XL-protein
Superior Biopharmaceuticals

PASylated enzymes

Therapeutic enzymes are widely applied to treat rare genetic disorders as well as various types of cancer. Despite the huge success of this protein class, there are issues which limit the desired therapeutic outcomes. While they often show an intrinsically short plasma half-life, enzymes of non-human origin are immunogenic. Conjugation with polyethylene glycol (PEG) is an attempt to tackle these issues. However, organ accumulation of the non-biodegradable PEG, the formation of anti-PEG antibodies and complement activation have been reported. The resulting PEG hypersensitivity can reduce drug efficacy in individual patients and the exposure to PEG via the food chain, cosmetics or by recent Covid-19 vaccinations may further emphasize this problem. PASylation® , the genetic fusion or chemical conjugation with a conformationally disordered polypeptide of Pro, Ala, and/or Ser, is a superior alternative to PEG. It offers an elegant solution to overcome these problems and to create a novel generation of therapeutic enzymes with enhanced efficacy and safety.

Extended plasma half-life

- Expanded hydrodynamic volume leading to extended circulation time
- Reduced injection frequencies

Immunogenicity shielding

- The hydrated, bulky PAS polypeptide can interfere with immune recognition of antigenic enzyme epitopes

Efficient & cheap production

- Genetic fusion: high yields, homogenous product & reduced costs
- Compatible with various industry standard expression systems

Biodegradable PEG alternative

- PAS overcomes PEG hypersensitivity
- No organ accummulation during chronic treatment

Related Publications:

Najjari A. et al. (2021) The effective control of hyperuricemia in cancer patients: A new recombinant conjugated variant of urate oxidase. *Asian Pac. J. Cancer Prev.* 22, 627-632.

Dublin, July 26, 2017, (PRNewswire): Jazz Pharmaceuticals and XL-protein GmbH enter into a license agreement on PASylation® technology to develop long-acting asparaginase product candidates.

Lerchner A. et al. (2016) Fusion of an alcohol dehydrogenase with an aminotransferase using a PAS linker to improve coupled enzymatic alcohol-to-amine conversion. *Protein Eng. Des. Sel.* 29, 557-562.

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