Polyphosphate is a primordial chaperone.

Gray MJ et al.

Molecular Cell. 2014 Mar 06; 53(5):689-699

https://doi.org/10.1016/j.molcel.2014.01.012

PMID: 24560923

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Classifications

Confirmation | Good for Teaching | Interesting Hypothesis | New Finding

Evaluations

Very Good ★★ 12 Mar 2014

Roberto Docampo

This elegant work reveals a novel role of polyphosphate as a chemical chaperone protecting bacterial cells from oxidative and other stresses. Polyphosphate is a linear polymer of a few to many hundreds of phosphate (Pi) residues linked by high-energy phosphoanhydride bonds. This ubiquitous polymer is found in bacteria, protists, and mammalian cells, and it was likely present prebiotically {1}. Recent work demonstrated that polyphosphate was able to suppress thermal aggregation of the enzyme glyceraldehyde 3-phosphate dehydrogenase without loss in the enzymatic activity {2}, and the present work confirms these results using luciferase and citrate synthase. The authors also demonstrate, using mutants deficient in polyphosphate kinase or exopolyphosphatase, that this protection also occurs in live bacteria.

References

1. Polyphosphate and its diverse functions in host cells and pathogens.

Moreno SN, Docampo R.

PLoS Pathog 2013; 9(5):e1003230

https://doi.org/10.1371/journal.ppat.1003230

PMID: 23658515

2. Effect of poly(phosphate) anions on glyceraldehyde-3-phosphate dehydrogenase structure and thermal aggregation: comparison with influence of poly(sulfoanions).

Semenyuk PI et al.

Biochim Biophys Acta 2013 Oct; 1830(10):4800-5

https://doi.org/10.1016/j.bbagen.2013.06.024

PMID: 23811344

Classifications

Interesting Hypothesis | Confirmation | New Finding

Cite this Recommendation:

Docampo R: Faculty Opinions Recommendation of [Gray MJ et al., Mol Cell 2014 53(5:689-699)]. In Faculty Opinions, 12 Mar 2014;

https://doi.org/10.3410/f.718285428.793491860

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Recommended 23.5

Score 23.5

❝ Relative citation ratio: **7.66**

★ Weighted sum of stars: **5.0**

↑ **Top 0.5%** in Cell Biology

3 Recommendations

0 ★★★ Exceptional

2 ★★ Very good

1 ★ Good

Learn more

Very Good ★★ 24 Apr 2014

 Tim Clausen  Marcin Suskiewicz

At least two long known but puzzling phenomena – i) that, in all organisms analysed so far, cellular ATP levels go down upon oxidative treatment and ii) that bacterial polyphosphate kinase (PPK) mutants are hypersensitive to various stresses – are explained by a recent study by Gray et al. establishing inorganic polyphosphate as an ubiquitous and general protein chaperone. Regarding ATP levels, it appears that, at least in E. coli, a rapid drop to below 50% of the normal concentration observed in response to the proteotoxic oxidant HOCl is minimised in ppk knock-out cells. This suggests that, upon oxidative stress, a substantial fraction of cellular ATP is diverted to the synthesis of polyphosphate, an isoenergic and reversible reaction catalysed in both directions by PPK. A large part of the study is dedicated to demonstrating that the polyphosphate levels thus achieved (about 50mM) are sufficient to confer protection from aggregation both globally and to specific model protein substrates. Polyphosphate turned out to be effective in vivo not only against oxidative agents, but also other stressors, suggesting it acts directly on client proteins and not by neutralising a particular stress type, as is indeed seen in in vitro assays. Interestingly, already with 2mM polyphosphate almost no aggregated proteins were observed in an experiment in which soluble and insoluble fractions of the E. coli lysate before and after heat shock were examined by SDS-PAGE. This, one could add, makes polyphosphate an interesting additive for recombinant production of aggregation-prone proteins. The fact that this inorganic polymer is already effective at mM and, in the case of some substrates, even nM concentrations, suggests it differs from chemical chaperones (osmolytes), which stabilise proteins indirectly by interacting with the solvent, and functions more like protein chaperones. In an assay in which luciferase was denatured in the absence and presence of polyphosphate, it was demonstrated that, while the substrate loses its activity in both cases, it can be later reactivated by the ATP-dependent chaperone system DnaK-DnaJ-GrpE if protected by polyphosphate. This observation leads to a fascinating, although still largely speculative, model. Upon oxidative stress, ATP levels go down and polyphosphate is produced, preventing protein aggregation in a holdase-like fashion. Due to the low ATP levels, active ATP-dependent refolding is down-regulated, as it would be anyway – as long as the stress is still present – leading to a futile unfolding-refolding cycle. Upon relief of stress conditions, ATP is recovered from polyphosphate and unfolded proteins, now released, can be refolded by the ATP-dependent molecular machines. Many questions remain to be answered. Does polyphosphate, long known to be a ubiquitous cellular component, have the same role in other organisms, including humans? What is the mechanism of its action? One can think of many others. However, the number of questions that now come to mind is a proof that the study by Gray et al. truly changes the way we think of protein quality control.

Classifications

Good for Teaching | Interesting Hypothesis | New Finding

Cite this Recommendation:

Clausen T and Suskiewicz M: Faculty Opinions Recommendation of [Gray MJ et al., Mol Cell 2014 53(5:689-699)]. In Faculty Opinions, 24 Apr 2014;

https://doi.org/10.3410/f.718285428.793493937

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Good ★ 18 Sep 2019

 Jean-François Collet  Camille Goemans

Hypochlorous acid (HOCl) induces both protein oxidation and aggregation, so bacteria need concerted efforts of chaperones and antioxidants to maintain proteostasis during stress. This study presents work from the Jakob laboratory that led to the identification of polyphosphate (polyP), an inorganic polymer synthesized from ATP, as a chemical chaperone able to stabilize bacterial proteins during HOCl stress. Accordingly, intracellular levels of polyP increase during HOCl stress as a result of both decreased hydrolysis and probably also increased synthesis, although this remains to be firmly established.

This Recommendation is of an article referenced in an F1000 Faculty Review also written by Jean-François Collet and Camille Goemans.

Classifications

New Finding

Cite this Recommendation:

Collet J and Goemans C: Faculty Opinions Recommendation of [Gray MJ et al., Mol Cell 2019 53(5:689-699)]. In Faculty Opinions, 18 Sep 2019;

https://doi.org/10.3410/f.718285428.793565264

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