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Bioactive Self-assembled Peptide Hydrogels for 3D Cancer Model Applications

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Purpose:
Investigation of the proliferation, invasion, and drug-resistance behavior of cancer cells requires the application of cancer models that mimic the tumor environment. Hydrogels, structurally similar to extracellular matrix (ECM), have been widely used in 3D cancer models [1]. Peptides with regularly alternating hydrophobic and hydrophilic amino acids and specific charge distributions can form nanoarchitectures resembling the ECM through non-covalent interactions. Furthermore, bioactive motifs such as cell adhesion units can be incorporated into the peptide sequences during the synthesis [1,2]. In this study, we designed peptide hydrogelators containing a fibronectin-binding motif, leucine-aspartic acid-valine (LDV) for 3D cancer model applications. Self-assembly properties and in vitro cell interactions of these peptide hydrogels were studied.

Methods:
Peptides were synthesized using the solid phase peptide synthesis method based on Fmoc chemistry. Matrix-assisted laser desorption/ionization-time of flight mass spectroscopy (MALDI-TOF-MS) and reverse phase high-pressure liquid chromatography (RP-HPLC) were used to assess peptide purity. Secondary structures of the peptides were determined using Attenuated Total Reflection-Fourier Transform Infrared (ATR-FTIR) spectroscopy. The morphological and viscoelastic properties of the hydrogels were evaluated using atomic force microscopy (AFM) and oscillatory rheometer measurements, respectively. A549 cells were encapsulated in the peptide hydrogel matrices. In vitro cell proliferation, cell viability, and spreading tests were performed using Alamar blue assay, live-dead assay, and DAPI and phalloidin staining, respectively.

Results:
Molar mass and purity of the peptides were confirmed by MALDI-TOF-MS and RP-HPLC. ATR-FTIR results indicated the formation of β-sheet structures. Nanofibrous network structures were observed in the AFM images of the hydrogels. The storage moduli determined via the frequency sweep measurements are comparable to those of the other peptide hydrogels. The hydrogels supported the proliferation of the cells, and the cells encapsulated in the hydrogels started to colonize in 3D morphology after 7 days.

Conclusions:
The designed peptide hydrogels containing LDV sequences have potential in 3D cancer model applications. Testing of the anticancer drugs in these 3D matrices is underway.

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