

Structural Basis of Substrate Recognition and Thermal Protection by a Small Heat Shock Protein

Wilson Chun Yu LAU

**Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University,
Hong Kong SAR, P. R. China**

Email: wilson-cy.lau@polyu.edu.hk

Small heat shock proteins (sHsps) bind unfolding proteins, thereby playing a pivotal role in the maintenance of proteostasis in virtually all living organisms. Structural elucidation of sHsp-substrate complexes has been hampered by the transient and heterogeneous nature of their interactions, and the precise mechanisms underlying substrate recognition, promiscuity, and chaperone activity of sHsps remain unclear. Here we show the formation of a stable complex between *Arabidopsis thaliana* plastid sHsp, Hsp21, and its natural substrate 1-deoxy-D-xylulose 5-phosphate synthase (DXPS) under heat stress, and report cryo-electron microscopy structures of Hsp21, DXPS and Hsp21-DXPS complex at near-atomic resolution. Monomeric Hsp21 binds across the dimer interface of DXPS and engages in multivalent interactions by recognizing highly dynamic structural elements in DXPS. Hsp21 partly unfolds its central α -crystallin domain to facilitate binding of DXPS, which preserves a native-like structure. This mode of interaction suggests a mechanism of sHsps anti-aggregation activity towards a broad range of substrates.