Challenging tumor hypoxia with a polymeric carrier system simultaneously encapsulating complementary therapeutic agents

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Nanotechnologies have been exploited for the co-administration of chemotherapeutics such as taxanes with a photosensitizer (PS) which produces singlet oxygen ($^1O_2$) upon irradiation with red light in the presence of molecular oxygen (O_2) targeting cancer cells (photodynamic therapy, PDT).[1] However, tumor tissues often suffer from hypoxic conditions, an inadequate supply of O_2 compromising PDT efficacy[2] and activating resistance to chemotherapy[3]. The HypoCyclo project aims to develop a novel combination of chemo- and photo-therapies for the effective treatment of Breast Cancer (BC), bypassing hypoxia-derived limitations. We focused on cyclodextrin polymers (pCyD), biocompatible carriers able to improve the solubility and stability of hydrophobic drugs under physiological conditions and to host multiple functional agents outperforming current cancer treatments. We will discuss a multi-modal pCyD i) loaded with paclitaxel (PCX) as chemotherapeutic agent, ii) decorated with Chlorin e6 (Ce6) for PDT, and iii) functionalized with an Oxygen Releasing Agent (ORA) to supply O_2 *in situ*[4]. Preliminary data will be presented showing the NMR, UV-Vis and ESI-MS characterization of synthesized anthracene derivatives selected as suitable ORA due to their capacity to form endoperoxides photochemically by trapping $^1O_2$ and releasing it upon cycloreversion[5]. We will further provide evidences of the successful co-encapsulation of PCX, ORA and Ce6 into βCyD-polymer, without affecting the properties and efficacy of each component.

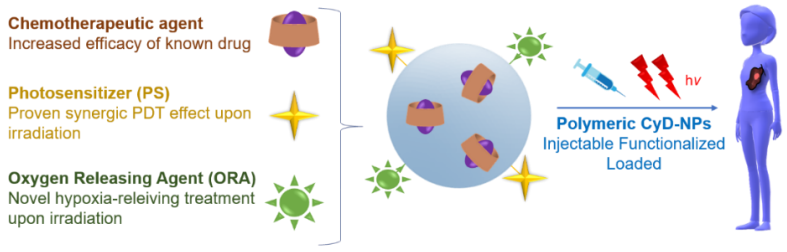

Figure 1. Design of a carrier based on co-encapsulation of three agents into the same CyD-polymer.

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References

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