Small heat shock proteins: cellular “first responders” under stress conditions

The human genome encodes ten members of the family known as “small heat shock proteins” (sHSPs). sHSPs act at the earliest stages of cellular stress to delay imminent and irreversible protein aggregation caused by partial protein unfolding. Numerous missense mutations in human sHSPs are associated with diseases that include early cataract, cardiomyopathies, and neuropathies. Though there is growing appreciation for their importance, little is known about how sHSPs work. Despite their moniker, small heat shock proteins exist as distributions of very large oligomeric species that have been refractory to structural and biochemical approaches until recently. Furthermore, human small heat shock proteins do not require heat for their activation. I will present our working model on the mechanism of activation of the human sHSP HSPB5, based on structural, biochemical, and functional studies under physiologically relevant stress conditions.