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Luciferin-Bioinspired Click Ligation Enables Hydrogel Platforms with Fine-Tunable Properties for 3D Cell Culture

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Abstract:

There is an increasing interest in coupling reactions for cross-linking of cell-encapsulating hydrogels under biocompatible, chemoselective, and tunable conditions. Inspired by the biosynthesis of luciferins in fireflies, here we exploit the cyanobenzothiazole-cysteine (CBT-Cys) click ligation to develop polyethylene glycol hydrogels as tunable scaffolds for cell encapsulation. Taking advantage of the chemoselectivity and versatility of CBT-Cys ligation, a highly flexible gel platform is reported here. We demonstrate luciferin-inspired hydrogels with important advantages for cell encapsulation applications: (i) gel precursors derived from inexpensive reagents and with good stability in aqueous solution (>4 weeks), (ii) adjustable gel mechanics within physiological ranges (E = 180–6240 Pa), (iii) easy tunability of the gelation rate (seconds to minutes) by external means, (iv) high microscale homogeneity, (v) good cytocompatibility, and (iv) regulable biological properties. These flexible and robust CBT-Cys hydrogels are proved as supportive matrices for 3D culture of different cell types, namely, fibroblasts and human mesenchymal stem cells. Our findings expand the toolkit of click chemistries for the fabrication of tunable biomaterials.

Keywords: bioinspired materials, 3D cell encapsulation, cyanobenzothiazole-cysteine click ligation, hydrogel, tunable gelation rate, bioactivity, luciferin adduct