Molecular chaperone keeps bacterial proteins from slow-dancing to destruction

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Just like teenagers at a prom, proteins are tended by chaperones whose job it is to prevent unwanted interactions among immature clients. And at the molecular level, just as at the high school gym level, it's a job that usually requires a lot of energy.

In new research, scientists at the University of Michigan and Howard Hughes Medical Institute have discovered how a protein chaperone called HdeA, which helps protect bacteria like the notorious Escherichia coli from the ravages of stomach acid, saves energy while keeping proteins from forming destructive clumps.

The research is described in a paper published online this week in the Proceedings of the National Academy of Sciences.

Proteins in disease-causing bacteria like *E. coli* unfold when they land in stomach acid after being accidentally ingested by humans and other animals. This unfolding stops the proteins from working and could spell doom for the bacteria if the chaperone HdeA didn't step in. HdeA works by binding very tightly to the unfolded proteins while the bacteria are in the stomach. By attaching to the bacterial proteins, the chaperone stops them from tangling like slow-dancing teens, which could kill the bacteria.

The researchers discovered how HdeA is then able to let go of the unfolded proteins as the bacteria pass into the small intestine so that the proteins refold instead of clumping together.

"HdeA uses a unique timed-release mechanism," said postdoctoral fellow Tim Tapley, who spearheaded the work. "If the proteins were released all at once they would likely clump together, killing the bacteria. What we found instead is that the chaperone HdeA lets go of them gradually, making it more likely that they fold back up into their proper form than clump together."

While most molecular chaperones consume large amounts of cellular energy in order to function, HdeA instead taps energy freely available in its living environment.

"In this way, HdeA is a bit like a wind powered machine, except that instead of harnessing wind, HdeA uses the energy from pH changes in the surrounding environment as the bacteria move from the acid stomach to the slightly alkaline small intestine," said James Bardwell, in whose lab the work was done. Bardwell is a professor of molecular, cellular and developmental biology and of biological chemistry, as well as a Howard Hughes Medical Institute Investigator.

More information: Proceedings of the National Academy of Science: www.pnas.org/

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