Research could lead to new drugs for major diseases

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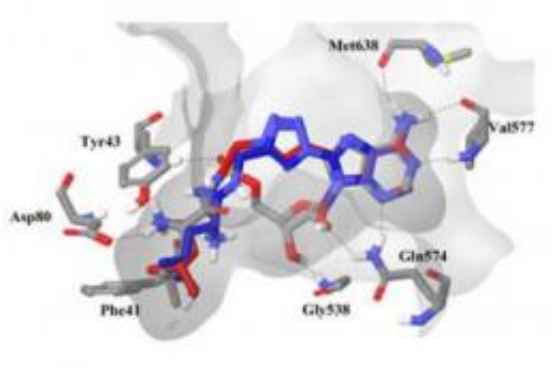

This is a molecular modeling image of a substance that binds to aminoacyl-tRNA synthetase. Credit: Photo: Per Fredrik Larsson

Researchers at the University of Gothenburg, Sweden, are working to develop substances that can prevent parasites, bacteria and fungi from producing essential proteins, research that could, in the long term, lead to new drugs for several major diseases.

The World Health Organization (WHO) has announced that aminoacyl-tRNA synthetases – a type of enzyme – are important targets for the development of new drugs for several major diseases such as cancer, various parasitic diseases and bacterial and fungal infections.

These enzymes are involved in the production of proteins (protein synthesis) in all organisms. Their job is to ensure that the right amino

acid is linked to the growing protein chain. These enzymes are essential for all living organisms.

Challenging research field

Researchers at the University of Gothenburg are currently undertaking basic research in this challenging field. The aim is to prevent the enzyme from producing proteins in bacteria, parasites or fungi, without stopping it from functioning in the human body.

"We're collaborating with researchers in several countries," says researcher Itedale Namro Redwan. "Our role has been to design and to synthesise substances that can be used for the development of drugs against parasitic diseases."

Looking for an effective substance

The enzymes' job of ensuring that the right amino acid is linked to the growing protein chain works in the same way in all types of cell, be they human or parasitic.

"The real challenge is identifying substances that act on enzymes in the parasite alone, without affecting the human enzymes at the same time," says Itedale Namro Redwan, who is making substances that can prevent bacterial and parasitic enzymes from functioning, but do not affect human enzymes. If this proves possible, it will help in the development of drugs for several major diseases.

"One of our main objectives has been to produce potent and selective substances that can be used to gain understanding of how these enzymes work. A greater understanding of their function would contribute to the development of medication for diseases like elephantitis."

Could prevent major diseases

Elephantitis, also known as filiaris, affects more than 120 million people in the developing world, and is caused by a worm that lives in the infected person's lymphatic vessels.

The potentially active molecules are being designed using computer-based molecular modelling techniques, with the resulting molecules subsequently synthesised via various chemical reactions.

"One of the best things about being a medicinal chemist is getting to plan a synthetic pathway that'll result in a specific substance, starting the reaction and then realising that the reaction's has worked," says Itedale Namro Redwan. "Better still is finding out that the molecule has performed as expected in a biological test."

The activity of the synthesised substances is assessed by partners through biological testing on, for example, aminoacyl-tRNA synthetase isolated from E. coli or filiaris parasites.

More information: The thesis "Design and Synthesis of Potential Aminoacyl-tRNA Synthetase Inhibitors" has been successfully publicly defended at the University of Gothenburg on 11 May 2012.

Provided by University of Gothenburg

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