Those amazing technicolor DNA dream machines

Prof. Yamuna Krishnan works on DNA nanotechnology. In order to understand how the basic building block of life, DNA, began to be used as construction material, we need to go back a bit.

The double helix structure of DNA was discovered by James Watson and Francis Crick in 1951, building on the work of Maurice Wilkins and Rosalind Franklin.

In the early 1980s, the scientist Nadrian Seeman, inspired by a woodcut called *Depth* by the artist M.C. Escher, theorized that the strands of DNA could be used for construction on the nanoscale, and laid the foundation for DNA nanotechnology. Then, in 2006 Paul Rothemund at Caltech devised a method to 'fold' DNA strands into two dimensional, 'designer' shapes on the nanoscale. This method of making designer DNA nanoshapes came to be known as DNA origami, after the Japanese art of paper folding. It was now clear that DNA could be used to make any imaginable shape on the nanoscale. But what might we use these shapes for? That was still a question that loomed large.

Prof. Krishnan's work broke that barrier by showing how one can transport designer DNA into specific locations inside living cells when they were injected inside living organisms so that they could probe the inner workings of cells. She first manipulated DNA strands to create 'nano-machines' that could measure specific chemicals. Then she discovered 'homing signals' that, when attached to these nanomachines, could be made to act like guided missiles. Except, instead of the 'seek and destroy' mission of a guided missile, Krishnan's devices 'seek and report' on the health status of cells. This work has major implications for biomedical imaging within living organisms.

Krishnan's devices act as scaffolding-like structures which are tipped with a fluorescent compound. Depending on the acidity of the cell in which the nanodevice finds itself, the tips of the device open or close. In higher acidity, it glows red and in lower acidity, it glows green. Krishnan demonstrated how they work inside a kind of small, soil-growing worm.

Her work spurred researchers to consider designer DNA nanodevices as drug delivery agents in cells. The more complex the scaffolding, the more functions it can carry out.

Very recently Krishnan found that her technology works in human cells isolated from a blood-draw to identify malfunctioning cells. She is now using her technology to develop blood tests for neurodegenerative diseases such as dementias that affect the elderly, and lysosomal storage disorders that affect infants and children.