MedicalXpress

A better delivery system for chemotherapy drugs

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Because cancer cells grow very quickly, chemotherapy is designed to target cells whose numbers grow rapidly. But this treatment comes with a heavy price — many healthy cells essential for body functions are also targeted and killed by the toxin. This dangerous side-effect has prompted researchers to seek better and more selective ways to kill cancer cells inside the body.

Prof. Daniel Wreschner of Tel Aviv University's Department of Cell Research and Immunology is now developing new antibodies — proteins produced by the immune system to fight infection — that bind to and kill off cancer cells exclusively. These antibodies, which target the cancer cells by binding to a protein called MUC1, can be used as an efficient drug delivery method, depositing a parcel of toxins directly into the belly of the diseased cells.

Prof. Wreschner's goal is to improve current methods of using antibodies to induce cancer cell death by utilizing different sub-regions in the MUC1 protein itself, which he believes are a superior target. His method has been shown to produce antibodies with a better ability to bind to cancer cells, which may heighten the efficacy of the antibodies and the toxins attached to them in treating cancer.

Recently reported in the journal *Cancer Research*, this research was carried out in collaboration with Ph.D. student Edward Pichinuk and undergraduate student Lotem Weiss in Prof. Wreschner's lab; Dr. Nechama I. Smorodinsky and Prof. Itai Benhar of the Department of

Molecular Microbiology and Biotechnology; and Dr. Daniel B. Rubinstein of the National Institutes of Health in the US.

Producing a stronger bond

In the transition from normal to cancerous, cells go through specific changes, including differences in make-up of the proteins on the cell surface or membrane. MUC1 is one of the proteins that are overproduced in many types of cancer, including breast and pancreatic cancers and leukemia. Labs around the world are working on methods to use this protein in order to accurately identify, access, and destroy cancer cells.

Currently, researchers are developing antibodies that target the "tandem repeat" of the protein, a section that repeats itself many times and therefore acts as a large bull's eye for antibodies. But targeting this section has a crucial flaw. "The tandem repeat is in the alpha section of the protein," explains Prof. Wreschner. "This alpha section can detach from the cell and be ejected into the bloodstream. At that point, the antibodies will bind to the alpha section in the blood, diminishing their ability to bind to the cancer cell."

But Prof. Wreschner is looking at MUC1 from a fresh perspective. His team's objective is to produce antibodies that have a much higher ability to bind to the proteins on the cell membrane. To do so, he is targeting the SEA domain of the protein, the "junction" which attaches it to the cell membrane. In the lab, this antibody has proven to have a high ability to bind to, enter, and then kill the diseased cell with its attached parcel of chemotherapy toxins. It is superior to antibodies already in use.

Addressing more cancer varieties

Prof. Wreschner says that there is much more research and development to be done before the antibody is available as a treatment option. He is looking for funding partners in order to bring it to a clinical stage.

While there are other FDA-approved medications on the market that use these principles, including Herceptin, used to treat breast cancer, and Erbitux, a treatment for colorectal and head and neck cancer, the advantage to the new antibody is that MUC1 is produced in a higher percentage of cancers. "People who are not eligible to be treated by antibodies already on the market could, following more research and development, likely be eligible for this one," Prof. Wreschner adds.

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