

# Quickly and Easily Generate Designer Photopatterned Hydrogel Matrices for Complex Microfluidic Tissue/Organ-on-a-Chip Devices

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## **Current *ex vivo* organoid models are unable to recapitulate spatiotemporal patterning of immune cells**

B lymphocytes and T lymphocytes play an essential role in protecting a host against pathogens. They go through several complex interactions to form germinal centers (GCs) where B cells can proliferate, increase antibody affinity, and differentiate into either memory B cells or long-lived plasma cells.

*Ex vivo* organoid models have accelerated our understanding of physiological, molecular, and cellular phenomenon and can support the study of GC formation and antigen response. However, the interactions that play a role in GC formation—including transcriptomic and epigenetic reprogramming, extracellular matrix remodeling, and cell-cell interactions—are complex, which limits the models that can show GC formation in human lymphoid follicles.

The established maleimide-functionalized poly(ethylene glycol) (PEG-MAL) hydrogel is an excellent biomaterial for primary immune cell survival and differentiation, but it is unable to recapitulate spatiotemporal patterning of immune cells as is seen *in vivo*. Its fast crosslinking prevents PEG-MAL patterning in complex microfluidic tissue/organ-on-a-chip and related devices. Alternative PEG polymers, such as vinyl sulfones and acrylates, do not support primary immune cell differentiation or survival *in vitro*. Furthermore, synthetic polymers as well as natural matrices (e.g., collagen, murine tumor matrix extract) are very challenging to pattern at the microscale to direct cellular activities.

## **Gain better spatiotemporal control and customization of hydrogel crosslinking and cell patterning**

Unlike PEG-MAL hydrogels, norbornene functionalized PEG (PEG-NB) hydrogels are crosslinked using a photoinitiated reaction with thiol groups. This reaction, through localization to the irradiated area, supports better spatiotemporal control of crosslinking and patterning. It represents a viable alternative to PEG-MAL by enabling facile cell patterning and the study of cell responses to antigens as well as culturing primary B cells *ex vivo*.

With this innovation, complex patterns (including biomolecular, cellular, and chemical gradients) can be generated in a synthetic hydrogel system using spatial patterning of the polymer network, proteins, multiple immune and non-immune cell types, and other non-cellular entities. This approach reduces timing and compatibility issues and offers designer flexibility compared to natural matrices.

### Summary Bullets

- Offers better spatiotemporal control and customization of hydrogel crosslinking and cell patterning
- Provides a viable alternative to PEG-MAL for culturing primary B cells ex vivo and studying their response to antigens
- Reduces timing and compatibility issues and offers designer flexibility compared to natural matrices

### Solution Advantages

- **Customizable design:** Using PEG-NB, this innovation results in highly tunable properties, including those that are structural, biophysical, and biochemical as well as degradation, polymeric and protein gradients, cell-based gradients.
- **Increased compatibility:** This approach offers designer flexibility comparable to natural matrices while (a) reducing the timing issues found with device injectability and crosslinking of PEG-MAL and (b) enhancing the immune cell compatibility found with other polymeric formulations like vinyl sulfone-PEG.
- **High throughput with high fidelity:** This approach enables the use of high-throughput microfluidic devices to study immune cells in a patterned space that mimics natural interactions.

### Potential Commercial Applications

PEG-NB can be used as an alternative to PEG-MAL for developing synthetic immune tissues in microfluidic devices for various applications, including:

- Diagnostics
- Disease modeling
- Regenerative medicine
- Immunotherapy
- Immunogenicity
- Drug screening

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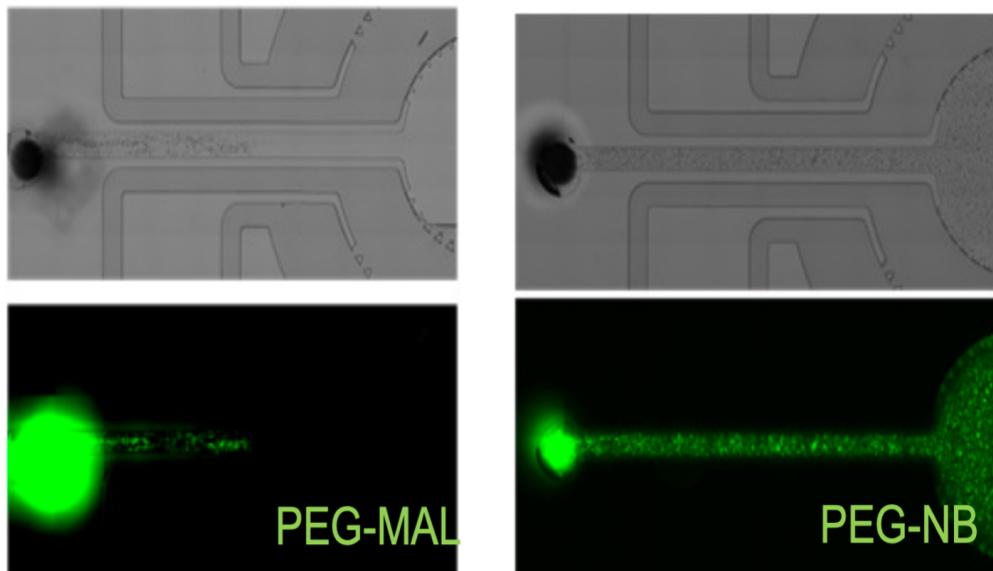
## IP Status

<p>Patent application has been filed</p>: US63/348191

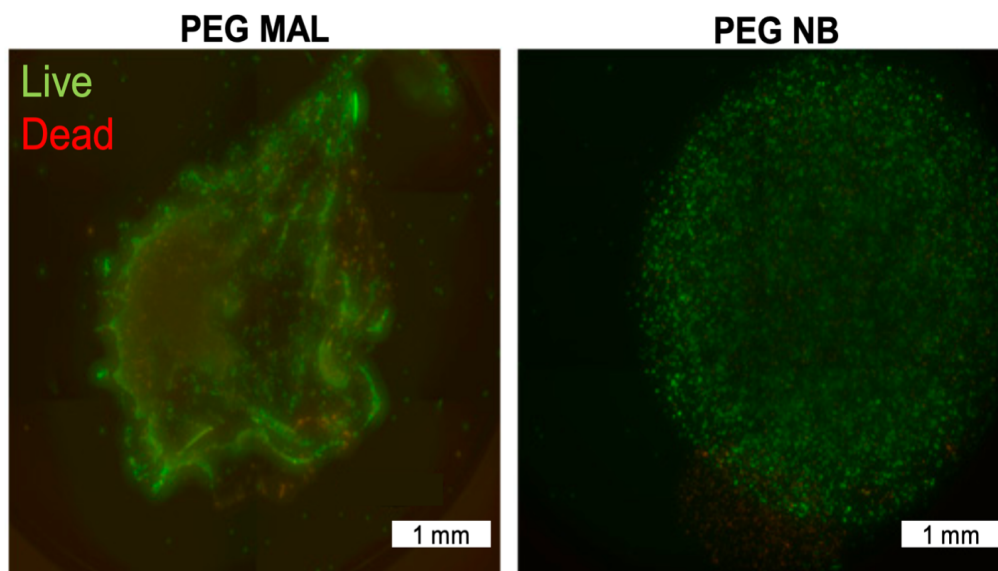
## Publications

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## Images



(left) Illustrates PEG-MAL crosslinking chemistry not supporting injectability or patterning in microfluidic devices. (right) Illustrates PEG-NB photoinitiated chemistry allowing cell patterning and injectability in microfluidic devices.



Both PEG-MAL and PEG-NB hydrogels shown encapsulating mammalian B cells; however, PEG-NB shows a higher homogenous cell distribution.

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