"Smart multifunctional GLA-nanoformulation for treating Fabry disease"

Ángel del Pozo
Smart4Fabry Consortium

Biopraxis, Hermanos Lumiere 5, Miñano, Spain
apozo@praxisph.com

Abstract (Century Gothic 11)

Lysosomal storage disorders (LSD) diseases are a group of rare diseases that currently lack a definitive cure. LSD incidence is about 1:5,000 - 1:10,000, representing a serious global health problem. One relevant LSD is the Fabry disease (FD), in which the deficiency in a-Galactosidase A (GLA) enzyme activity results in the cellular accumulation of neutral glycosphingolipids, leading to widespread vasculopathy with particular detriment of the kidneys, heart and nervous system. The current treatment for FD is the Enzyme Replacement Therapy (ERT), in which free GLA recombinant protein is administered intravenously to patients. ERT exhibits several drawbacks mainly related to the instability, high immunogenicity and low efficacy of the exogenously administered GLA to cross biological barriers, such cell membranes and blood brain barrier (BBB). In this scenario, a correct nanoformulation of the GLA enzyme is foreseen as a critical step to improve the ERT.
Precisely, the aim of Smart-4-Fabry EU project (#720942) is to achieve excellent quality control over the assembly of the different molecular components of a new liposomal nanoformulation of GLA, nano-GLA, for the treatment of Fabry disease. Nanoformulated GLA has already shown to have better PK/PD profile than free GLA and higher efficacy in vivo [1]. Smart-4-Fabry project will advance nano-GLA from an experimental PoC (TRL3) to preclinical regulatory phase (TRL5-6). A one-step method based on the use of green CO_2, will be used for the manufacturing of this novel nanoformulation under GMPs [2]. The final GLA nanoformulation will have tailored transport of GLA through cell membranes and BBB

References

[1] "*a-Galactosidase-A-Loaded Nanoliposomes with Enhanced Enzymatic Activity and Intracellular Penetration*", I. Cabrera, I. Abasolo, J.L. Corchero, E. Elizondo, P. Gil Rivera; E. Moreno, J. Faraudo, S, Sala, D. Bueno, E. Gonzalez-Mira, M. Rivas, M. Melgarejo, D. Pulido, F. Albericio, M. Royo, A. Villaverde, M. Garcia-Parajo, S. Schwartz Jr., N. Ventosa, J. Veciana, *Adv. Healthcare Mater.* **7**, 829-40 (2016).Authors, Journal, Issue (Year) page

[2] "Multifunctional Nanovesicle-Bioactive Conjugates Prepared by a One-Step Scalable Method Using CO2-Expanded Solvents", I. Cabrera, E. Elizondo, O. Esteban, J.L. Corchero, M. Melgarejo, D. Pulido, A. Cordoba, E. Moreno, U. Unzueta, E. Vazquez, I. Abasolo, S. Schwartz Jr., A. Villaverde, F. Abericio, M. Royo, MF Garcia-Parajo, N. Ventosa, J. Veciana, Nano Letters. 13, 3766-3774 (2013).

Figures

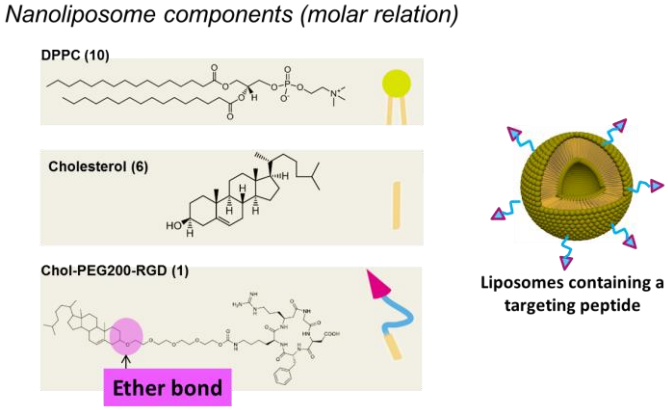

Figure 1: Modified (patent protected) lipids and lipsome strcuture