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Binding determinants of the small heat shock protein, αB-crystallin: recognition of the "IxI" motif

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(Note: With the exception of the correction of typographical or spelling errors that could be a source of ambiguity, letters and reports are not edited. The original formatting of letters and referee reports may not be reflected in this compilation.)

Acceptance letter 06 November 2012

Thank you for transferring your manuscript to The EMBO Journal. We have considered the manuscript in detail, as well as the included original referee reports. In addition, I sent the manuscript also to an expert in the field and trusted referee of the journal, for arbitrating input and feedback on the overall significance and suitability of this work for The EMBO Journal. Based on these considerations and the positive advisory comments copied below, I am please to inform you that we have decided to accept the study for publication in our journal.

A formal letter of acceptance including detailed information on further proceedings will be sent to you shortly.

Thank you for this contribution to our journal, and please consider us again for publication of your most exciting work in the future!

With best regards,

Editor
The EMBO Journal

Arbitrating referee 1 - comments:

This study addresses a controversial point about binding of peptide sequence extensions into binding pockets, in particular whether the crystal structures and solid state NMR data for human alphaB-crystallin, in which a characteristic motif within a sequence extension is observed to be bound into pockets within the "alpha-crystallin domain" of a partner chain, is relevant to the solution state.

Work described Baldwin et al 2011, and another NMR paper recently published by similar authors (http://www.ncbi.nlm.nih.gov/pubmed/22916679), conclude that these peptide extensions are largely unbound in solution. In my opinion the Klevit paper is good and does not overstate anything. It is pivotal to the controversy as it uses a solution based NMR technique and finds sufficient evidence to indicate whether a particular peptide binds or does not. The Klevit paper sees no major disparity between solid and their solution based techniques. The biophysics is obviously complicated but having all experimental data published is clearly needed. Is this important? These small heat shock proteins are presumed to function in cytoprotection, with the most recent claim published in Nature this month apparently pinning down their function to maintaining calcium homeostasis to prevent necrosis. These small heat shock protein binding sites are candidate functional binding sites, and their manipulation is of wide application in many human diseases.

