New Analysis Method Can Lead to Better Cancer Drugs

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While proteins on the surface of cells are the targets for most drugs, refined methods are needed to analyse how these membrane proteins are organised. Researchers at Karolinska Institutet have developed a new DNA-based analytical method that could contribute to the development of future drugs for breast and other cancers. The study is published in Nature Nanotechnology.

The efficacy of most drugs in clinical use is attributable to their interaction with proteins on cell membranes (see fact box). It is therefore essential to understand how these proteins operate in health and disease.

Many of the proteins on the cell membrane are distributed into functional units, domains of nano-scale dimensions (i.e. 10-6 mm).

NanoDeep: a refined method

Membrane proteins are analysed using super-resolution microscopy, a technique limited by the fact that only a small number of membrane proteins – normally three – can be analysed at the same time.

Researchers at <u>Karolinska Institutet</u> have now developed a method that increases this number. This non-microscope-based method for analysing entire populations of cells is called NanoDeep (NANOscale DEciphEring of membrane Protein nanodomains).

Interval of 10 nanometres

The method is based on the use of DNA analysis to translate information on membraneprotein organisation. There are no limits to the number of such proteins that NanoDeep can analyse simultaneously. Their work has not only enabled the researchers to corroborate previous findings but also led to new discoveries. "NanoDeep currently has a resolution in the 10 nanometre interval, that's 10 billionths of a metre, which surpasses many other methods of super-resolution microscopy," says the study's last author Ana Teixeira, researcher at the Department of Medical Biochemistry and Biophysics, Karolinska Institutet. "NanoDeep has the potential to bring new insights into the regulation of membrane protein function."

Cancer recurrence

Using NanoDeep, the researchers have been able to describe protein environments surrounding the membrane receptor Her2, a membrane protein that transmits information to proteins inside the cell.

Her2 is over-represented in breast and other types of cancer. A better understanding of Her2 will improve the chances of developing new drugs that prevent most recurrences of such cancers. The new method has been developed to be as simple as possible.

"Our method makes the use of information on the spatial organisations of proteins at a nanoscale more accessible as a diagnostic tool in clinical tests," says the <u>study</u>'s first author, postdoctoral researcher Elena Ambrosetti. "It can also be used as a tool for developing new kinds of drug designed to affect the function of membrane proteins."

Read the original article on Karolinska Institutet.