Accepted Manuscript

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PII: S0003-9861(16)30386-1

DOI: 10.1016/j.abb.2016.10.002

Reference: YABBI 7382

To appear in: *Archives of Biochemistry and Biophysics*

Received Date: 20 July 2016

Revised Date: 13 September 2016

Accepted Date: 3 October 2016

Please cite this article as: M. Heirbaut, F. Lermyte, E.M. Martin, S. Beelen, T. Verschueren, F. Sobott, S.V. Strelkov, S.D. Weeks, The preferential heterodimerization of human small heat shock proteins HSPB1 and HSPB6 is dictated by the N-terminal domain, *Archives of Biochemistry and Biophysics* (2016), doi: 10.1016/j.abb.2016.10.002.

The preferential heterodimerization of human small heat shock proteins HSPB1 and HSPB6 is dictated by the N-terminal domain

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Abstract

Small heat shock proteins are ATP-independent molecular chaperones. Their function is to bind partially unfolded proteins under stress conditions. *In vivo*, members of this chaperone family are known to preferentially assemble together forming large, polydisperse heterooligomers. The exact molecular mechanisms that drive specific heteroassociation are currently unknown. Here we study the oligomers formed between human HSPB1 and HSPB6. Using small-angle X-ray scattering we could characterize two distinct heterooligomeric species present in solution. By employing native mass spectrometry we show that such assemblies are formed purely from heterodimeric building blocks, in line with earlier cross-linking studies. Crucially, a detailed analysis of truncation variants reveals that the preferential association between these two sHSPs is solely mediated by their disordered N-terminal domains.

Keywords: HSP20; HSP27; heterooligomers; native mass spectrometry; chaperone, small-angle x-ray scattering

Abbreviations: sHSP(s), small heat shock proteins; MS, mass spectrometry; SDS-PAGE, sodium dodecyl sulfate polyacrylamide gel electrophoresis; yADH, yeast alcohol dehydrogenase; HEWL, hen egg white lysozyme; DTT, dithiothreitol; ACD, α-crystallin domain; SAXS, small-angle X-ray scattering; SEC, size-exclusion chromatography; NTD, N-terminal domain; CTD, C-terminal domain; SUMO, small ubiquitin modifier

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