Photosensitizers for photodynamic therapy: from photophysics to assisted delivery.

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Theoretical studies have been employed in photodynamic therapy to predict and understand the optical and photophysical properties of photosensitizers. This is particularly helpful, when a new class of compounds is considered as photosensitive drug, such as BODIPYs. Insights on the deactivation mechanism, upon radiation, could suggest substitution patterns to enhance their efficacy as photosensitizers. [1] The overall efficacy of the treatment, though, is not only due to the light-response of the drug, but arise from the effectiveness of the different stages represented in Figure 1.

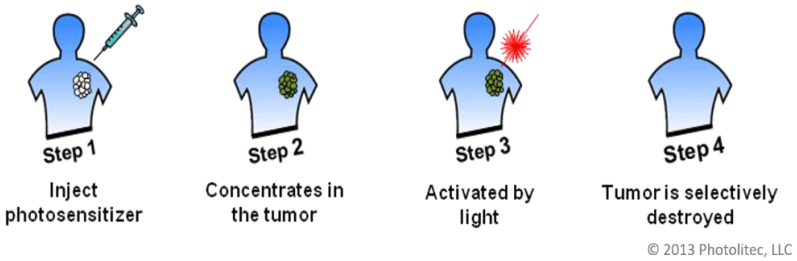

Figure 1. *Schematic representation of photodynamic therapy treatment stages.*

The hydrophobicity of porphyrin derivative photosensitizers, such as Temoporfin, prevents an easy administration of the drug. This problem has been addressed engaging nano-carriers, such as liposomes, for an assisted delivery. Calorimetric measurements showed that the thermal stability of the liposome is enhanced when the photosensitizer is embedded inside it. [2] In order to explain this behaviour, all-atom classical molecular dynamics simulations have been performed. Specifically, the disaggregation process of the drug/bilayer structure induced by high temperatures has been modelled. These challenging simulations, which involve half a million of atoms and simulation times of hundreds of nanoseconds, are feasible thanks to the use of GPU-based hardware. Understanding the nature of the interactions responsible for the altered stability of the carrier, when loaded with the drug, is expected to help formulating improved nano-carriers for extremely hydrophobic drugs.

References

[1] M. De Vetta, L. González, I. Corral, in preparation, (2017).

[2] N. Dragicevic-Curic, M. Friedrich, S.Petersen, D. Scheglmann, D. Douroumis, W. Plass, A. Fahr, *International Journal of Pharmaceutics,* **412** (2011), 85-94 .