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Harnessing and enhancing the natural properties of albumin as a drug carrier by rational protein engineering

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Human serum albumin is the most abundant serum protein and has a long history of safe use in biopharmaceutical products. It has many features that contribute to the molecule being naturally well designed as a drug carrier, including its high solubility and stability, long circulatory half-life and the potential to attach therapeutic candidates by fusion or conjugation. We will describe Veltis® albumin variants designed to enhance two of these aspects, long circulatory half-life and drug attachment by conjugation, whilst maintaining solubility, stability and its inherent low immunogenicity. The long circulatory half-life of albumin in the human body (around 19 days) derives in part from the size of the molecule, whereby it resists filtration through the kidneys and in part from its association with the neonatal Fc receptor (FcRn). Albumin binds to FcRn under acidic conditions in the endosome and is rescued from lysosomal degradation back to the plasma where it is released under neutral pH conditions. We will describe our rational design of variants to enhance binding to the receptor under acidic conditions, whilst retaining release at neutral pH, resulting in a greater than two-fold improvement in half-life. Short half-life is a significant challenge for many peptide and protein therapeutics; fusion or conjugation to Veltis engineered albumins offers the potential of monthly dosing. We will also present thio-engineered albumin variants to improve drug efficacy by increasing the drug-albumin ratio whilst maintaining FcRn-binding capabilities and half-life extension. Rational protein design has enabled us to enhance specific properties of albumin related to drug delivery whilst retaining the numerous other features which contribute to the molecule being naturally well designed as a drug carrier.

Biography

Karen Bunting is a Science Director at Albumedix, heading Molecular Biology and Fermentation within Research and Technical Development. Prior to the formation of Albumedix, she has joined Novozymes Biopharma UK in 2011 as a Senior Research Scientist and later as Science Manager. She has 20 years' experience in Structural Biology and Protein Engineering. At Albumedix her primary research focus has been the design and engineering of albumin variants to optimize the circulatory half-life of therapeutic agents. Prior to joining Novozymes, she led a research team at the University of Nottingham focusing on structural analysis of protein-protein and protein-DNA interactions, following on from Post-doctoral work at the Institute of Cancer Research in London. She has obtained BSc in Microbiology from Imperial College, London and PhD in Crystallography from Birkbeck College, London.

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