Light-triggered release of drugs in vivo: amplification strategies, response to new wavelengths, and application to a clinical challenge

Awardee: Adah Almutairi
Award: New Innovator Award
Awardee Institution: University of California, San Diego

Co-authors: Carl-Johan Carling, Jason Olejniczak, Viet Anh Nguyen Huu, Noah J.J. Johnson, Sha He, Arnold Garcia, Jing Luo, Kang Zhang
Co-author Institution: University of California, San Diego

This presentation will cover several recent advances in the development of light-degradable polymers as tools for biological research and drug delivery, including a strategy for chemically amplifying the light signal to accelerate degradation, a polymer that degrades upon single-photon absorption of red light, novel upconverting structures enabling efficient conversion of more biologically compatible wavelengths, and application of a previously reported polymer to the treatment of disease. The chemical amplification strategy relies on phototriggered unmasking of acidic groups that hydrolyze adjacent ketals, which overcomes ketals' requirement of low pH for efficient degradation. Particles composed of the photocaged-acid/ ketal polymer degrade rapidly upon brief irradiation. The red light-degradable polymer incorporates a photocage not previously used in responsive materials, which cleaves in hydrophobic environments (unlike coumarins). Particles composed of this polymer, when subcutaneously injected and irradiated through tissue, release sufficient drug to significantly reduce carrageenan-induced paw inflammation in mice. Our advance in the upconversion field is the application of uniform shell deposition to overcome dopant concentration quenching, allowing unprecedented upconversion efficiencies at 800 nm. Absorption of this wavelength rather than the 980 nm employed by current structures avoids the potential for tissue heating, as water's absorption of 800 nm infrared is much lower. Finally, we have evidence that a UV-degradable polymer (Fomina et al., *J Am Chem Soc* 2010) may be useful for the delivery of anti-angiogenics in the eye to treat macular degeneration. This strategy would preserve clinician control over dose timing while reducing the frequency of intravitreal injections. UV-degradable particles are stable in the eye for months and release a therapeutically effective dose of a small molecule anti-angiogenic; the irradiation required for release is well-tolerated by the eye.