News
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*****Ranney presents findings of magnetic targeting for drug delivery to organs.

DALLAS -- Dallas scientists have shown that they can use magnetism to help the body resist infection by targeting drugs to a specific organ.

Dr. David Ranney, assistant professor of Pathology and director of the Laboratory of Targeted Diagnosis and Therapy at The University of Texas Health Science Center at Dallas, reported the findings at the meeting of the Federation of American Societies for Experimental Biology in St. Louis April 3.

Ranney's new technique involves tiny spheres of protein, one-twentieth the size of a red blood cell, containing magnetite and a peptide that attracts circulating neutrophils (white blood cells). The microspheres of human albumin were injected into the bloodstream of rats and magnetically targeted to the lungs where they dissolved to release the peptide hormone FMLP (N-formyl-methionyl-leucyl-phenylalanine). The FMLP attracted neutrophils to the area, enhancing the body's resistance in the targeted tissue.

The magnetite is the guide for the spheres. An external magnet placed at the tissue to be targeted stops the magnetite-containing microspheres in the capillaries and holds them there long enough to pass through the capillary walls into the tissue.

"Within five minutes they pass through the capillaries into the tissue, and the drug or hormone is time-released in the tissue from 15 minutes to 10 hours," says Ranney. "This is the first time that a biomodulator, a substance that changes the host response, has been entrapped, released and tested in vivo. This technique has one of the highest levels of targeting of any system devised -- 80-90 percent of the hormone reached the targeted tissue."

About five years ago when Ranney was at Northwestern University, he and others reported using the technique to deliver a cancer drug, Adriamycin, to tumors in rats. A dose one-tenth the size of the normal chemotherapy dose caused regression of sarcomas in 92 percent of the animals.

"Fighting a tumor with a freely circulating drug is like waxing your kitchen floor by standing at the front door and dumping a tub of wax into the house," says Ranney. "Most of the wax will end up on the carpet, but some of it will probably get to the kitchen and wax it. In this case, the carpet is the liver, the gastrointestinal tract, the hair that falls out --"

With drugs taken orally or by the usual kind of injection most of the drug goes to the liver, spleen and bone marrow and is wasted and often toxic. With targeted drugs, much smaller doses can be directed to the area or the tumor that needs treatment, and with only a small amount wasted, very little of the drug circulates throughout the body. This would mean a great reduction in side effects.

Ranney cautions that the techniques are still at least two years away from human experimentation. He was one of three inventors of the microsphere production technique at

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Northwestern and is currently testing it in conjunction with the Eli Lilly and Company.

Possible future uses of the target technique include:

*treatment of burns, trauma, immunosuppression, cancer (Hodgkin's disease) or severe localized infection;

*testing effectiveness of drugs, especially in arthritis or adult respiratory distress syndrome following trauma;

*targeted gene splicing in a specific area;

*increased efficiency of monoclonal antibody drug delivery;

*enhancement of organ images done with nuclear magnetic resonance.

Transplant recipients may die of infection because their immune systems are suppressed by drugs to avoid rejection of the transplanted organ. With this technique, says Ranney, the immunosuppressive drug can be delivered only to the area of the new organ, leaving the immune system intact in the rest of the body.

So far, at the usual doses, the magnetic microspheres show no adverse effects in animals. The albumin is dissolved and absorbed by the body. The drug acts mainly in the target organ where it is later degraded. The magnetite breaks down partly into a soluble form of iron, which is excreted in the urine. Most of the remaining magnetite is removed by white blood cells and accumulates in the liver. "It is non-inflammatory in our studies," says Ranney. "We know also that coal miners who breathe in magnetite can accumulate the compound in their lungs for years without ill effects."

The researcher is trained as a pathologist, immunologist, biochemist and surgeon.

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