Cellular and Molecular Nanomechanics and Human Disease States

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Abstract

We explore possible connections among mechanics, biochemistry, and medicine at the cell and subcellular levels specifically in the context of several broad human diseases. For this purpose, we investigate the molecular changes induced by invasion of parasites or from exposure to chemicals agents occurring naturally in the human body, the consequent changes in the mechanical response of the cell and the cytoskeleton, and possible implications for disease progression. The two cases considered are: human red blood cells invaded by the malaria parasite *Plasmodium falciparum* and Panc-1 pancreatic epithelial cancer cells. In the former case, it is shown by recourse to large deformation optical tweezers stretching at the picoNewton force level that parasitization leads to significant stiffening and cytoadherence of the red blood cell. Possible consequences for biological and physiological responses are probed. Gene inactivation and cell biomechanics experiments specifically designed to explore the contributions to cell mechanical response from specific proteins transferred from the parasite to the cell cytoskeleton are also undertaken. Molecular-level simulations of the cytoskeletal network of the entire human red blood cell are performed to identify how molecular network geometry influences cell shape, deformation and alterations to deformability induced by certain hereditary hemolytic disorders. We also demonstrate very different chemomechanical pathways associated with the nanomechanical response of the Panc-1 cell and their implications for tumor metastasis. The presentation will conclude by demonstrating how the foregoing experiments and simulations can be incorporated into novel microfluidic devices for disease diagnostics and drug efficacy assays.