5a effect the researches observed particular to the mouse model used? Will it be true for other cancers? Would it translate to human disease? Despite these questions, which must be addressed with further studies, sa Gorter, "It is still an impressive study showing to my knowledge for the first time that complement (C5a) can promote tumor progression."