ECM stiffness affects the ability of cancer-killing cells to search and kill target cells

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Cytotoxic T lymphocytes (CTLs) are immune cells that can recognise and kill targets such as cancer cells.[1] Cell migration is crucial for CTLs to find and kill their targets.[2] However, the ability of CTLs to migrate and kill in three-dimension (3D) is still not fully understood.[3] One aspect that influences migration is the extracellular matrix (ECM), the environment where cells migrate. However, the ECM *in vivo* has complex properties and thus, it is difficult to determine how each property affects cell migration. One way to deconvolute the combined effects of ECM properties is through reducing the ECM *in vivo* and mimicking the essential ECM properties *in vitro*. In our work, we aim to understand how ECM stiffness influences the migration and killing of CTLs in well-defined biomimetic ECMs based on poly(ethylene glycol) hydrogels. The migration and killing assays were performed in high-throughput manner using 3D bioprinter, time-lapsed fluorescence microscopy, and computational tools. With these biomimetic ECMs, we learned that CTLs migrated faster and killed more target cells in soft than in stiff ECM. We found out that this difference in killing efficiency is determined by the length of contact time between CTLs and target cells rather than the number of contacts formed. These insights can potentially advance cancer therapy.

References:

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