Source : www.thehindu.com Date : 2021-05-16

NEW APPROACH TO DRUG DELIVERY COMBINES BIOLOGICS AND ANTIBODY-DRUG CONJUGATES

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Illustration: Khushboo Singh.

A type of nanoparticle designed by researchers from University of Massachusetts, Amherst, in the U.S., embodies a new approach to treating diseases that could potentially revolutionise the field. This combines concepts of biologics and antibody–drug conjugates to produce protein–antibody conjugates that can be used for targeted drug delivery – in the case of pancreatic cancer cells, for example. The team has tested the mechanism in cell lines in the lab and now plans to move on to studying it in mouse models. Their research is published recently in the journal *Angewandte Chemie.*

The new concept, namely, Protein–Antibody Conjugates or PACs, combines two different approaches to drug delivery. One is biologics, where the idea is to target a defective protein in the system by delivering proteins to it. An example of this is the case of insulin treatment. If a person is short of insulin, which is a protein, they are given a shot of this protein which balances the system.

The reason this works is because we need a circulation of insulin outside the cells and not inside the cells. “Now, we have 20,000 proteins and when one of these is malfunctioning, we have no way of taking that protein specifically inside the cell. That is a big problem in biologics,” explains Sankaran Thayumanavan, Distinguished Professor of Chemistry at Department of Chemistry, University of Massachusetts, who led the research. “It will be a gamechanger if we can take the protein inside the cell. So, people have been looking at protein delivery for a while.”

The other concept is of using antibodies for drug delivery. Antibodies are something the body produces to detect a foreign substance inside the body. “We can develop antibodies to recognise anything that does not belong in our bodies. That includes cancer cells as well. If there is something different on the surface of a cancer cell compared to a healthy cell, you can design the antibody that selectively goes to the cancer cell,” he explains. Drug molecules can be attached to the antibody, forming drug–antibody conjugates.

Prof Thayumanavan’s group developed protein–antibody conjugates or PACs, which have a protein attached to the antibody, and this conjugate can zero in on, say, pancreatic cancer cells.

This could have an impact on incurable diseases. Most drugs work this way: If the protein has a particular shape – bent concave like a cup for example, the drug is designed to fit into the bent portion, like a key into a lock, so that the protein’s function is inhibited, and it cannot function. But some of the proteins have an open structure, it is difficult to design a drug that can bind to it, because it is so wide.

However, using a protein molecule, which is typically large, can solve this problem.

Pancreatic cancer is an example. “There are [types] that are considered undruggable. In 90% of pancreatic cancers, this is the case. We know what we should target but we do not know how to design drugs that will bind. But with proteins we know we can design molecules that will bind to the target,” says Prof. Thayumanavan.

In a telling analogy, he compares the protein–antibody conjugate to an addressed envelope containing the drug. The antibody plays the role of the address and indicates the cell where the drug should precisely be delivered.

The group also realises that biology involves complexity and that this method may well fail if it is not tuneable. “In our lab we are already developing three different polymer platforms, each of which has its own tuneability… the concept is real, and it is important at the molecular level we understand how to tune it,” he says.

The researchers are planning to test this concept in mouse models as the next step.

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