

IIT-Kanpur scientist-led team designs nano-machines that can correct anomalies inside living cells

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In a feat that may be clinically significant in near future, researchers led by a young structural biologist from the Indian Institute of Technology-Kanpur have created nano-size machines that can crawl inside living cells to correct anomalies often linked to diseases.

These 'nano-machines' are made of fragments of antibodies and can be made to selectively target signalling events inside living cells. "They can be designed in such a manner that they regulate one arm of the signalling mechanism while leaving others completely untouched," said IIT scientist Arun Kumar Shukla, who led a multi-institutional team for this work, which appeared in journal *Nature Nanotechnology* on Monday.

The technique may have therapeutic potential in certain diseases which otherwise are considered untreatable, such as type I diabetes and retinitis pigmentosa, a class of genetic disorders that result in progressive loss of eyesight.

The scientists showed that these specially prepared antibody fragments work by targeting selective functions of a class of proteins inside the cell called beta-arrestins. Beta-arrestins are significant because they regulate the action of a family of receptors called G-Protein-Coupled Receptors (GPCR) found on the surface of each living cell.

Physiological receptors

These receptors are at the centre of every physiological process in our body. For example, we see things when photons (light particles) fall on rhodopsin molecules

(GPCR receptors present in the retina), get the smell when the receptors in nostril cells get activated, and flee when an impending danger approaches us as GPCRs in different types of cells receive chemical cues in the form of hormones. These receptors also regulate everything from heartbeats to immune response. Scientists have already identified nearly 1,000 different GPCRs in the human body.

According to Shukla, beta-arrestins play a critical role in impeding the normal function of GPCR, particularly in cells that are not healthy, normal cells. "Beta-arrestins that bind with GPCR proteins pull the latter inside the cells and form a complex with another class of proteins called clathrin. Such complexes are typically headed for doom."

The scientists found that

the antibody fragments prevent beta-arrestin proteins from binding to clathrin and thus help the receptors stay at the cell surface longer, where they continue to do their normal function. "What these antibody fragments do here is to hinder beta-arrestin-GPCR complex from binding to clathrin, which is a sure-shot way to destruct the receptor," Shukla said.

He, however, said their work was currently only a proof of concept. As a next, they plan to find a way to deliver these tiny antibody fragments inside lab-bred cells so that they can explore their actual potential.

Apart from IIT-Kanpur researchers, their mpatriots from the Central Drug Research Institute, Lucknow, and a few universities in the US and Canada were part of the team.