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Probing cell mechanical properties with microfluidic devices

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Exploiting flow on the micron-scale is emerging as a method to probe cell mechanical properties with 10-1000x advances in throughput over existing technologies. The mechanical properties of cells and the cell nucleus are implicated in a wide range of biological contexts: for example, the ability of white blood cells to deform is central to immune response; and malignant cells show decreased stiffness compared to benign cells. We recently developed a microfluidic device to probe cell and nucleus mechanical properties: cells are forced to deform through a narrow constrictions in response to an applied pressure; flowing cells through a series of constrictions enables us to probe the ability of hundreds of cells to deform and relax during flow. By tuning the constriction width so it is narrower than the width of the cell nucleus, we can specifically probe the effects of nuclear physical properties on whole cell deformability. We show that the nucleus is the rate-limiting step in cell passage: inducing a change in its shape to a multilobed structure results in cells that transit more quickly; increased levels of lamin A, a nuclear protein that is key for nuclear shape and mechanical stability, impairs the passage of cells through constrictions. We are currently developing a new class of microfluidic devices to simultaneously probe the deformability of hundreds of cell samples in parallel. Using the same soft lithography techniques, membranes are fabricated to have well-defined pore distribution, width, length, and tortuosity. We design the membranes to interface with a multiwell plate, enabling simultaneous measurement of hundreds of different samples. Given the wide spectrum of diseases where altered cell and nucleus mechanical properties are implicated, such a platform has great potential, for example, to screen cells based on their mechanical phenotype against a library of drugs.