Artificial Extracellular Matrix Proteins with Enhanced Biological Activity

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Biomaterials have been modified with short RGD peptides to promote cell adhesion. Cell responses on RGD surfaces are similar, but generally not identical to those on fibronectin. Hence, there is great interest to engineer materials with enhanced biological activity. In particular, efforts to incorporate full-length fibronectin type III domains into engineered biomaterials have not been reported.

We have prepared artificial extracellular matrix (aECM) proteins that combine full-length fibronectin type III domains 9 and 10 with repeating elastin-like domains that confer tunable mechanical properties. Cell culture experiments with Rat-1 fibroblasts showed that aECM proteins containing full-length cell-binding domains promoted faster cell spreading than shortened sequences. The rapid cell spreading behavior was a result of a 10-fold increase in the binding affinity of $\alpha_5\beta_1$ integrin to aECM containing domains 9 and 10 (FN910m).

The aECM proteins containing these full-length fibronectin domains also promoted *in vitro* wound healing responses comparable to those observed on fibronectin. Cells migrated with higher speeds on these aECM proteins compared to that with a short RGD sequence, as a result of higher phosphorylated-FAK signaling. Interestingly, the contribution of proliferation to wound closure on all three aECM proteins was much more significant compared to that on fibronectin. This was consistent with higher levels of phosphorylated-ERK1/2 signaling observed on the aECM proteins.

Overall, aECM proteins containing full length cell-binding domains have enhanced biological activity, leading to faster cell attachment and rapid wound healing. This demonstrated the promise of aECM proteins for use in surgery and regenerative medicine.