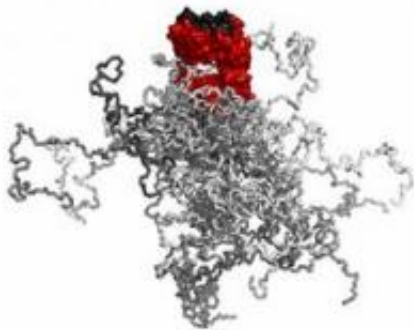


Researchers prolong the half-life of biopharmaceutical proteins

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Structure of a PASylized antibody fragment.

Many biopharmaceuticals comprise small proteins that are quickly eliminated from the body. Scientists at the Technische Universitaet Muenchen (Germany) combine such small proteins with a kind of molecular balloon that swells and thus prolongs the half-life of the proteins in the body. The TUM spin-off XL-Protein GmbH has now started to further develop this new technology with blockbuster potential.

People who suffer from [hepatitis B](#) are often treated with the tissue hormone interferon. However, there is a problem: Interferon is a very small [protein](#), which is filtered from the blood via the kidneys after only a short time. For the patient this means a high-dose injection every other

day to keep the effect of the substance from wearing off prematurely.

However, interferon stays in the body much longer when chemically coupled with a synthetic PEG (polyethylene glycol) molecule. PEG is a random coil long-chain polymer string that swells by adsorbing water. That way the PEG molecule becomes large enough that it does not fit through the fine pores of the kidneys - the attached interferon remains in the circulatory system longer, and the patient will need an injection only every one to two weeks.

Using [genetic engineering](#), TU Muenchen scientist Prof. Arne Skerra and his coworkers from the Chair of Biological Chemistry at the Center for Life and Food Sciences Weihenstephan have now developed an amino acid string that tangles up similarly to PEG and also swells in the presence of water. However, unlike many PEG compounds, there is no danger of this biological polymer accumulating in the body. In fact - over an extended period of time - it is discharged or biologically broken down. That happens because this amino acid string (polypeptide) consists of three of the 20 naturally occurring amino acids: proline, alanine and serine, or in short, PAS.

The protein substance interferon, which itself consists of [amino acids](#), can thus be easily generated in "PASylated" form. In first trials with animals, TUM scientists established that PASylated interferon has a half-life in the blood that is prolonged by a factor of 60, which should allow a significant extension of dosing intervals during medicinal therapy.

A further advantage is the simplified biotechnological production: The DNA segments carrying the information for the PAS amino acid sequence and for the interferon can simply be attached to each other and then, for instance, used for transforming bacteria. The bacteria then produce the PASylated [interferon](#) in one piece, thus making much fewer production steps necessary in comparison with the chemical coupling of

PEG. According to Skerra, "this will lead to a significant drop in production cost."

In principle all small proteins currently used as medication or in development in pharmaceutical companies - for example, growth factors or functional antibody fragments - can be PASylated. Thus there could be a huge market for the new technology. Consequently, Prof. Skerra and his team initiated the founding of a new biotech company, XL-Protein GmbH (<http://www.xl-protein.com>), which started its operations last spring. "Our technology has the potential to give birth to a whole new generation of blockbuster medications," the TUM biochemist is convinced. Several of the new drugs are already at an advanced stage of preclinical development.

Source: Technische Universitaet Muenchen

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