Health & Medicine

Cell Out

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Brent Stockwell made headlines last year by discovering a previously unknown type of cell death. He found that substances that react with oxygen, such as rusting iron, can accumulate in a cell to the point where oxidation tears the cell apart. “It’s a pretty violent process,” says Stockwell, a Columbia associate professor of biological sciences and chemistry. “The cell becomes overwhelmed in a sea of hydrogen peroxide, essentially bleaching itself to death. It completely disintegrates within a few hours.”

The story gets better: Stockwell recently discovered that cancer cells can be prompted to produce excessive iron, resulting in the self-destructive oxidation process. His research team screened 40,000 natural and manmade compounds and identified two, RSL3 and RSL5, that cause iron production in cancer cells to kick into overdrive. These two compounds are found naturally in plants and take on their lethal power only in the presence of a cancer-causing protein called Ras oncogene. Scientists have known for years about this dangerous mutant protein. But they had not yet found a compound that could kill it or, as Stockwell has done, trick the protein into destroying the same cancer cells that it spawns.

The findings appear in the March 24 issue of the journal Chemistry & Biology, in a paper coauthored with Columbia postdoctoral researcher Wan Seok Yang.

The discovery accomplishes a central goal of cancer research: to identify compounds that attack tumor cells without affecting healthy cells. Stockwell says the breakthrough could help scientists develop cancer drugs with fewer side effects than those that target all rapidly proliferating cells, including noncancerous cells whose destruction leads to hair loss and nausea.

“This information will help us discover new features of cancer-cell biology,” says Stockwell, who notes that the Ras oncogene is found in many, but not all, types of cancer cells. “The approach we’ve taken is general and can ultimately be applied to many different mutant genes and to many kinds of cancers.”

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