

In vivo polysialylation to enhance the pharmacokinetic profile of therapeutic proteins and immunomodulation

An important factor for the clinical and commercial success of protein based drugs lies in optimal bioavailability, which is a major challenge for pharmaceutical industry. It has been shown that Polysialic acid (PolySia), large negatively charged sugar chains, has the ability to modulate protein pharmacokinetics, bio-distribution and bioavailability. In addition, PolySia contributes to anti-inflammatory processes.



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BACKGROUND

PolySia is a unique glycopolymer of α 2,8-linked sialic acid residues, originally identified on neural cell adhesion molecule (NCAM) of vertebrates. PolySia mediates diverse biological functions and has great potential in therapeutic use. Chemical or in vitro PolySia engineering has made a remarkable impact on pharmacokinetic properties of recombinant therapeutic glycoproteins. Here we demonstrate the in vivo protein PolySia by intensive glyco-engineering of a plant-based expression platform.

TECHNOLOGY

Nicotiana benthamiana plants are well suited for the generation of therapeutic glycoproteins with defined glycan structures. By genetic deconstruction and overexpression of mammalian glycosylation proteins we have developed plant glycosylation mutants which can efficiently synthesize mammalian like disialylated N-glycan structures. To further elongate disialylated structures towards PolySia we transiently expressed two human polysialyltransferases in our engineered plants along with Ig5FN1, the naturally polysialylated domain of NCAM. HPLC analysis of the plant produced Ig5FN1 exhibited N-glycans carrying a chain length exceeding 40 sialic acid residues.

AT A GLANCE ...

Available for

- License Agreement
- Collaboration
- Assignment

Keywords

- Polysialic acid
- Polysialylation
- Glycopolymer
- Plant expression system

IPR

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Video

<https://youtu.be/6YktgQ1hRyg>

APPLICATION OF POLYSIA

One of the major concerns in recombinant biologics is rapid clearance from blood stream. The attachment of polymers like PolySia is a promising approach to overcome this limitation and PolySia may be used in immunological processes like anti-inflammatory treatments or tissue regeneration.

BENEFITS

- PolySia is a natural product thus biodegradable and non-immunogenic
- PolySia protects proteins from degradation
- Extended half-life provides low frequency of dosage-applications
- Extended half-life improves pharmacological activities
- PolySia has anti-inflammatory activities and protects from cytotoxicity

COOPERATION OPPORTUNITIES

On behalf of University of Natural Resources and Life Sciences Vienna, TransMIT GmbH is looking for cooperation partners or licensees for further development in Germany, Europe, US, and Asia.

A TECHNOLOGY OF



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