UCLA Chemistry & Biochemistry

Physical Chemistry Seminar

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Activatable Imaging Nanoagents for the Self-Reporting Delivery of Cancer Therapeutics

Activatable nanoagents are those that enhance their signal output (magnetic or fluorescent) upon interacting with specific changes in the biological environment (pH, enzymatic activity) of areas of disease. A key activatable nanoagent developed in our lab is based on iron oxide nanoparticles (IONPs). Even though IONPs have been extensively studied as MRI contrast agents, their use as drug delivery agents is rather new. Particularly, the changes in MR signal observed upon drug release is a phenomenon not previously reported, until recently described by our lab. We have developed a method that encapsulates drugs and fluorescent dyes within the hydrophobic pockets of the polymeric coating surrounding the iron oxide nanoparticle. The cargo within the polymeric coating is stable at physiological pH, but it is released at lower pH. In our method, the drug is never conjugated to the polymer surrounding the nanoparticle, but rather is entrapped via hydrophobic interactions in internal hydrophobic pockets within the polymer. In particular, we have developed various iron oxide nanoparticle formulations that change their magnetic water relaxation properties upon drug release triggered by changes in pH. The main idea is to generate a nanoagent that only produces a signal upon interaction with the designated cellular target, minimizing background signal and increasing signal-to-noise ratio upon release of a drug. Furthermore, radioisotopes (such as ^{89}Zr) can also be encapsulated within these nanoparticles, generating a nanoparticle that can be tracked by both MRI and PET. Finally, our lab has developed binding magnetic relaxation (bMR) nanosensors. These activatable nanosensors change their water relaxation upon binding of molecular targets to small molecules on the nanoparticle surface. Using this method, we have identified small molecules that bind to various toxins and cellular receptors for potential use in diagnostic and targeted therapeutic applications.

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