Breakthrough for more efficient drug development

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Developing new drugs is a highly costly and time-consuming process. Of 20 candidates, 19 are normally rejected because they don't work or have unwanted side effects. Now a research team led by Professor Lars Baltzer at Uppsala University has produced a tiny molecular "binder" that has the potential to change this landscape radically.

The study, published today in the prestigious journal Angewandte Chemie, presents the concept of a tiny polypeptide consisting of 42 amino acids to which virtually any target-seeking organic molecule can be bound. In the body it then seeks out the designated sites to be treated. What's unique about the polypeptide is that it dramatically enhances the properties of the little molecule in a simple and very general way.

"This produces superbinders. They bind more strongly and more specifically than other alternatives," says Lars Baltzer, professor of organic chemistry, who believes it will be possible to rapidly develop new drugs much more readily with this new concept.

The whole concept goes against the grain of what is usually done in drug development. Traditionally it's usually a matter of synthesizing drugs from A to Z, with certain requirements needing to be met in order to succeed. Drugs should be low molecular (500 Da), be highly fat soluble, and have no more than ten binding sites in order to pass through the cell membrane. But the majority are ineffective or toxic, and nowadays there are also ways to get larger molecules through cell membranes. Recently therapeutic antibodies have emerged as an alternative. They're large

(150,000 Da) and bind to the outside of cells, which they then "block."

The new peptide is 5,000 Da or only 1/30 as large as a typical antibody, which is smaller than was thought possible. But according to Lars Baltzer nature has always signaled that this should work.

"The human growth factor hGH uses 35 amino acids to bind to its receptor, but it turns out that only six of them are critical. The rest can be replaced without significantly changing the function. There's really nothing very special about placing a general peptide on a small molecule, but nobody has done it before," he says.

In this study the peptide was successfully bound to the inflammation marker CRP, which is an indicator of a risk of premature death in heart patients, among other things. Several other studies are underway and are proving to be equally successful.

These findings are of great importance to industry, and several large companies have shown their interest. The spin-out company that was previously formed out of Baltzer's research team is now going to further develop the concept to be able to help the drug industry determine at a considerably earlier stage than today whether a drug candidate is worth pursuing or not.

Provided by Uppsala University