A better way to design fusion protein drugs

March 23 2016

New software developed at A*STAR could help scientists design sophisticated biopharmaceutical drugs that demand the joining of proteins together. The tool, which is freely available online, allows researchers and drug developers to input the protein fragments desired and pick the best 'linkers' accordingly.

Lead platform developer Dong-Yup Lee, a chemical engineer at the A*STAR Bioprocessing Technology Institute (BTI) and the National University of Singapore, says he is "very open to collaborating with other researchers, especially from biopharma companies, who are looking for suitable linkers for their synthetic fusion protein drugs."

Lee and his colleagues described the software in the journal *Bioinformatics*.

The choice of a suitable peptide linker can be complicated, and is often overlooked in the design of antibodies and other complex drugs or biotechnology tools that involve joining two different proteins. Yet with an unsuitable linker, the attached proteins might not fold properly. They might also be expressed at low levels, or have impaired activity.

To improve the process of linker selection, Lee and his colleagues developed a web-based platform called SynLinker, which contains a database of 2,150 naturally occurring peptide linkers plus another 110 artificial or empirical linkers. Users can search SynLinker by linker length, amino acid composition, solubility and other features that affect linker flexibility and function. After picking from multiple candidate

linkers, users can then model their desired fusion protein constructs with each linker. "The prediction of a possible conformation of the fusion protein is a unique feature of SynLinker," Lee says.

Lee's team has used SynLinker to select suitable linkers for fusion enzymes that allow scientists to study human drug metabolism in laboratory model organisms. Lee explains that he and his colleagues are expressing these fusion systems in a yeast strain, and they are "currently being validated experimentally for functional testing via collaboration with the microbial group from BTI."

Similar bioinformatics tools existed, but have now ceased. The one called LINKER is no longer online, and the other, known as LinkerDB, is no longer being updated or improved. SynLinker is important to the biomedical research community as it provides the most current and thorough resource of its kind. "SynLinker is the only up-to-date available online resource for selecting linker candidates in synthetic fusion protein design," Lee says.

SynLinker is freely available online. "We also provide online help information and tutorial video to guide the users to use SynLinker," Lee says.

More information: Chengcheng Liu et al. SynLinker: an integrated system for designing linkers and synthetic fusion proteins: Fig. 1., *Bioinformatics* (2015). DOI: 10.1093/bioinformatics/btv447

Provided by Agency for Science, Technology and Research (A*STAR), Singapore

from https://phys.org/news/2016-03-fusion-protein-drugs.html