Interaction between Human Serum Albumin and an Anionic-Fluorinated Porphyrin

Andreia Filipa da Costa Tuna[1]*, Otávio Augusto Chaves[1] and Carlos Serpa[1]

[1]Centro de Química de Coimbra (CQC), Departamento de Química, Universidade de Coimbra, Rua Larga, 3004-545 Coimbra, Portugal

*andreia.dacostatuna@gmail.com

Human serum albumin (HSA) is the most abundant globular protein in the bloodstream, being responsible for the biodistribution of both endogenous and exogenous compounds which directly impact the pharmacokinetic profile of drugs.[1] In this sense, the present work reports via molecular docking calculations and spectroscopic measurements the interaction between HSA and an anionic tetrapyrrolic macrocycle which presented feasible photosensitizer capacity to photodynamic therapy of cancer (PDT) (**TPFFS$_4$**).[2] The HSA structure presents three main binding sites (subdomains IIA, IIIA, and IB),[1,3] and molecular docking calculations suggested subdomain IB (site III, an electrostatic positive pocket) as the main region for **TPFFS$_4$**. The UV-Vis spectra indicated a hyperchromic effect at 280 nm and a bathochromic shift at Soret band of porphyrin (~ 400 nm) in the proportion HSA:**TPFFS$_4$** of 1:1, indicating an interaction in the ground-state. The steady-state fluorescence measurements corroborated with this hypothesis and indicated that **TPFFS$_4$** might perturb the microenvironment around the tryptophan residue (a hypsochromic shift). The Stern-Vomer (K_{SV} ~ 0.90 – 1.25 × 10^5 M^{-1}) and quenching rate constant (k_q ~ 1.42 – 2.15 × 10^{13} $M^{-1}s^{-1}$) values indicated that the fluorescence quenching mechanism is dependent of **TPFFS$_4$** concentration: static process until proportion 1:1 for HSA:**TPFFS$_4$** and dynamic at higher porphyrin concentration.[1,3] These data is in accordance with the obtained time-resolved fluorescence trend. The modified Stern-Volmer binding constant (K_a ~ 1.11 – 8.13 × 10^4 M^{-1}), enthalpy (ΔH ~ 51.0±6.4 $kJmol^{-1}$), entropy (ΔS ~ 0.254±0.021 $kJmol^{-1}K^{-1}$), and Gibbs' free energy change (ΔG < 0 $kJmol^{-1}$) showed that the binding is moderate, entropically driven and spontaneous.[3] Overall, **TPFFS$_4$** showed good binding parameters with HSA being able to be biodistributed by this protein in the human bloodstream.

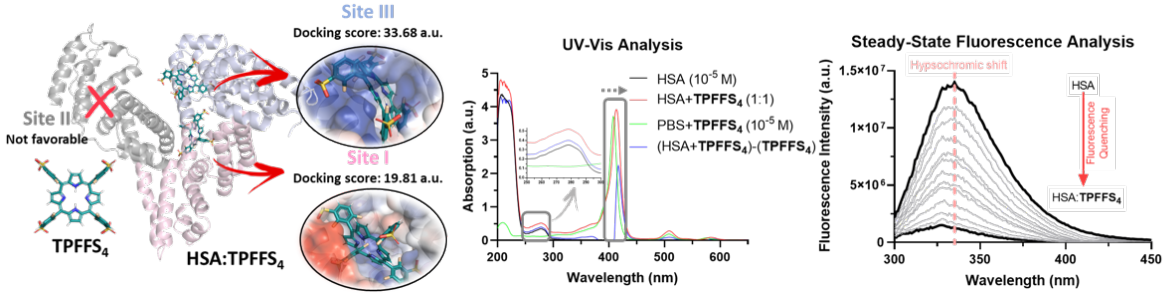

Figure. *Molecular docking and spectroscopic analysis for HSA:**TPFFS4**.*

References

[1] S. Naveenraj, S. Anandan. *J. Photochem. Photobiol. C* **2013**, *14*, 53-71.

[2] B. Pucelik, R. Paczyński, G. Dubin, M.M. Pereira, L.G. Arnaut, J.M. Dąbrowski. *PLoS ONE* **2017**, *12*, e0185984.

[3] T.V. Acunha, O.A. Chaves, B.A. Iglesias. *J Porphyr. Phthalocyanines* **2021**, *25*, 75-94.