Focus on kinetics for better drug development

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Credit: Leiden University

Potential drugs that seem promising in the lab, but don't show any activity in a person: they cost the industry an incredible amount of time and money. That's why Indira Nederpelt focuses on a more efficient search for new drugs in her PhD, by determining the kinetics of a potential drug earlier on in the drug development process.

Importance of kinetics

Many diseases can be treated by activating or blocking a particular receptor in the body with a drug. 'For decades the affinity of a drug was

the main focus of drug discovery– the attraction between the molecule and the receptor,' says Nederpelt. 'Since the past ten years, some researchers prefer to look at the speed at which a molecule binds to the receptor and how long that molecule stays on the receptor – also called the kinetics. There are still many sceptics, but in my research I show how important these kinetics actually are.'

From milliseconds to hours

'The main consensus in my field is that the kinetics of different medicines are roughly the same. As a proof of concept I developed novel assays and showed with these assays that the kinetics of medicines can vary tremendously: some medicines bind to the receptor in milliseconds, others need minutes and sometimes even hours,' Nederpelt explains. In the ideal case, a number of exceptions excluded, a drug quickly binds to the receptor and stays there for a long time. If that is the case, a patient can take the medicine less often, for instance only once a week instead of twice a day.

Endogenous substances

'During my PhD I thought, aren't we forgetting something?,' Nederpelt says. 'Our body produces endogenous substances. When these substances bind to the receptor, the drug cannot bind this receptor. If you don't include this in your research, chances are that a potential drug suddenly shows no activity in the human body. Therefore, I looked at two receptors in my research, so-called G protein-coupled receptors.' For the first time, Nederpelt determined the kinetics of the endogenous substances that belong to these receptors. The endogenous substance belonging to the first receptor appeared strikingly slow. Of the two endogenous substances that belong to the second receptor, one turned out to be fast and one turned out to be slow.

Situation in the body

'By determining the kinetics of the endogenous substances, you can predict more accurately which molecules are promising as a drug,' Nederpelt explains. If an endogenous substance binds to the receptor very fast, a medicine needs to bind to the receptor even faster in order to do its work. I hope that this research shows other researchers how important the kinetics of both the medicine and the endogenous substances are. My ambition is that determining the kinetics is included in the standard tests of pharmaceutical companies. In doing so we can get better drugs on the market faster and help the patient of the future,' Nederpelt concludes.

Provided by Leiden University

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