1 An engineered pathway for the formation of protein disulfide bonds.

Masip L, Pan JL, Haldar S, Penner-Hahn JE, DeLisa MP, Georgiou G, Bardwell JC, Collet JF
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Recommendations:

Good 12 Mar 2004

Tracy Palmer
F1000 Microbiology
University of Dundee, Dundee, UK.

NEW FINDING

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This article describes a fascinating example of bacterial protein engineering in action. The authors imposed strong evolutionary pressure on the monomeric cytoplasmic disulfide reductase thioredoxin to compensate for lack of a periplasmic disulfide bond insertion machinery. Remarkably the mutants they isolated that could oxidize disulfides in the periplasm all resulted in the conversion of thioredoxin to a dimer that was bridged by a [2Fe-2S] cluster. This highlights how simply cofactors can be gained through protein evolution.

Disclosures
None declared

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Abstract:

ABSTRACT

We have engineered a pathway for the formation of disulfide bonds. By imposing evolutionary pressure, we isolated mutations that changed thioredoxin, which is a monomeric disulfide reductase, into a [2Fe-2S] bridged dimer capable of catalyzing O2-dependent sulfhydryl oxidation in vitro. Expression of the mutant protein in Escherichia coli with oxidizing cytoplasm and secretion via the Tat pathway restored disulfide bond formation in strains that lacked the complete periplasmic oxidative machinery (DsbA and DsbB). The evolution of [2Fe-2S]
thioredoxin illustrates how mutations within an existing scaffold can add a cofactor and markedly change protein function.

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