In Silico Hit Prediction - ZeptoHit

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Organisation

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SCOPE OF THE METHOD

The Method relates to	Human health
The Method is situated in	Translational - Applied Research
Type of method	In silico

DESCRIPTION

Method keywords

in silico analysis

hit discovery

phenotypic activity

Scientific area keywords

computational modelling

artificial intelligence

machine learning

bioinformatics

Method description

ZeptoHit is a technology based on Artificial Intelligence (AI) which accelerates hit discovery. With only a protein sequence as information, ZeptoHit can quickly and efficiently recommend promising hits, without any limitations. Its search for promising compounds goes much beyond chemical structures similar to known hits. Furthermore, ZeptoHit can accurately make predictions for proteins that have no known modulator or binder. ZeptoHit can be seen as a very smart filter which will predict promising compounds across millions of possibilities. These compounds can later be screened and validated in a wet lab in a low throughput screening campaign.

Method status

Internally validated
Published in peer reviewed journal

PROS, CONS & FUTURE POTENTIAL

Advantages

ZeptoHit has been learning from millions of examples of hits. With only a protein sequence as input, it can generate a list of likely hits, with a high accuracy. Thanks to this wide knowledge it is capable of:
- identifying not only the on-target hits, but also the off-target hits so that adverse effects can better be anticipated;
- identifying hits even in the case of unknown compounds;
- drug discovery teams working on novel compounds do not start from a blank page but can already start identifying possible hits;
- identifying hits even in the case of novel targets. Also here, pharma researchers can pre-screen a novel target even if it is not well known or studied;
- predicting the type of bioactivity: the solution does not only predict if there will be a hit but also predicts the type of expected bioactivity: activation, inhibition...;
- prioritizing compounds that are synthesizable and available so they can be rapidly tested.

The benefits of using ZeptoHit are the following:
- Screen only the compounds with a likely promising bioactivity on humans so to reduce unnecessary costs and animal testing efforts;

- Considerably decrease time and cost of drug discovery efforts;
- Increase chances of success through the identification of possible adverse effects due to off target hits;
- Filter out non promising leads in order to concentrate screening efforts on promising leads;
- Decrease risk of drug development projects by having the widest possible search of promising leads, instead of missing out on some valuable compounds.

Challenges

The method is probabilistic, even if the hit rate is considerably higher than the state of the art. This means that we always work with partners who have mechanistic or phenotypic assays to validate the predictions of ZeptoHit.

Modifications

ZeptoHit is constantly modified so its predictions constantly improve. Also, it is developed in parallel with ZeptoWard, our ADMETox prediction model, so we can select, from the project start, not only promising compounds, but also safe ones, so animal testing is not performed in vain.

REFERENCES, ASSOCIATED DOCUMENTS AND OTHER INFORMATION

References

https://www.frontiersin.org/articles/10.3389/fphar.2022.856804/full

Links

Zeptohit : in silico hit discovery

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