



Tailoring the lifespan of drugs

Jan Terje Andersen

UiO Bepartment of Molecular Biosciences

The Faculty of Mathematics and Natural Sciences

Translational research: The importance of academic-industrial partnership in turning basic research into products



Short-lived biological and chemical drugs

1. A major challenge for the therapeutic use of many drugs is their short lifespan.

- 2. Removed very rapid from the body (minutes, hours, few days).
- 3. Limits their therapeutic efficacy.



4. <u>Expensive</u> treatment, <u>large doses</u> required, <u>burden</u> for the patient.

5. Many promising drug candidates will never reach the marked due to these obstacles!



Why are they eliminated from the body?



- The drugs are small.
- The drugs are removed via the kidneys, excreted in to the urine.
- The drugs are quickly broken down/ metabolized in the liver that receives up to 60 liters of blood each hour.



Albumin as a carrier of drugs

ALBUMIN is an ideal protein that can be utilized as a carrier of drugs!

- Why ALBUMIN?
- It has a unique half-life of <u>3 weeks</u>.
- It is <u>not removed</u> from the blood via the kindeys or the liver.
- It is a very <u>stable</u> protein, <u>soluble</u> in water.



We and others have discovered why albumin is not removed quickly from the body

ALBUMIN is rescued from degradation due to binding to the **neonatal Fc receptor (FcRn)**.



The AlbufuseTM technology



Fusion to albumin extends the lifespan of drugs

Is it possible to enhance the lifespan of albumin beyond that of nature?

Molecular engineering of the ALBUMIN-FcRn interaction



<u>Our secret</u>

We know how FcRn binds ALBUMIN

-We can design new ALBUMINs with improved binding to FcRn

Bioinformatics and biotechnological tools

Design of "super"-ALBUMIN



• A single point mutation (1/585) is enough to alter binding to FcRn dramatically!

ALBUMIN with a range of FcRn binding strengths

AlbufuseTM Flex variants



Superior lifespan of AlbufuseTM Flex variants beyond that of natural albumin



Tailoring the lifespan using Albufuse Flex variants

AlbufuseTM FLEX: reduced frequency of dosing and improved bioavailability



Centre for Immune Regulation Department of Molecular Biosciences

OUS-HF Rikshospitalet Department of Immunology



Inger Sandlie Jan Terje Andersen





Centre for Molecular Biology and Neuroscience (CMBN) Department for Medical Microbiology. Department of Medical Biochemistry

> Oslo University Hospital

Bjørn Dalhus Magnar Bjørås







Muluneh B. Daba

Stian Foss



ss Algirdas Grevys



Jørund Sollid Jostein Dalland



HELSE • • SØR-ØST