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Small molecule modulators for temporal control of gelation and hydrogel mechanics

Stanford researchers have designed a new 3-dimensional (3D) hydrogel cell culture system that models native tissue environment with precise control over gelation and degradation properties. Current 3D cell culture methods often use animal-derived proteins, which are xenogeneic and lack consistency across batches. In addition, enzymatic methods used to retrieve cells from the culture system can result in non-specific cleavage and downstream phenotypic effects.

To address the current challenges, the Stanford group designed a new, fully chemically defined hydrogel system. Using small molecule modulators, the gelation and degradation properties of the hydrogel can be finely tuned. In short, the system consists of: a polymer with chemically reactive functional groups, a small molecule competitor, and a small molecule catalyst. The competitor allows for adequate mixing of the hydrogel to achieve homogenous cell distribution and can be used to modulate the material properties of the hydrogel. Depending on the timing, addition of the competitor can also disrupt the hydrogel network, which allows for easy cell retrieval. Addition of the catalyst serves to alter the crosslinking bond exchange rate, which mimics the cell's ability to remodel its extracellular environment in native tissue. Together, this carefully designed hydrogel system can be used as a in vitro model to recapitulate native tissue for both research and clinical settings.

Applications

- Research tool for 3D cell culture platforms
- In-vitro models for drug delivery or cancer research
- Clinical tools for tissue engineering, regenerative medicine or personalized medicine

Advantages

- Homogenous and chemically defined hydrogel
- Non-animal, xenogeny-free culture system
- Cell-friendly retrieval method: elimination of non-specific protein cleavage caused by enzymatic degradation of traditional hydrogels
- Recapitulation of the native tissue environment
- Potential for both research and clinical translation

Patents

- Published Application: WO2023215881
- Published Application: 20250290045

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