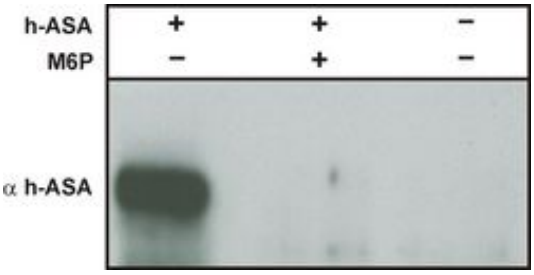
Technology Offer

Man6P-specific single chain antibody fragment for detection of mucolipidosis and optimization of enzyme production for ERT

Reference Number 14-00022

Challenge

Inherited metabolic disorders mucolipidose (ML) type II/III result from deficiency of a specific transferase, responsible for the formation of mannose-6-phosphat (Man6P)-modified glycoproteins. Without Man6P, the glycoproteins are not destined for lysosomes and escape outside the cells. The deficiency may be overcome by enzyme-replacement therapy (ERT), which, however, requires expensive production and downstream-processing and does not ensure provision of therapeutically active enzymes, i.e. those carrying Man6P.



Immunoprecipitation of recombinant human arylsulfatase A (h-ASA) from medium of cultured cells overexpressing h-ASA using antibody M6P-1.
h-ASA was visualized by immunoblot using a specific antibody (? h-ASA). The precipitation could be inhibited by addition of Man6P (M6P).

Technology

A high-affinity Man6P-specific single-chain antibody fragment has been developed, which allows specific and rapid detection of Man6P-containing proteins. The antibody fragment has been shown to facilitate easy diagnosis of ML II and ML III (Mueller-Loennies et al., 2010, Am J Pathol 177:240f; Makrypidi et al., 2012, Mol Cell Biol 32:774f). Man6P content also represents a critical quality attribute of enzymes used for ERT. Accordingly, the antibody fragment possesses great utility in evaluating manufacturing processes to improve yields and quality of therapeutic enzymes, as well as in optimizing and controlling their production (Madhavarao et al., 2014, Biotechnol Appl Biochem 61:184f).

Commercial Opportunity

The technology is offered for in-licensing.

Development Status

The inventors have generated a recombinant antibody fragment, specifically binding to Man6P. The protein expresses well in a prokaryotic host, can be purified to homogeneity, is stable over several months at 4°C and can be immobilized on affinity media without loss of activity.
It has been succesfully demostrated that the antibody fragment allows:

- easy diagnosis of ML II and III by western blots
- histological staining of lysosomes
- selective purification in a one-step procedure of recombinant high-affinity uptake forms of lysosomal enzymes on affinity media (see figure)
- control and optimzation of production processes of therapeutic enzymes for the treatment of lysosomal storage disorders

Patent Situation

Proprietary access to scAb-fragment expressing clone.

Further Reading

Schröder et al (2010) Site-specific analysis of N-linked oligosaccharides of recombinant lysosomal arylsulfatase A produced in different cell lines. Glycobiology 20:248-259
Müller-Loennies et al (2010) A Novel Single-Chain Antibody Fragment for Detection of Mannose 6-Phosphate-Containing Proteins. Application in Mucolipidosis Type II Patients and Mice. American Journal of Pathology 177: 240-247
Madhavarao et al (2014) Evaluation of butyrate-induced production of mannose-6-phosphorylated therapeutic enzymes using parallel bioreactors. Biotechnol Appl. Biochem 61: 184-192

Forschungszentrum Borstel
Leibniz-Zentrum für Medizin und Biowissenschaften

Licensing Contact:
Dr Torsten Stachelhaus
Technology Manager
T: +49 40 1888 43 48
stachelhaus@ascenion.de

Ascenion GmbH
Herzogstraße 64
D-80803 München
T: +49 89 318814-0
info@ascenion.de
www.ascenion.de