Molecular nanomechanics in human health

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Abstract

Mechanical forces play a crucial role in a myriad of biological processes including numerous diseases and disorders [1]. However, molecular nanobiomechanics are barely considered in modern medicine. Our research line focuses on atomic force microscopy (AFM) to investigate the effect of mechanical forces in proteins and enzymatic reactions that are relevant to human pathologies. In the past years, we have investigated how force affects the chemistry of thioredoxins, a class of enzymes that regulate the redox balance in cells. We showed that force regulates their chemistry, revealing several mechanisms for disulfide bond reduction that were hidden in standard bulk assays [2,3]. Importantly, these enzymes seem to be important during HIV-1 infection by reducing disulfide bonds in human CD4, the primary receptor of the virus. Using AFM techniques we have investigated the mechanics of CD4. We observed that force might trigger mechanical unfolding of CD4 and subsequent disulfide bond reduction in CD4 by Trx enzymes. Further experiments demonstrated, for the first time, that an antibody that blocks HIV-1 infection produces a mechanical effect on CD4 by preventing mechanical unfolding. We suggest that mechanical force might be important during HIV-1 infection which may change our understanding of the mechanism of infection. This observation might offer new avenues to explore novel treatments focused in the mechanics of proteins and enzymes, that is, *mechanopharmacology*.

References

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[3] Perez-Jimenez R et al. Nat Struct Mol Biol*,* **16(8),** 2009, pp 890-6.