

Scientists answer how bacteria fight toxic fluoride

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Yale researchers have uncovered the molecular tricks used by bacteria to fight the effects of fluoride, which is commonly used in toothpaste and mouthwash to combat tooth decay.

In the Dec. 22 online issue of the journal [Science Express](#), the researchers report that sections of [RNA messages](#) called riboswitches - which control the expression of genes - detect the build-up of fluoride and activate the defenses of bacteria, including those that contribute to [tooth decay](#).

"These riboswitches are detectors made specifically to see fluoride," said Ronald Breaker, the Henry Ford II Professor and chair of the Department of Molecular, Cellular and Developmental Biology and senior author of the study.

Fluoride in over-the-counter and prescription toothpastes is widely credited with the large reduction in dental cavities seen since these products were made available beginning in the 1950s. This effect is largely caused by fluoride bonding to the enamel of our teeth, which hardens them against the acids produced by bacteria in our mouths. However, it has been known for many decades that fluoride at high concentrations also is toxic to bacteria, causing some researchers to propose that this antibacterial activity also may help prevent cavities.

The riboswitches work to counteract fluoride's effect on bacteria. "If fluoride builds up to toxic levels in the cell, a fluoride riboswitch grabs the fluoride and then turns on genes that can overcome its effects," said Breaker.

Since both fluoride and some RNA sensor molecules are negatively charged, they should not be able to bind, he notes.

"We were stunned when we uncovered fluoride-sensing riboswitches" said Breaker. "Scientists

would argue that RNA is the worst molecule to use as a sensor for fluoride, and yet we have found more than 2000 of these strange RNAs in many organisms."

By tracking fluoride riboswitches in numerous species, the research team concluded that these RNAs are ancient - meaning many organisms have had to overcome toxic levels of fluoride throughout their history. Organisms from at least two branches of the tree of life are using fluoride riboswitches, and the proteins used to combat fluoride toxicity are present in many species from all three branches.

"Cells have had to contend with fluoride toxicity for billions of years, and so they have evolved precise sensors and defense mechanisms to do battle with this ion," said Breaker, who is also an investigator with the Howard Hughes Medical Institute. Now that these sensors and defense mechanisms are known, Breaker said, it may be possible to manipulate these mechanisms and make fluoride even more toxic to bacteria. Fluoride riboswitches and proteins common in bacteria are lacking in humans, and so these fluoride defense systems could be targeted by drugs. For example, the Yale team discovered protein channels that flush fluoride out of cells. Blocking these channels with another molecule would cause fluoride to accumulate in [bacteria](#), making it more effective as a cavity fighter.

Fluoride is the 13th most common element in the earth's crust, and it is naturally present in high concentrations throughout the United States and elsewhere. Its use in [toothpaste](#) and its addition to city water supplies across the United States sparked a controversy 60 years ago, and the dispute continues to this day. In the United Kingdom, and in other European Union countries, fluoride is used to a much lesser extent due to fierce public opposition.

The new findings from Yale only reveal how

microbes overcome fluoride toxicity. The means by which humans contend with high fluoride levels remains unknown, Breaker notes. He adds that the use of fluoride has had clear benefits for dental health and that these new findings do not indicate that [fluoride](#) is unsafe as currently used.

Provided by Yale University

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