Contribution ID : **37** Type : **Poster**

Synchrotron light in the structural studies of human transferrin for its application as a drug transporter in the central nervous system

Wednesday, 23 June 2021 14:40 (0:10)

Abstract

Human serum transferrin (Tf) is a ˜80 kDa glycoprotein that transits the blood plasma, whose function is to transport iron from its absorption site towards every cell through the blood vessels. Its structure consists of two homologous lobes, an N-terminal lobe and a C-terminal lobe, which can each bind a metallic ion, mainly Fe3+, through a coordination bond with octahedral geometry1–3. This important protein has been proposed as a potential drug transporter due to its transport mechanism across the blood-brain barrier4,5. To determine the feasibility of such system, a thorough structural and bioanalytical characterization of transferrin is essential, for which synchrotron light is a powerful resource. X-ray crystallography is one of the most widely used approaches for structure determination, and several Tf models have been obtained so far2,3,6–8; however, further research is necessary to generate high resolution models. Besides, a plethora of non-conventional crystallization techniques are available for crystal growth optimization, which in turn provides higher quality crystallographic data9–11. Therefore, the current project is exploring several of these methods for growing high quality transferrin crystals, being counter diffusion one of the main bets. Another powerful technique is Small Angle X-ray Scattering (SAXS), which has been able to provide information for Tf regarding its stability and behavior in solution12. Since transferrin's iron release mechanism has been shown to be pH dependent1, SAXS analyses at different pH conditions are being performed to study its conformation states throughout the stages of its iron binding and release cycle.

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Session Classification : Poster Session