Cell adhesion is essential for the hierarchical organization of all multicellular organisms. In regenerative biology, the engineering challenge is to identify the critical, biological design rules that control tissue functions in engineered environments. Exciting recent discoveries have now shown that, in addition to soluble and adhesive cues, cells respond to tissue and biomaterial mechanics to regulate diverse cell functions, including differentiation, metastasis, and barrier functions. Cell surface adhesion proteins mechanically couple cells to the extracellular matrix and to adjacent cells, and it is increasingly clear that these adhesion proteins are crucial mechanical and signalling hubs that read the mechanical environment to regulate cell functions. Several findings document the tension sensing function of integrins, which mediate cell-matrix adhesion. However, our recent discovery that intercellular adhesion proteins are also tension sensors expands the system of adhesion and signalling proteins that co-ordinately regulate cell shape, cell movements, and regulate the integrity of tissue barriers. This talk focuses on our combined use of engineering and biochemical approaches to determine how cells read their mechanical environment and transmit this information across the cell membrane and through tissues. These findings reveal crucial biological design parameters governing information transfer at cell-cell and cell-matrix interfaces, and their consequences for tissue engineering and for understanding and treating disease.