

Highlight—Chaperone Proteins Are Evolution’s Helping Hand

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Accepted: August 24, 2016

Chaperone proteins are a guiding force within the cell. Not only do they usher newly minted protein molecules into their correct functional shapes but it seems that in doing this, they also can promote genetic diversity in a somewhat unexpected way.

In a new paper in *Genome Biology and Evolution*, Aguilar-Rodríguez et al. (2016), explore the role chaperone DnaK plays in buffering deleterious mutations and promoting evolution.

“Chaperone proteins could be considered sentinels of the cell,” says Fares. “That’s pretty interesting in itself, but if you look at what consequences that has, it’s even more fascinating.”

Simply as a byproduct of their function (making sure other proteins fold into their native conformation) chaperones (also called heat shock proteins) can accelerate the rate at which other proteins evolve. They do this by “buffering” mutations. Even if an error enters the DNA sequence, the chaperone still helps the protein fold into the correct form. Thus, whether mistakes accumulate in the genetic code or not, natural selection is blind to mutations that occur in proteins that are clients of chaperones.

To do the experiment, researchers used a hypermutable clone of *Escherichia coli* (one lacking a DNA-repair mechanism). They raised 68 parallel and independent colonies (along some control populations) for 85 days (with a new petri dish being inoculated for each line each day). They then analyzed the evolutionary rates of DnaK clients (proteins folded by the chaperone DnaK) in the *E. coli* they had raised, along with the clients in *Salmonella enterica*, and 83 other gamma-proteobacteria.

Author David Alvarez-Ponce says, “experimental evolution, in my opinion, is one of the next frontiers in evolutionary experiments.” Despite being interesting to study evolution in nature, unfortunately “so many factors are playing a role at the same time. If a gene evolves quickly, you don’t know if it’s because a relaxed period of selection, or maybe it’s because of positive selection,” says Alvarez-Ponce.

The team chose to examine the effects of DnaK because the field has traditionally used other chaperones, specifically Hsp90 or GroEL. The researchers wanted to know if DnaK

would also buffer mutations, despite the fact that its folding mechanism is different. (It did.)

But, if chaperones keep mutations cryptic in the population, how does buffering contribute to evolution?

“I consider evolution anything that produces a change in the genetic structure of the population,” says Fares. “What is neutral in a single environment might not be in a different environment. That mutation might do something very important if that environment changes.”

Enriching a population for mutations increases the possibility that population could evolve novel functions in the future. Natural selection will decide if these mutations will be useful in the future.

The paper is especially interesting, says Jennifer Wernegreen, researcher at Duke University who was not involved in the work, “because the authors demonstrate the buffering effects of DnaK at very different time scales: mutation accumulation experiments in *E. coli* (spanning ~1,870 generations), as well as deeper genome comparisons that span multiple lineages of gamma-proteobacteria.”

She thinks the combination of experimental and evolutionary comparisons builds a robust case for the author’s conclusion that DnaK buffers deleterious mutations and significantly accelerates protein evolution.

Fares believes this work will be interesting to other researchers in several ways.

From simply a mechanistic point of view, many biochemists might be interested in the precise workings of buffering: DnaK, Hsp90 or GroEL all have different ways of folding proteins.

“And the question is, whether all three also have different ways of buffering mutations,” poses Fares, “so there is a lot of biochemistry work to do there.”

He’s also interested in understanding how buffering ability translates into the origin of novel functions in evolution. And if it is possible to increase genetic variation within a population, he’d also like to know how to find novel functions in that population.

“So what we can do is domesticate chaperones by increasing their expression for instance in a molecular system and see

if an enzyme can acquire other functions that were potentially hidden in its code," Fares says.

This could translate into biotechnological advances, by fostering enzymes that are capable of new chemical functions, such as making a biodegradable plastic for instance.

"If we can domesticate chaperones to explore other paths, it's not difficult to realize that we can actually explore all possible functions that an enzyme may have and therefore produce 'cellular factories' to explore enzyme potential," Fares says.

Fares lab is working toward making an increased exploration of enzyme function a reality. Watch this space.

Literature Cited

Aguilar-Rodríguez J, et al. 2016. The molecular chaperone DnaK is a source of mutational robustness. *Genome Biol Evol.* 8(9):2979–2991.

Highlights editor: George Zhang