Tuning the Properties of Supramolecular Colloidal-Probes for Hydrogen Peroxide

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Hydrogen peroxide (H_2O_2) plays an important role in normal metabolic pathways in cells. However, its presence is not always beneficial to cellular health, since a high concentration of H_2O_2 has been correlated to diseases such as cancer and arthritis. This has prompted the development of systems that respond to H_2O_2 concentrations as imaging agents or drug carriers, in efforts to improve current treatments. Despite continued progress in the development of H_2O_2 probes and responsive systems, challenges remain regarding adequate biocompatibility, and the specificity for targeting a desired diseased site. Boronic esters are functional groups selective to H_2O_2 that are used in H_2O_2-responsive systems. Previously, we had synthesized boronic ester probes (BEPs) using a variety of boronic ester aldehydes and measured their photophysical properties upon oxidation with H_2O_2. We found that BEPs had interesting fluorescent properties after oxidation and could serve as turn-on probes in biological environments. We also have developed colloidal particles termed supramolecular Hacky Sacks (SHS) suitable for the encapsulation of BEPs achieving a supramolecular micro-probe with the potential of imaging H_2O_2 microenvironments in living cells. SHS are formed from thermo-responsive supramolecular G-quadruplexes formed via the self-assembly of guanosine derivatives. Preliminary studies of the probes showed a need to shift the fluorescence of the BEPs to longer wavelengths (red-shift) to perform more effective in vitro studies. In addition, varying the hydrophobicity of BEPs could preserve the turn-on properties for a longer period of time taking advantage of the hydrophobic core of the SHS. Herein, we will present the synthesis of new BEPs via a Claisen-Schimdt condensation, using acetophenone and 4-boronic ester naphthaldehyde, and the Knoevenagel condensation using different boronic ester aldehydes and malononitrile, increasing the conjugation and the excitation wavelength of these molecules. Also, we synthesized BEPs with different aromatic ketones with 4-formylphenyl boronic acid pinacol ester. These BEPs were synthesized with reasonable yields and were characterized by UV/Vis spectroscopy, fluorescence spectroscopy and 1D/2D NMR. We will highlight the photophysical properties in solution and within SHS enabling the comparison with previously developed probes. These studies represent important progress towards the development of supramolecular imaging micro-probes based on the integration of BEPs and SHS, which provides the initial steps towards cell-based studies.