Title: Evidence for chaperone function in mechanosensation

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Abstract text:

The small heat-shock proteins (sHSPs; HSPBs) are a family of molecular chaperones involved in stress response. Their canonical function is to prevent irreversible aggregation of denatured or partially denatured proteins. However, sHSP binding partners have been identified that interact without prior denaturation, suggesting a separate function. Several of these partners are involved in the mechanical translation of chemical signals and are key components in systems that underlie cell or tissue viscoelastic properties, such as the muscle sarcomere and the actin cytoskeleton. Though sHSP association with the cellular support network is long established, little is understood about the purpose or mechanism of these interactions. Here we discuss results that demonstrate a propensity for sHSP-mediated stabilization of mechanosensing protein domains at the atomic level which leads to stiffening at the macro scale. We focus on the interactions of HSPB5 (αB-crystallin) with cardiac titin within the sarcomere, and of HSPB1 (HSP27) with the actin-binding protein filamin C, and primarily draw upon native mass spectrometry and gas phase unfolding experiments in conjunction with *ex vivo* tissue assays. We postulate that sHSPs are able to recognize certain proteins prone to mechanical stress and bind them proactively such that physiological tensile forces do not lead to full unfolding, thus both preventing downstream aggregation and aiding cells and tissues in the maintenance of elastic properties essential to their function.