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Safety And Effectiveness Of Therapeutic Virus That Fights Cancer Enhanced By Mayo Clinic Researchers

Mayo Clinic researchers working with colleagues in Germany have devised a much-needed multilevel safety feature for viruses used to treat cancer. In the process of making cancer-killing viruses more specific to cancer tumor cells, they report having improved the therapeutic effectiveness of viruses. They did this by engineering a modified measles virus that turns on only in the presence of secretions specific to malignant cancer cells.

In effect, the Mayo Clinic virus makeover uses proteins secreted by cancer cells as the unique key to the virus' ignition. Their report on the topic appears in the August edition of Cancer Research (http://cancerres.aacrjournals.org/).

The investigation was performed in laboratory mice that were transplanted with a human cancer. The process is still experimental -- and thus, years away from clinical use in humans. However, the Mayo results may be immediately useful in designing improved cancer treatments for humans. "Our work shows that oncolytic measles virus particle activation can be made dependent on substances secreted by cancer cells, and this enhances safety," explains Roberto Cattaneo, Ph.D., lead researcher on the Mayo team. "By doing this, our study broadens the safeguarding strategies possible to tightly restrict the targeted virus to cancer cells."

Significance of the Mayo Clinic Research
The Mayo researchers say their contribution is a key advance because it provides a method of designing a therapeutic virus that is safe, stable and that reliably targets and kills cancer cells. Importantly, it appears to greatly reduce the possibility that the virus would erroneously turn on and harm the patient by causing unintended infection.

As such, the Mayo innovation of the cancer-activated virus is a helpful safety advance for the promising experimental field of "oncolytic virotherapy." The phrase refers to the natural ability of certain viruses to kill cancer cells. It's a promising approach that has been known for nearly a century -- but constrained by safety concerns. Measles virus is one example of an oncolytic virus. For example, the live attenuated Edmonston measles vaccine strain can reduce or eliminate human lymphoma, myeloma, ovarian cancer and glioma tumors that are transplanted into laboratory mice.

Enhanced Safety and Effectiveness
The success of oncolytic virotherapy depends on restriction of viral growth to cancer cells --and only cancer cells -- to prevent unintended rogue infections elsewhere in the healthy body. The Mayo cancer-activated virus adds one more layer to a multiple safeguard system, so it now consists of three levels. The resulting enhanced security system now works at the level of:

* activation of the virus particle

* receptor recognition necessary for the virus to enter a cancer cell

* ability of the virus to multiply preferentially in cancer cells

These multiple safeguards are specific to and dependent on cancer cells -- and are therefore vital to fully transforming viruses into safe therapeutic agents.

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Collaboration and Support
Others on the research team include: Christoph Springfeld, M.D., Ph.D.; Veronika von Messling, D.V.M.; Marie Frenzke and Guy Ungerechts, M.D., Ph.D. In Langen, Germany, Christian Buchholz, M.D., collaborated. The work was supported by Mayo Clinic and the Siebens Foundation, the National Institutes of Health and research scholarships from the German research foundation and the Bundesministerium für Bildung und Forschung.

Contact: Bob Nellis
Mayo Clinic