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Intracellular Mechanics-Based Drug Screening for Cancer Metastasis

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In 2007 alone, close to 1.5 million new cancer cases and over half of a million deaths from cancer are projected to occur in US. In general, cancer is much easier to be successfully treated before metastasis; the five-year survival rates for most of the cancers in the metastatic stage are lower than 10%. The origin of cancer is due to genomic instability; however, the genomics or proteomics studies focus on this phenomenon cannot thoroughly elucidate how cancer metastasis proceeds. During this process, cancer cells protrude and conquer their physical barriers, resist shear stress, establish anchorages and finally settle in a new environment. Each development in this process involves mechanical forces. Thus, whether force generation and cancer cells' mechanical properties can be integrated into the current mainstream of cancer research and offer new insight is worthy of being investigated. To measure the change of cell mechanics, specifically intracellular mechanics, a tool that least disrupts the probed cell's behavior and, simultaneously, can obtain real time quantitative measurement is necessary. To satisfy these criteria, we have developed a technique, ballistic intracellular nanorheology (BIN), in which we trace and analyze the trajectories of nanospheres that have been ballistically bombarded into the cytoplasm of individual cells. This technique allows us to probe the effects of chemical or mechanical stimuli on intracellular mechanics in various types of cells, on culture dishes or in a three-dimensional matrix. BIN is, currently, the first and only method available that can be applied to perform such tasks. Using this technique, we have gained detailed information about how the cytoskeletal remodeling pathways control the intracellular mechanics. We have also obtained information on the tempo-correlation between agonists and intracellular mechanics and how cells utilize their intracellular mechanics to react extracellular shear stress. These studies have set the framework for us to understand the mechanical mechanism of cancer cell metastasis on a molecular level. In this talk, I will describe the working principal using this technique to screen cancer drugs that prevent cancer metastasis.