Application of fragment-based drug discovery to membrane proteins

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Stellingen

Behorende bij het proefschrift:

Application of fragment-based drug discovery to membrane proteins

The mild Schiff's base chemistry can be used to functionally immobilize membrane proteins, provided detergent is present above the critical micelle concentration at all times.

This thesis, chapters 3 - 5

Immobilizing native membrane fragments containing overexpressed membrane proteins makes it possible to better mimic the native environment by co-immobilization of other important players of the signalling cascade.

This thesis, chapter 3

Using an immobilized reference membrane protein with low fragment binding properties enables one to identify specific fragment binding to a target in fragment-based screening.

This thesis, chapters 4 - 5

Although finding the appropriate protocol for inserting membrane proteins in nanodiscs may be demanding, the benefits which follow include easier membrane protein handling and fewer artefacts in protein analyses due to the absence of detergent.

This thesis, chapter 6

Increasing linker length between the immobilized protein and the surface can substantially increase the functionally immobilized protein population by providing more space for extramembranous domain movement.

This thesis, chapter 3
Bieri, C. et al. 1999. Nat. Biotechnol. 17, 1105 - 1108

There is a trade-off between the probability of detecting binding and the probability of finding a good match between ligand and target, but using sensitive biophysical methods such as NMR can be a solution.

Hann, M. et al. 2001. J. Chem. Inf. Comput. Sci. 41, 856 - 864

Screening fragments is amenable to finding lead products with better starting bioavailability profiles, thereby reducing the often laborious chemistry efforts required to remove initial unwanted functional groups.

Hajduk, P. J. et al. 2002. J. Med. Chem. 45, 5628 - 5639

"The need to tailor drug treatments requires a more systematic approach to integrating and interpreting information spanning genes, proteins, pathways, targets, diseases, drugs, and patients."

Jentzsch, A. et al. 2009. Linked Data on the Web workshop at WWW2009

Make sure the only separation anxiety you have during research is one that concerns your purifying device.

Always enjoy research as if it were a fun puzzle. Just bear in mind that unlike research, the puzzle has an end.

It's not about how much you give, it's about how little you expect back.

Hopefully, linking data and open source information accessible to all will soon become a concept that will unleash all the hidden potential there is in collaboration as opposed to competition.

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