Biomechanical properties of cells are important determinants of cell behavior and organ function in normal and disease states. Understanding the link between cell biomechanics and the delicate balance between human health and disease holds great promise for predicting disease onset and progression and for developing effective therapies. In the context of sickle cell disease, this presentation addresses questions of how biological processes lead to structural changes in the cell that are accompanied by changes in mechanical characteristics, how those changes influence disease state, and how therapeutic strategies can be developed and evaluated. Probing cell biomechanics for insights into the pathophysiology of disease has important implications for the treatment of individuals with sickle cell disease and individuals with other diseases that have a biomechanical basis.