Hiring antibodies as nanotechnology builders

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Artistic representation of the strategy adopted in the work. Antibodies, by binding to antigen-conjugated DNA tiles, induce the assembly of tubular nanoscale structures. Credit: Ella Marushchenko

What if we could use antibodies as functional tools for nanotechnology applications? A group of researchers at the University of Rome Tor Vergata started from this simple question, and the results of their research are now published in *Nature Communications*.

Nanotechnology enables the design and fabrication of molecular structures at nanoscale dimensions with great potential for many fields, including biomedicine. A convenient way to make such nanostructures is to employ synthetic DNA as the building material. These days, it is possible to design and synthesize DNA strands that, via simple and predictable interactions, bind to each other like Lego bricks and form beautiful 2-D and 3-D geometries in a controllable and precise fashion. To date, many nanoscale shapes have been created using DNA bricks, ranging from nanoboxes to more complex geometries such as a nanoscale "Mona Lisa." For practical application of these nanostructures, however, their assembly and disassembly should be guided by molecular cues of clinical relevance.

Now, a research group at the University of Rome Tor Vergata has shown that it is possible to recruit antibodies as molecular builders to build or dismantle DNA nanostructures.

The function of antibodies is to recognize and bind to foreign molecules or proteins. For this reason, antibodies are ideal biomarkers because they are produced specifically to target foreign molecules in the blood. Each antibody has its own target and therefore does its job in a highly specific and precise way.

"This project started a couple of years ago when we realized that this amazing functionality of antibodies to recognize and bind to a specific molecule could be repurposed for nanotech applications," says Francesco Ricci, professor at the University of Rome Tor Vergata and senior author of the manuscript. "We had the idea of utilizing antibodies as molecular workers to build nanoscale structures."

Simona Ranallo, a post-doc researcher in the group of Prof. Ricci and first author of the manuscript, says, "To do this, we employed DNA bricks that bind to each other and form nanostructures of tubular shape

.We then re-engineered such bricks with recognition tags (antigens) so that their assembly is initiated by a specific antibody. The nanotube structure can thus only built up when the antibody is present in the sample."

Ricci says, "Antibodies are highly specialized workers. There are thousands of distinct antibodies, each recognizing its own antigen. We took advantage of this amazing feature and designed different bricks that can assemble with different specific antibodies. Then we took a step further. We engineered our DNA bricks so that they not only assemble into the desired nanostructure in the presence of a specific antibody, but they can also be completely dismantled by a second antibody worker."

This strategy demonstrates the possibility to design intelligent nanostructures that can be built and destroyed in the presence of a specific biomarker. This has potential applications in the biomedical field, in diagnostics or therapeutics.

More information: Simona Ranallo et al. Orthogonal regulation of DNA nanostructure self-assembly and disassembly using antibodies, *Nature Communications* (2019). DOI: 10.1038/s41467-019-13104-6

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