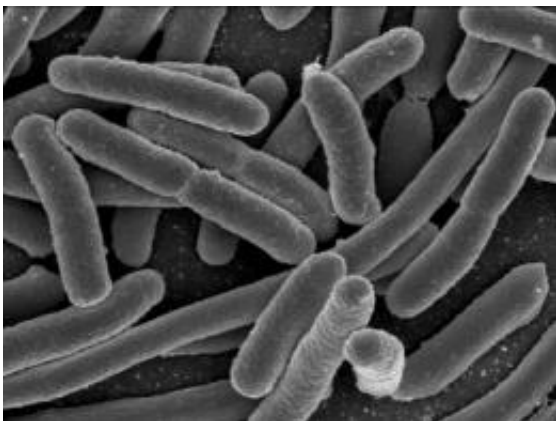


Drug kills cells through novel mechanism

December 10 2009



MIT and Boston University researchers have discovered that the drug hydroxyurea kills bacteria by inducing them to produce molecules toxic to themselves — a conclusion that raises the possibility of finding new antibiotics that use similar mechanisms.

Hydroxyurea inhibits the enzyme critical for making the building blocks for DNA, so for decades it has been used to study the consequences of inhibiting DNA replication in *E. coli*, yeast and mammalian [cells](#). It is also sometimes used in chemotherapy to halt the growth of cancer cells.

The research team, led by biologist Graham Walker of MIT and bioengineer James Collins of Boston University, showed that cells don't die after hydroxyurea treatment because their [DNA replication](#) is

blocked, but because the blockage sets in motion a chain of cellular events that culminates in the production of hydroxyl radicals. Those radicals are highly reactive and can damage cellular molecules such as nucleic acids, lipids and proteins.

Collins has previously shown that three different antibiotics, which each inhibit different cell processes, all lead to production of hydroxyl radicals, which play a role in killing the cells.

"This naturally leads to the thought that one could perhaps find a new class of antibiotic that acts further down the chain(s) of events that stimulate hydroxyl radical production," says Walker.

The findings could also aid in the development of adjuvants — small molecules that would enhance the lethality of current antibiotics, says Collins.

The researchers exposed *E. coli* to hydroxyurea, provoking them to activate a DNA repair system called SOS. This response keeps the cells alive for several hours, but eventually produces hydroxyl radicals that kill the bacteria.

In future studies, Walker hopes to delve further into the mechanism of bacterial response to hydroxyurea and the sequence of events that ultimately kills them.

More information: "[Hydroxyurea](#) Induces Hydroxyl Radical-Mediated Cell Death in *Escherichia coli*," Bryan Davies et al. *Molecular Cell*, Dec. 11, 2009.

www.cell.com/molecular-cell/fulltext/S1097-2765%2809%2900865-X

Source: Massachusetts Institute of Technology ([news](#) : [web](#))

Citation: Drug kills cells through novel mechanism (2009, December 10) retrieved 1 May 2024 from <https://phys.org/news/2009-12-drug-cells-mechanism.html>

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