

# Potential new medicines show promise for treating colon cancer, asthma

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In what they described as the opening of a new era in the development of potentially life-saving new drugs, scientists today reported discovery of a way to tone down an overactive gene involved in colon cancer and block a key protein involved in asthma attacks. Those targets long had ranked among hundreds of thousands that many scientists considered to be "undruggable," meaning that efforts to reach them with conventional medicines were doomed to fail.

"These substances represent an entirely new class of potential drugs," study leader Gregory Verdine, Ph.D., told the 241st National Meeting & Exposition of the American Chemical Society, being held here this week. "They herald a new era in the drug-discovery world."

Verdine cited estimates that conventional medicines, most of which belong to a family termed "small molecules," cannot have any effect on 80-90 percent of the proteins in the body known to be key players in disease. Throwing up their hands in frustration, scientists had even begun to term these prime targets for battling disease as "untouchables" and "undruggable."

The new substances are not small molecules, but "stapled peptides," named because they consist of [protein](#) fragments termed peptides outfitted with chemical braces or "staples." The stapling gives peptides a stronger, more stable architecture and the ability to work in ways useful in fighting disease.

"Our new stapled peptides can overcome the shortcomings of drugs of the past and target proteins in the body that were once thought to be undruggable," Verdine said. "They are a genuinely new frontier in medicine."

In one advance, Verdine and colleagues at Harvard University described development of the first stapled peptides that target colon cancer and asthma attacks. The colon cancer stapled peptides inhibit activity of a protein called beta-catenin that, when present in a hyperactive form, causes cells to grow in an aggressive and uncontrolled way. That protein normally helps keep certain cells, including those lining the colon, in good health. But the abnormal protein has been directly linked with an increased risk of colon cancer and other types of cancer, including those of the skin, brain, and ovaries.

When added to human [colon cancer](#) cells growing in laboratory cultures, the stapled peptides reduced the activity of beta-catenin by 50 percent. In patients, that level of reduction could be sufficient to have a beneficial impact on the disease, Verdine suggested.

Verdine also reported development of the first stapled cytokines, which show promise for fighting asthma. Cytokines are hormone-like proteins secreted by cells of the immune system and other body systems that help orchestrate the exchange of signals between cells. The stapled cytokines moderate the activity of a cytokine called interleukin-13, which asthma patients produce in abnormally large amounts that contribute to asthma attacks.

Current asthma drugs, he noted, tend to treat the underlying symptoms of [asthma](#), particularly inflammation. By contrast, stapled cytokines could treat the underlying causes of the disease. Verdine's team is collaborating with a pharmaceutical firm on efforts to further develop the stapled peptides.

Provided by American Chemical Society

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