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Abstracts of papers presented at the

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Enhanced in vitro culture of leukemic cells: insights from collagen scaffolds and carboxymethyl cellulose-polyethylene glycol gel

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Background: Studying chronic lymphocytic leukemia (CLL) in vitro is challenging due to its complexity and dependency of CLL cells on their microenvironment. An integral part of the natural CLL microenvironment is the three-dimensional (3D) spatial organization, which facilitates frequent cell-to-cell and cell-to-matrix contacts. Therefore, we aimed to mimic the natural tissue architecture by implementing a 3D in vitro culture. We hypothesized that compared to conventional culture, the additional dimension and increased cell-to-matrix contacts would enhance the prosurvival stimuli in CLL cells.
Methods: We cultured CLL cells in two materials: (i) collagen scaffolds, or (ii) gel composed of carboxymethyl cellulose and polyethylene glycol (CMC-PEG). We assessed cell distribution, morphology, and viability via microscopy, and measured the metabolic activity by AlamarBlue assay. Gene expression (MYC, VCAM1, MCL1, CXCR4, CCL4) was analyzed using qPCR to understand the effects of novel culture approaches on adhesion, apoptosis, and intercellular interactions of CLL cells co-cultured with bone marrow stromal cells (BMSCs) in 3D.
Results: The materials facilitated cell-to-cell and cell-to-matrix interactions due to scaffold structure and aggregate generation. CLL cells in CMC-PEG displayed similar or higher metabolic activity than in conventional culture. Compared to conventional culture, we observed the following effects: (i) a lower expression of VCAM1 in both materials, (ii) a higher expression of CCL4 in collagen scaffolds, and (iii) a lower expression of CXCR4 and MCL1 (proapoptotic transcript variant 2) in collagen scaffolds, while it was higher in the CMC-PEG gel.
Conclusion: Our findings suggest that the introduction of material into the in vitro 3D culture impacts CLL cells' apoptosis and interactions. While the expression of proapoptotic MCL1 is either suppressed (collagen) or elevated (CMC-PEG) in 3D materials, culture in both CMC-PEG and collagen can enhance the expression of certain genes associated with CLL-BMSCs interaction.
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