Exploiting Multivalency in Mechanobiology

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Understanding how mechanical forces can switch the structure-function relationships of proteins, and thus cell signalling, is essential to establish the fundamental principle of the rapidly emerging field of mechanobiology. Much progress has been made in the molecular understanding of how forces can change the structure of proteins, thereby destroy binding epitopes or alternatively open them up. Protein stretching is thus exploited by cells to sense mechanical stimuli and physical factors in their environment which then regulates gene transcription processes and subsequently cell decision making. To probe the tensional state of extracellular matrix fibers in healthy and cancer, we have developed a peptide probe that can sense the tensional state of fibronectin in organ tissues, as fiber stretching destroys its multivalent binding epitope. Fundamental molecular mechanisms will be discussed, as well as our efforts to translate such mechanobiological principles into the clinic.