

P002 Integrin $\alpha_v\beta_3$ lateral clustering promotes focal adhesion stability and fibronectin matrix organization

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Integrin clustering is essential for focal adhesion formation and adhesion-dependent cellular functions. In this study we characterized the effect of nanoscale variations in spacing between RGD ligands on cell migration and focal adhesion dynamics. Furthermore, we determined the effects of integrin lateral clustering on fibronectin (FN) fibril formation and organization. Nanopatterned surfaces presenting RGD-biofunctionalized gold dots, surrounded by passivated gaps were used. The clustering of associated integrins is modulated by varying the inter-dot spacing between 58 and 108nm. Cell-surface attachment is not sensitive to pattern density, while the formation of stable focal adhesions and persistent spreading is. Thus, cells plated on 108nm-spaced pattern exhibit delayed spreading with repeated protrusion-retraction cycles compared to cells on 58nm pattern and the adhesion sites undergo rapid turnover and contain reduced levels of zyxin. FN matrix deposition in cells adhering to RGD-nanopatterned surfaces is apparent on both types of pattern, but on the larger spacing FN is not organized into a network and rather present at cell-cell junctions. These findings indicate that a critical lateral spacing between integrins is essential for the establishment of mature and stable adhesions, which induce efficient cell spreading, formation of focal adhesions and FN matrix assembly.