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Oral Presentation

Protein aggregation into bacterial inclusion bodies is a specific kinetically driven process

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Background

Bacterial inclusion bodies are major bottlenecks in protein production and are hampering the development of top priority research areas such as structural genomics. Inclusion body formation was formerly considered to occur via non-specific association of hydrophobic surfaces in folding intermediates rendering biologically inactive protein. Increasing evidence, however, indicates that protein aggregation in bacteria is a rather specific event which might result in active inclusion bodies [1,2].

Results

Here, first we have used fluorescence resonance energy transfer and microscopy to investigate the degree to which unrelated proteins expressed in the same cells coaggregate with one another. Our data reveal that in bacteria, protein aggregation is a specific event even among highly aggregation-prone polypeptides expressed at high levels.

Second, we have investigated the effect of a large set of single-point mutants of one of these proteins on its specific activity once deposited in inclusion bodies. We find that the activity of such aggregates significantly correlates with the predicted aggregation rates for each mutant.

Conclusion

Overall the data in this study confirms that *in vivo* protein aggregation depends on molecular recognition and suggests that rationally tuning the kinetic competition between folding and aggregation might result in highly active, inclusion bodies. The exploration of this technology during recombinant protein production would have a significant biotechnological value.

References

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