GRAPHENE OXIDE-PEPTIDE NANOFIBERS AS PLATFORMS FOR CELL BIOACTIVE RESPONSES

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1 BACKGROUND

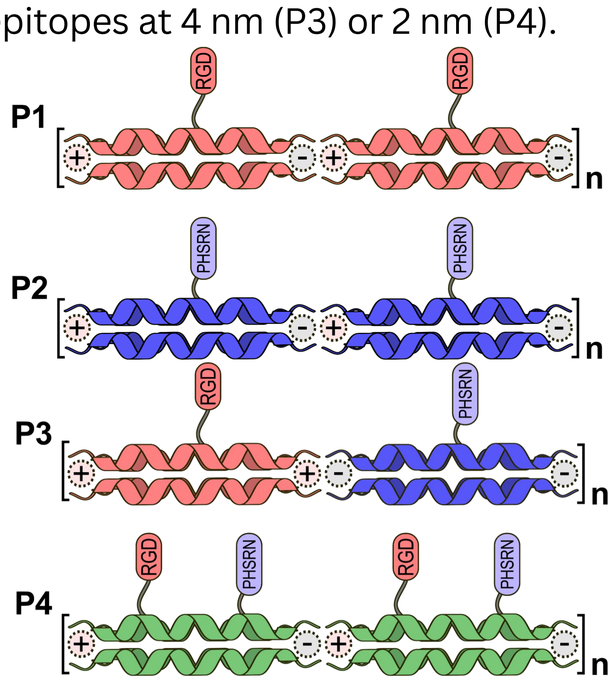
Cellular adhesion to the extracellular matrix (ECM) regulates essential processes, including proliferation, migration, and differentiation. Several studies have focused on mimicking the characteristics of the ECM by developing and modifying biomaterial surfaces, optimizing protein adsorption to promote early cell attachment and spreading. (1) Cellular interactions with the scaffold can be coordinated through peptide functionalization with the canonical RGD motif and its synergistic partner, PHSRN, two key fibronectin-derived epitopes that promote integrin-mediated cell adhesion. (2)

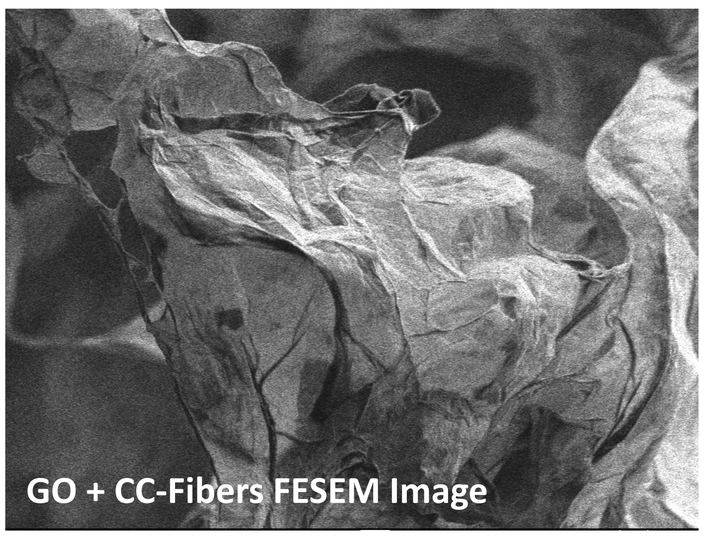
β-sheet peptides are commonly used as biomimetic scaffolds in tissue engineering owing to their ability to form nanofibrous hydrogels that mimic the ECM. However, their self-assembly mechanism offers limited control over the relative positioning of multiple functional domains, such as RGD and PHSRN. (3)

Coiled-coil (CC) peptides, in contrast, rely on a predictable heptad-repeat architecture that allows functional domains to be placed at defined, controllable distances, while also self-assembling into nanofibrous structures. (3,4) This combination of structural predictability and nanostructure formation makes coiled-coil scaffolds particularly well suited to reproducing the RGD–PHSRN synergy that drives integrin-mediated adhesion.

2 SCAFFOLD DESIGN AND CHARACTERIZATION

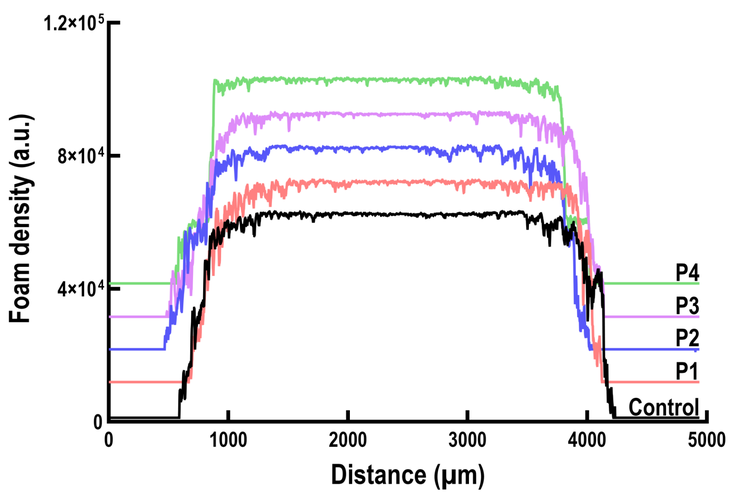
In this study, we designed a biomimetic scaffold based on coiled-coil tetramers that self-assemble into long nanofibers via electrostatic interactions and are functionalized only with RGDS (P1) or PHSRN (P2) epitopes, or with both epitopes at 4 nm (P3) or 2 nm (P4).





To evaluate cellular response, these nanostructures were integrated into graphene oxide (GO) foams, which were chosen as the supporting scaffold owing to their superior surface area, mechanical resilience, and biocompatibility. (5)

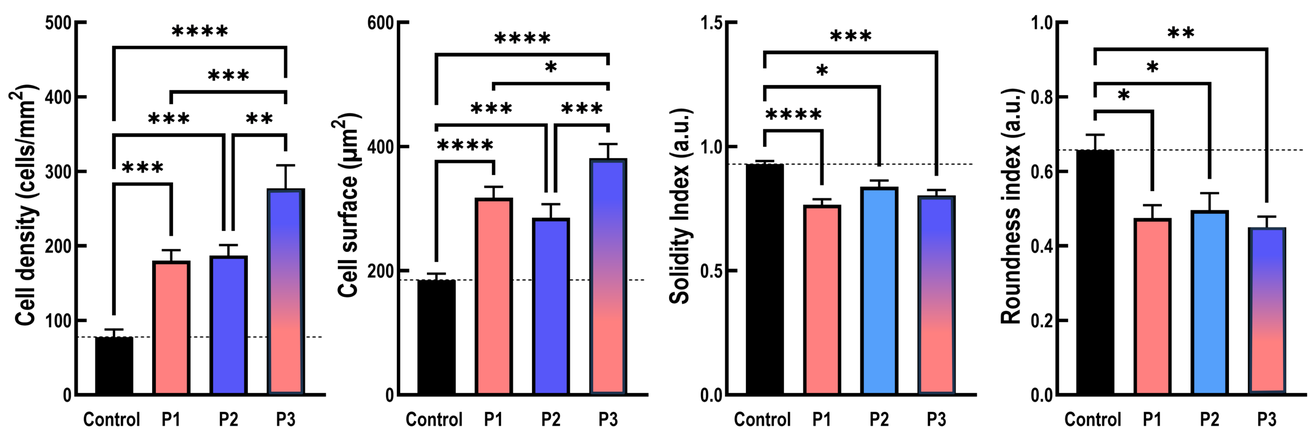
Hybrid and control GO foams had equivalent optical densities, confirming that the integration of peptide fibers does not alter the density or structural homogeneity of the foam, thus providing a consistent physical substrate for subsequent cell studies.

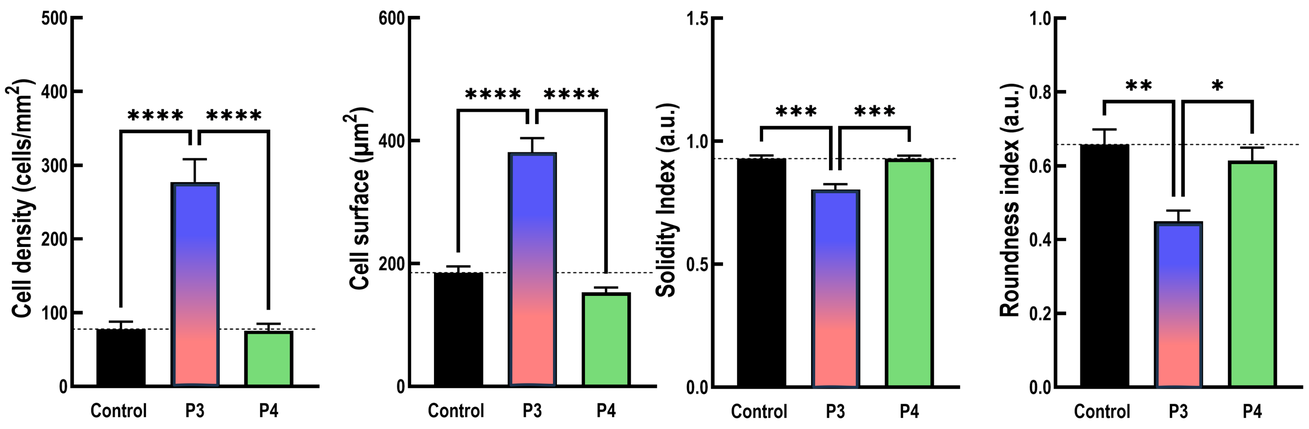


3 BIOACTIVITY OF THE HYBRID SCAFFOLDS

Spatial disposition determines the bioactivity of the scaffold: while functionalization with either the RGDS (P1) or PHSRN (P2) motifs increased the cell adhesion and spreading of SH-SY5Y cells compared to the control, the combination of both motifs at a distance of 4 nm (P3) resulted in a synergistic improvement.

In contrast, reducing the distance between RGDS and PHSRN to 2 nm (P4) severely compromised scaffold bioactivity, decreasing SH-SY5Y cell density and spreading to levels even lower than the control.





4 CONCLUSIONS

- Monofunctionalized RGDS or PHSRN peptide fibers significantly improved SH-SY5Y cell adhesion and spreading compared to the control.
- A precise 4 nm epitope spacing is essential for SH-SY5Y adhesion and spreading on GO scaffolds, whereas shorter distances compromise bioactivity.
- These functionalized GO scaffolds represent a highly tunable platform for advanced biomedical applications.

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