

Drugging the undruggable: Advances toward next generation of disease fighters

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After decades of dreaming the drug developer's impossible dream, scientists finally are reporting progress in making drugs that target the "untouchables" among the body's key players in health and disease. They are the hundreds of thousands of proteins that many scientists considered to be "undruggable," meaning that previous efforts to develop a drug against them had failed.

Scientists described advances toward these drugs today during a special symposium, "Drugging the Undruggable," at the 240th National Meeting of the American Chemical Society. The advances could lead to a new generation of medicines for treating cancer, diabetes, and other major diseases, they said.

In one advance, scientists today reported on a new family of potential drugs that are capable of blocking a key protein that's involved in the development of cancer. Called "stapled peptides," the substances get their name from chemical "braces" that hold the peptides, or [protein fragments](#), in a compact shape that gives them high stability in comparison to their unfolded versions. The three-dimensional shape is critical for the peptide to function normally and help orchestrate body processes. The chemical stapling allows them to resist destruction by enzymes, easily penetrate cells, and bind to biochemical machinery within cells.

Their report indicated that the stapled peptides prevented the growth of [cancer cells](#) in a group of test animals, a key advance toward the start of

clinical trials in a group of cancer patients.

"Stapled peptides represent an entirely new class of potential drugs," said study leader Gregory Verdine, Ph.D., who has been studying the molecules for the past decade and helped pioneer their development.

"They herald a new era in the [drug-discovery](#) world."

There are hundreds of thousands of proteins in the human body, many of them with links to human disease. However, only a tiny fraction — about 20 percent — of these proteins is considered "druggable." Thanks to a new generation of drug discovery technologies, that tiny fraction is now on the rise.

"The entire pharmaceutical industry has been working on drug-design platforms that focus on this little sliver of human drug targets and this limits the drug arsenal available to doctors," said Verdine, a chemical biologist at Harvard University in Cambridge, Mass. "What's required is an entirely new class of drugs that overcome the shortcomings of drugs of the past."

In addition to "stapled [peptides](#)," scientists described new insights into how proteins interact with other proteins, the use of small molecules to target and treat cancer, and related topics. The presenters included scientists from government, industry, and academia.

Provided by American Chemical Society

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