The reversible fibrillation of a periplasmic small heat shock protein; Protein Engineering Lab, Faculty of Engineering, Tottori University

Citation: Miyawaki, S., Uemura, Y., Hongo, K., Kawata, Y., and Mizobata, T. (2018) Acid-denatured small heat shock protein HdeA from *Escherichia coli* forms reversible fibrils with an atypical secondary structure. *Journal of Biological Chemistry*, Papers in Press.

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Highlights:

- The small periplasmic molecular chaperone HdeA from *E. coli* is a "conditional chaperone" that is activated only by losing its original native structure by acid denaturation.
- Miyawaki *et al*. found that in its acid activated state, HdeA was also susceptible to forming inactive fibrillar aggregates that closely resembled amyloid fibrils seen in a variety of neurological diseases.
- HdeA fibrils also showed a number of characteristics that are not commonly seen in typical protein amyloid fibrils.
- The findings in Miyawaki *et al*. are relevant to understanding the general phenomenon of protein aggregation and fibrillation, and also may lead eventually to novel methods of preventing and controlling infection by Gram-negative bacteria such as *E. coli*.

Researchers of the Protein Engineering Laboratory of the Faculty of Engineering, Tottori University have discovered an unusual characteristic of the dynamic structural properties of HdeA, a "conditionally activated" molecular chaperone protein that resides in the periplasm of *E. coli*.

HdeA is a small, dimeric protein whose role in *E. coli* is to protect the structural stability of various proteins in the periplasm that are endangered by sudden shifts of the environment to very low pH. HdeA is an example of a "conditionally active" molecular chaperone, which is activated only under these low pH conditions. The method by which HdeA accomplishes this is rather interesting, in that HdeA utilizes its own acid-denatured state as the active molecular chaperone form; HdeA must lose its own native structure in order to help other proteins.

Miyawaki and coworkers found that, when HdeA is activated as a molecular chaperone, this protein is also susceptible to forming long, fibrillar aggregates that closely resemble the amyloid fibrils observed in various neurological disorders. These fibrils are not active as molecular chaperones, and the fibril forming reaction is in fact in competition with the molecular chaperone activity of HdeA. HdeA also displayed a number of interesting characteristics that are not commonly seen in protein amyloid fibrils, such as the ability to recover a quasi-native state upon returning to neutral pH.

The results from Miyawaki *et al*. provide interesting insights regarding the general phenomenon of protein aggregation and fibrillation. And additionally, the finding that HdeA, a crucial component of the acid-tolerance mechanism of Gram-negative bacteria, is susceptible to inactivation through fibrillation might lead to the development of novel methods to prevent and treat the infections caused by such microorganisms.

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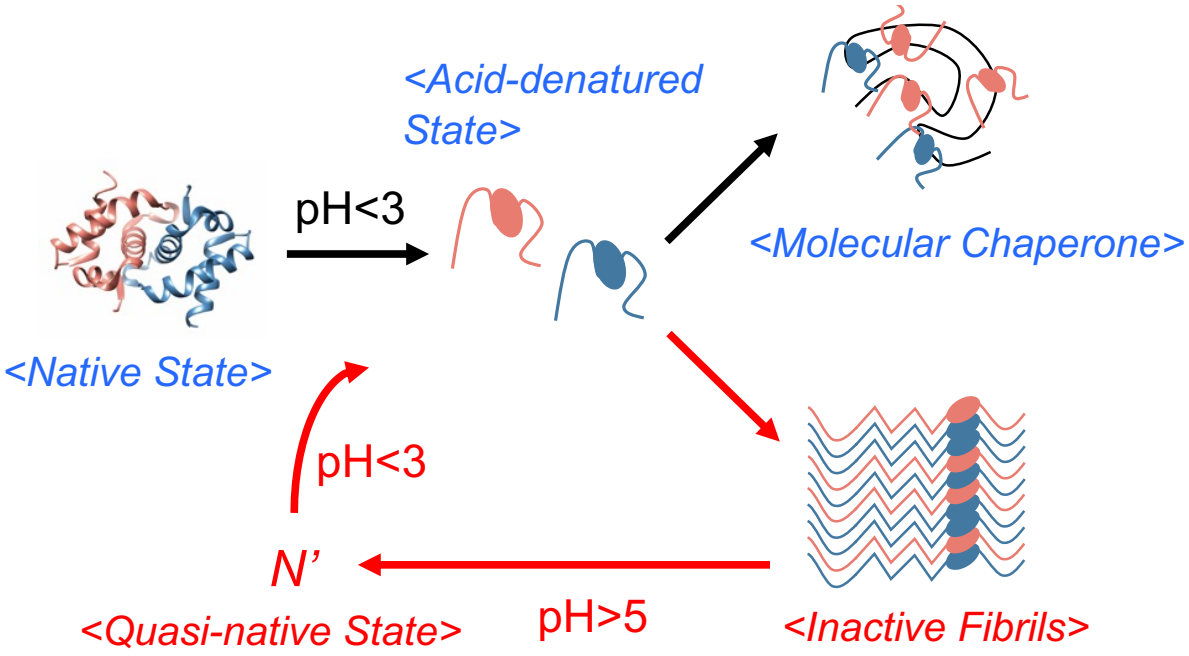

The reversible fibrillation of the periplasmic molecular chaperone HdeA from *E. coli.* Details in red highlight the results from the present study.