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Inside job: new radioactive agents for colon cancer work inside cells

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Johns Hopkins scientists have developed a potentially novel way to fight colorectal cancer using tiny molecules to deliver potent barrages of radiation inside cancer cells, unlike current treatments that bind to the surface of cells and attack from the outside and cause unwanted side effects.

In laboratory studies with normal and cancer cells, the new radiation delivery system proved able to specifically target colon cancer cells, and what's left over is likely to be easily filtered out by the kidneys because the delivery system's molecules are so small.

As reported online in PLoS One on October 3, Hopkins colorectal cancer specialists John Abraham, Ph.D., and Stephen Meltzer, M.D. -working with the notion that small molecules generally make better treatment packages-designed small bits of protein only 10 amino acids long as the foundation for their drugs. By contrast, antibodies used to deliver radiation or chemicals can be over one thousand amino acids long.

The team attached radioactive phosphorous, P32, as a test of how well their peptides worked and "to our surprise, our first tests showed that cells were ingesting these molecules, thus transferring the radiation inside and killing them by breaking up their DNA and proteins," Abraham says.

While cautioning that the new radiation delivery system is still far from

ready for use in people, Abraham notes that P32 gives off high energy that can penetrate through 5 millimeters of human tissue, making it a good candidate to tackle colon cancer since colon cancer cells can often form large, thick tumors into which drugs may not penetrate very well. In addition, P32-labeled peptides may serve another valuable use: to find small metastases or recurrences of colon tumors while they are still small enough to treat. Images of the body can be taken of the labeled peptides as they bind, revealing where stray tumor cells may be nesting.

Abraham, Meltzer and their team then designed and tested a variety of P32-peptides on 18 normal and cancerous human cell samples. The most potent peptide, MA5, could bind to adenocarcinoma cells, which make up 95 percent of all colon cancers, 150 times more strongly than other cell types and be transferred inside cells within 2 hours.

Source: Johns Hopkins Medical Institutions