Visualizing chaperone-assisted protein folding.

Horowitz S et al.

Nature Structural & Molecular Biology. 2016 07; 23(7):691-697

https://doi.org/10.1038/nsmb.3237

PMID: 27239796

Show Details

Classifications

Good for Teaching | Interesting Hypothesis | New Finding | Technical Advance

Evaluations

Exceptional ★ ★ ★ — 13 Jul 2016

Michael B Sherman

The paper presents one of the first attempts to determine the structural ensemble of a protein being folded interacting with a chaperone. A new methodology was developed to enable visualizing the ensemble using X-ray crystallography and molecular dynamics simulations. Although the results present just a glimpse into the process, it is quite promising in yielding useful techniques for dealing with a very complex and very dynamic process.

Classifications

Interesting Hypothesis | New Finding | Good for Teaching | Technical Advance

Cite this Recommendation:

Sherman M: Faculty Opinions Recommendation of [Horowitz S et al., Nat Struct Mol Biol 2016 23(7:691-697)]. In Faculty Opinions, 13 Jul 2016;

https://doi.org/10.3410/f.726388165.793520641

Copy to clipboard

Exceptional ★ ★ ★ 16 Jan 2017

Robert Poole

This article represents an important technical and scientific advance. It shows how a technique based on X-ray crystallography, called residual electron and anomalous density (READ), can reveal how Spy (a bacterial periplasmic chaperone) interacts with the substrate protein immunity protein 7 (Im7). Horowitz, Bardwell and others show a remarkable series of snapshots showing how a substrate can 'explore' a folding landscape while bound to a chaperone. As well as clarifying chaperone action, it describes a new method for determining heterogenous structural assemblies and is therefore of wide-ranging applicability.

Classifications

New Finding Technical Advance

Cite this Recommendation:

Poole R: Faculty Opinions Recommendation of [Horowitz S et al., Nat Struct Mol Biol 2017 23(7:691-697)]. In Faculty Opinions, 16 Jan 2017;

https://doi.org/10.3410/f.726388165.793527053

Copy to clipboard

Less

Very Good ★ ★ 14 Feb 2017

Tim Clausen Julia Leodolter

How can one visualize a substrate during chaperone-assisted folding? In this paper, Horowitz et al. first attempt to obtain a crystal structure of the substrate Im7 bound to the chaperone Spy. While they observed a well resolved cradle-shaped structure for the chaperone, the substrate was only visible as a pretty disperse, "not-buildable" electron density filling the cradle. Apparently, the substrate was bound at a distinct pocket of the chaperone; however, it did so in various conformations.

To resolve individual conformations of the captured unfolded poly-peptide, the authors developed an elegant structural biology approach, which they termed READ (residual electron and anomalous density) method, a procedure situated in-between protein crystallography and molecular dynamics simulations. To delineate the position of the substrate proteins inside the cradle, they 1) used the residual electron density and 2) marked selected residues with iodine to localize them by their anomalous signal. Together, this provided suitable constraints for subsequent molecular dynamics simulations and to determine the possible conformations of the bound substrate.

In their final ensemble model, substrate conformations corresponding to unfolded, partially folded and native-like states appear. These data provide direct insight how chaperone-mediated protein folding may proceed.

Classifications

New Finding Technical Advance

Cite this Recommendation:

Clausen T and Leodolter J: Faculty Opinions Recommendation of [Horowitz S et al., Nat Struct Mol Biol 2017 23(7:691-697)]. In Faculty Opinions, 14 Feb 2017;

https://doi.org/10.3410/f.726388165.793528394

Copy to clipboard

Less