Researchers map trends in drug development

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Credit: University of Copenhagen

From a drug perspective, G protein-coupled receptors are the most utilised cell receptors in the body. They are uniquely accessible at the cell surface, and a third of all drugs sold in the US target them.

A new mapping by the University of Copenhagen and Uppsala University of all these drugs on the market and currently tested in clinical trials has been published in the prestigious journal *Nature Reviews Drug Discovery*. The mapping reveals trends for how this type

of drug targets a larger number or receptors, takes advantage of new scientific principles and fine-tunes to achieve higher safety through more specific target interactions and cellular signalling.

"We can see the future trends when we compare the drugs on the market with those undergoing clinical trials. We can see, based on a number of parameters, that the new drugs targeting these receptors have more precise effect, become more complex and have fewer side effects," says Alexander Hauser, a PhD student at the Department of Drug Design and Pharmacology.

In recent years, researchers have learned more - largely through 3D atomic structures - about how G protein-coupled receptors are built and thus how they function. This knowledge appears to now have translated into drug development. The mapping shows that future drugs can be more specific affecting fewer receptors, resulting in fewer side effects.

There is also an increasing shift from small chemical drugs to far more complex biological protein drugs, and binding of drugs multiple sites on the receptor. These drugs can thereby fine-tune their effect and be even more precise.

The mapping was carried out under the leadership of Associate Professor David Gloriam, and also examines the trends in relation to the illnesses being targeted through this type of receptor. The researchers compared the number of drugs available on the market for a given disease with the number currently undergoing clinical trials.

"A lot of clinical trials are being done for Alzheimer's and obesity, for which there are virtually no approved drugs on the market. We also see many clinical trials related to asthma, diabetes and cancer. Far from all the drugs undergoing clinical trials will end up being approved products. But this mapping offers a good impression of where the focus is," says

David Gloriam.

The mapping also shows there is great potential for further research into these receptors. Over half the G protein-coupled receptors do not yet have a drug that targets them. There is therefore considerable untapped potential. Most of the untargeted receptors are related to genetic and immune system disorders.

G protein-coupled receptors

The GPCR superfamily comprises 800 receptor proteins on human cells. They sit in the cell membrane and relay important signals from the outside into the cells.

Drugs can affect them in a multitude of ways. Essentially, when a substance binds to a receptor it can trigger a cascade of cellular signals. It can then forward a whole series of signals in the body.

One-third of all drugs approved by the US Food and Drug Administration (FDA) target this type of receptor in human cells.

More information: Alexander S. Hauser et al, Trends in GPCR drug discovery: new agents, targets and indications, *Nature Reviews Drug Discovery* (2017). DOI: 10.1038/nrd.2017.178

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