Tricolor Visible Wavelength-Selective Hydrogels for Cell Encapsulation and Release

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Statement of Purpose: Over the past decade, photoresponsive biomaterials have birthed a surge of innovation in targeted drug delivery and 4D cell culture. Compared to other material-modifying stimuli (e.g., pH, enzymes, heat etc.), light is a particularly powerful stimulus, uniquely affording spatiotemporal control in an orthogonally specified manner with different wavelengths.[1] Despite its established promise in laboratory settings, significant challenges remain in pushing these technologies to the clinic. Current photosensitive materials are constrained by their reliance on high-energy UV light which is poorly penetrant through human tissue, limiting the depths to which they may be used for *in vivo* treatment. Additionally, photoresponsive materials developed thus far most typically respond to one or potentially two distinct wavelengths, thereby missing significant opportunities for reaction multiplexing by taking advantage of the entire spectrum of visible and IR light. In this work, I will discuss our recent results in designing and synthesizing a series of visible light-responsive cytocompatible polymer crosslinkers for next-generation hydrogel photodegradation.

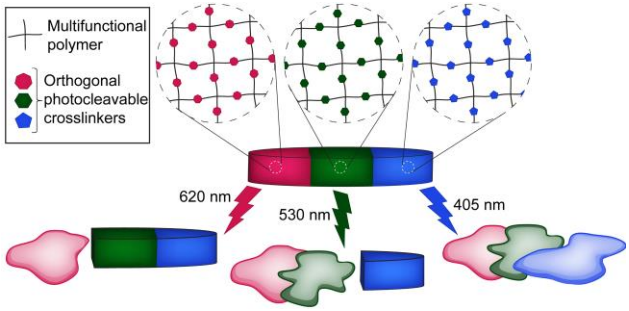

Figure 1. Tricolor degrading hydrogels. PEG-based hydrogels degrade selectively under irradiation at three different wavelengths.

Methods: A series of three crosslinkers was synthesized based on well-established photochemistries of ruthenium polypyridyl complexes[2] and *ortho*-nitrobenzyl moieties[3]: RuPink, RuOrange, and *o*NB. The crosslinkers were found to be selectively photocleaved at 617 nm, 530 nm, and 405 nm irradiation respectively. These three crosslinkers formed stable hydrogels with multifunctional strained alkyne-bearing poly(ethylene glycol) (PEG) via bioorthogonal strain-promoted azide-alkyne cycloaddition (SPAAC). The resulting hydrogels were highly light sensitive and were successfully utilized to encapsulate and deliver mammalian cells.

Results: RuPink and RuOrange demonstrated exceptionally high photoefficiencies under low-energy light activation. Hydrogels based on these crosslinkers degraded rapidly and showed highly tunable stiffness with light exposure, degrading under irradiation through up to 2 cm of tissue. Cell viability throughout the encapsulation and release process was similarly high to in previously reported PEG-based hydrogels and sustained in extended culture.

Conclusions: The work presented here represents the first report of an entirely visible three-color selectively responsive biomaterial. The new crosslinkers reported are remarkably photoefficient, form rapidly softening hydrogels, and are highly cytocompatible over long periods of time. These materials represent the next generation of multiresponsive materials for deep tissue drug delivery.

References:

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