Photo by Alex Wang, UT Austin

News of the RCSA Community

New molecule can tangle up DNA for more than 2 weeks

Brent Iverson, a member of the RCSA Board of Directors, leads a research team at the University of Texas at Austin that has created a molecule with unusual properties, even for advanced biochemical research.

It's a molecule Iverson calls a "threading tetra-intercalator." It can tangle itself inside the double helix of a DNA sequence and can stay there for up to 16 days before the DNA liberates itself, much longer than any other molecule reported.

Researchers say it may be an important step along the path to someday creating drugs that can go after rogue DNA directly. Such drugs would be revolutionary in the treatment of genetic diseases, cancer or retroviruses such as HIV, which incorporate viral DNA directly into the body's DNA.

"If you think of DNA as a spiral staircase," says Iverson, "imagine sliding something between the steps. That's what our molecule does. It can be visualized as binding to DNA in the same way a snake might climb a ladder. It goes back and forth through the central staircase with sections of it between the steps. Once in, it takes a long time to get loose. Our off-rate under the conditions we used is the slowest we know of by a wide margin."

He says the goal is to be able to directly turn on or off a particular sequence of genes.

"Take HIV, for example," he says. "We want to be able to track it to wherever it is in the chromosome and just sit on it and keep it quiet. Right now we treat HIV at a much later stage with drugs such as the protease inhibitors, but at the end of the day, the HIV DNA is still there. This would be a way to silence that stuff at its source."

Iverson notes, however, that researchers are still a long way from reaching that goal.

In order to synthesize their binding molecule, Iverson and his colleagues begin with the base molecule naphthalenetetracarboxylic diimide (NDI). It's a molecule that Iverson's lab has been studying for more than a decade.

His results were published in *Nature Chemistry* and presented recently at a colloquium at New York University. Iverson is a professor of chemistry and chair of the department of chemistry and biochemistry at UT Austin.

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