

New compounds trigger cancer cell suicide

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By Martin F. Downs

NEW YORK (Reuters Health) - Scientists believe they have found a new way to get tumor cells to self-destruct, a discovery that may eventually lead to better drugs to fight cancer.

Dr. James A. Wells and Jack T. Nguyen, researchers at Sunesis Pharmaceuticals, Inc., in South San Francisco, California, found two synthetic compounds that triggered programmed cell death, or apoptosis, in cancer cells.

Normal human cells only last for so long before a chemical program switches on and kills them. This prevents uncontrolled cell growth and keeps the body in good working order. But in cancer cells, the mechanism is often faulty, and the cells don't die.

"We were looking for things that would induce cell death," Wells told Reuters Health.

"We took a cell, a whole cell, and we basically punctured the membrane, and then we took the goo out of the cell, and then we screened the goo against the small-molecule library," he said.

The small-molecule library was a set of roughly 3,500 compounds. Two of the compounds triggered apoptosis, according to a report in the online Proceedings of the National Academy of Sciences.

The researchers knew they had found what they were looking for when they detected an enzyme called caspase-3.

"Caspase-3 is the actual henchman that goes around and executes the cell," Wells said.

The compounds were tested on whole normal cells and a variety of cancer cells -- including breast, lung, ovarian, skin and leukemia tumor cells.

One of the compounds triggered apoptosis in the cancer cells while having little effect on normal cells. It appeared to be most effective against the leukemia cells.

The other compound wasn't as potent in whole cells, although it was potent in the other tests. The researchers speculate that it had difficulty passing through the cell membrane.

The study shows that these compounds might work against cancer cells that are resistant to other cancer drugs.

Some chemotherapy agents now in use target a gene called p53, which regulates cell growth. But in many cancer cells, p53 is mutated, so drugs aiming to trigger apoptosis by that route don't work.

The research seems promising, but it could be several years before any new cancer drug comes from it.

"These compounds should be considered as very early leads. They would need a lot more work," Wells said. "Going forward, we would be enhancing the potency of the drug-like properties of the molecule, and studying the molecules in animals."

Wells said that Sunesis Pharmaceuticals, of which he is co-founder and president, might team up with another pharmaceutical company to develop a drug, or they might decide to do it in-house.

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