

Research Team Seeks to Develop New Treatments for Cancer, HIV, Alzheimer's

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It all began in 1986 when plant scientists set out to get deeper purple petunias but got the complete opposite—white petunias. In the late 1990s, researchers working with fruit flies and *C. elegans* (a nematode worm commonly used in genetics studies) set out to understand this strange phenomenon.

Their work revealed a new biological pathway, RNA interference (RNAi), which is mediated by short-interfering RNAs

Fast forward to 2010. An interdisciplinary team of MSU researchers is studying RNA and siRNAs with the goal of developing better therapeutics for diseases such as cancer, HIV, Alzheimer's, or any other disease where a protein is causing or worsening the disease (In photo at right, clockwise from bottom left: Greg Baker, professor of chemistry; Georgina Carballo, PhD student in chemistry; S. Patrick Walton, associate professor of chemical engineering and materials science; Amanda Portis, PhD student in chemical engineering and materials science; and Christina Chan, the George W. Bissell professor of chemical engineering and materials science.)

"Researchers are excited because this gives us another tool for developing therapeutics that are very specific for one protein that is being expressed that shouldn't be expressed," says S. Patrick Walton, associate professor of chemical engineering and materials science. "So if we want to knock out or knock down the expression of a protein, we now have a new way to do this very specifically. RNAi has the potential to treat or cure a vast array of diseases.

"The unique characteristic of siRNA-based drugs is that they use a natural pathway in our cells to generate the therapeutic effect," says Walton. "This system can be more specific and have fewer side effects as opposed to an approach that uses drugs to change a cell's natural function."

The research team, which includes Christina Chan, the George W. Bissell professor of chemical engineering and materials science, and Greg Baker, professor of chemistry, is attempting to design the active molecules (the siRNAs) for maximal activity by understanding the mechanism of how they work, specifically at the level of how they interact with the proteins that are involved in this pathway and how they can be delivered with the highest efficiency. The goal is to design siRNAs that can achieve the strongest therapeutic effect at the minimum dose.

Chan and Walton will be working primarily on the design and testing of the siRNAs; Baker's major contribution will be in helping to design polymeric nanoparticles—polymers that form nanoscale structures that can encapsulate the siRNAs and deliver them specifically to a particular cellular target. The combination of improved siRNA design with improved delivery efficiency addresses the two major limitations of current siRNA-based therapeutics.

The work is being funded by a four-year \$940,000 grant from the National Institutes of Health.

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