DNA ARTISAN

McGill University's Hanadi Sleiman looks to DNA as a template to pattern materials like nanotubes that act as smart delivery systems for therapeutics.

By **Melora Koepke**

Hanadi Sleiman's tastefully decorated office at McGill University's Department of Chemistry is dominated by a large picture window revealing the spires and rooftops of the 190-year-old Montreal institution. Displayed on the windowsill are several DNA knick-knacks: Francis Crick and James Watson bobble head dolls and a model of the iconic double helix. "This model of DNA is accurate down to the structure of nucleotides and bases," Sleiman says, contemplating the intricate model.

DNA — its mystery, its still-untapped potential for scientific innovation — has long fascinated Sleiman who, as a post-doctoral student, studied under French chemist Jean-Marie Lehn, winner of the 1987 Nobel Prize for his pioneering work in supramolecular chemistry. Sleiman and her research team, which works out of a bright, airy new laboratory in McGill's Otto Maass Chemistry Building, is expanding upon Lehn's work, focusing on the supramolecular chemistry of DNA. Backed by a number of funding agencies, including NSERC, the Sleiman Research Group uses the unique chemistry of DNA to design new nanomaterials for drug delivery, diagnostic tools and anti-tumour therapeutics. "It's not just the molecule of life — now we

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DNA designer, Hanadi Sleiman

can do something with it. It's the difference between studying what's there and making your own versions of it," Sleiman says. Sleiman was at Stanford University in the late 1980s completing her PhD in organic chemistry when she attended a lecture by Lehn on supramolecular chemistry — a discipline that examines the noncovalent interactions between molecules, from molecular self-assembly to molecular recognition. At the time, Sleiman had the idea that she would focus on the synthesis of small molecules for her post-doctoral work. Lehn, ever the visionary, articulated a challenge to his audience, which included Sleiman, to "learn how to control the interactions between molecules the way nature controls them," she recalls. Soon, Lehn predicted, scientists could combine supramolecular "components to make something: a machine, a functional molecule, a device, whose function is greater than the sum of its parts."

Lehn's talk changed the course of Sleiman's studies, propelling her along a journey of scientific discovery to her current position as one of Canada's foremost researchers in supramolecular chemistry and DNA nanotechnology.

Although nanotechnology is still considered an emerging field, nature itself already builds on this scale; a double strand of DNA is about two nanometres wide. Moreover, DNA is wonderfully programmable; sequences can be created that bind only to each other in certain ways. Combine that with excellent structural properties and DNA becomes one of the most promising templates to pattern materials with nanoscale precision. Sleiman and her team have used it to create one-, two- and three-dimensional nanostructures, including DNA nanotubes, which have a variety of possible applications. For example, they could act as templates for the growth of nanowires, aid in the structural determination of proteins, or even provide new platforms for genomics applications. Nanotubes could also act as "smart" delivery systems for therapeutics, or become implantable nanoelectronic devices to sense, predict and diagnose disease. "We're hoping this will be a whole new generation of molecules," Sleiman says.

One of Sleiman's major innovations has been the incorporation of synthetic organic or metal-based linking molecules into the DNA structure. These act as the junctions, or corners, of the supermolecules and allow many short DNA sequences to be linked together in a modular way. Using this strategy, the team recently developed nanotubes that can selectively encapsulate molecular "cargo," in this case gold nanoparticles, along the DNA nanotube length. This cargo can then be released by the nanotubes in response to specific external stimuli. The innovation could be used to deliver cancer drug molecules directly to tumours thus reducing the toxic effects on the body and enhancing efficacy.

The research is at a crucial juncture, Sleiman says. "This is the time for the field of DNA nanoscience to start producing useful things." Easier said than done. For example, while DNA structures hold promise for biological applications, their ability to resist enzymes, to penetrate into cells and their safety in organisms all need to be examined and optimized. "There is a bright future and a lot of possibilities in DNA assembly, but there is still a lot of work to be done," says Sleiman.

Sleiman isn't focusing solely upon DNA nanoscience. Other areas of research relate to her background synthesizing small molecules and polymers. Her team also works on designing and synthesizing biomimetic materials. Among some of the group's research highlights, their work on the creation of hybrid polymer-DNA and gold nanoparticle DNA structures were selected as editor's choices in *Science* and *Nature*.

Sleiman's science may be complex, but behind it is the simple but lofty goal of contributing to society in a meaningful way. This passionate sense of purpose grew out of the most dire of circumstances — war. The eldest of two children, Sleiman grew up in a family that emphasized achievement. Born in Beirut in 1965, Sleiman's mother, Leila El-Horr, was a journalist, her professor father, Farouk Sleiman, chair of the biology department at Lebanese University Beirut. A happy home life was interrupted on Sleiman's 10^{th} birthday by the thud of falling bombs — malevolent heralds of the 15-year Lebanese Civil war. But the fear and devastation of that protracted conflict entrenched a sense of resolve in the precocious young girl. "If you're going to school and there's snipers and there's bombs, it gives you a resilience," Sleiman says. "You internalize the fact that no matter what happens around you, you're going to get that education."

As the war worsened, Sleiman became determined to leave her beleaguered nation. "When I was in university, it was really tough, because the war got worse," she recalls. "At that point, I said to myself, 'I'm going to get really great grades so I can go to a really good graduate school and make it out of here.' "

Sleiman received a B.Sc. in chemistry with high distinction and was accepted to Stanford University when she was only 20 to do a PhD in organic chemistry. It was at Stanford that Sleiman met her future husband, Bruce Arndtsen, who also became a chemistry professor at McGill. The couple has two children, Ryan, 12, and Maya, 7, both born while Sleiman's career as an academic and researcher was in its early stages. By becoming the first female faculty member to have a child in the chemistry department in 1999, Sleiman broke through a glass ceiling of sorts — embracing her role as academic researcher and mother. McGill was supportive of their star researcher's dual demands and, as it turns out, the children adapted well to their mother's career. "I remember when Maya was two months old; I was invited to a conference to give a speech that was very important for my career. I held her in my arms as I paced back and forth, practicing my speech. She lay in my arms happily while I practiced."

It is a lesson that Sleiman hopes to pass on to her female students: motherhood and a career in science is not a contradiction in terms. Many female students have "internalized societal pressures" telling them that they can't be both mothers and researchers, says Sleiman. "I tell them if they follow their dreams, they'll be happier people as a result. And they'll be passing on this happiness to their children; I really do think it's a gift to my boy that he is growing up knowing that women are active contributors to society."

Sleiman has always shown such support and empathy for students, which is one of the reasons she was recognized several years ago with McGill's Leo Yaffe Award and Principal's Prize for excellence in teaching. She has also been recognized for academic achievement, winning, most recently, the Strem Award for Pure or Applied Inorganic Chemistry from the Canadian Society for Chemistry and McGill's William Dawson Scholar Award (McGill's equivalent to a Canada Research Chair Tier II).

Research and teaching in tandem has given Sleiman the means to "try to transform the world." As a researcher, orchestrating and manipulating nature's tiniest particles, she seeks positive changes for humankind. As a teacher, the change is more immediate, but no less lofty because of it. "As a teacher, you really see your impact, it's a person who's changed by you." ACCN