Dynamic cell-material interactions measured using passive microrheology

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Scaffolds that mimic aspects of the extracellular matrix while providing a 3D microenvironment cells can degrade and remodel during migration is an area of growing interest with applications in wound healing, tissue engineering and stem cell expansion. Cells do not reside in their microenvironment, they actively reengineer the scaffold to meet specific requirements that maximize the efficiency of cellular processes. Although biomaterials provide an initially well-defined microenvironment for the cells, little is known about the extent of cellular interaction with the matrix. The lack of quantitative and predictable information about this process has limited advances in biomaterial design. To bridge this gap, we use microrheological characterization to quantitatively measure the microenvironment directly around a 3D encapsulated human mesenchymal stem cell (hMSC), the pericellular region, during dynamic remodeling and degradation. hMSCs degrade a synthetic hydrogel network through two pathways, MMP secretion that digests the peptide cross-linker and myosin II regulated adhesion and reversible remodeling of the network. This facile technique measures spatial changes in material properties with sensitivity that can discriminate between areas where the cell adheres to the matrix as well as areas degraded due to cell-secreted matrix metalloproteinase cleavage of the peptide cross-linker. This work provides a foundation and technique to quantitatively capture matrix remodeling during cellular migration, which will further design of tunable synthetic materials that will enhance and direct cell motility.