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News Release

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Scientists watch as *E. coli* bacteria evolve heat resistance under stress:

Experiment turns up the heat on natural selection, reveals new details of an evolutionary mechanism

Scientists in Munich report evidence that high concentrations of the molecular "chaperone" proteins GroEL and GroES – intracellular machines that can stabilize folding proteins under stress – play a critical role in increasing the maximum temperature at which *E. coli* bacteria can grow. Massively and permanently elevated levels of the GroE proteins were found in bacteria adapted, step-wise over a period of years, for growth at 48.5 degrees C. This genomic change persisted for more than 600 generations, and molecular analyses ruled out other mechanisms that might account for the increase in heat resistance. The researchers' findings, published in the June 18 edition of the Journal of Biological Chemistry, have important implications for both fundamental evolutionary studies and biotechnology applications.

In addition to being a well established resident of the human digestive tract, *Escherichia coli* is at home in the lab. It is a model organism as important to biological research as brewer's yeast, the fruit fly, and the mouse. Having evolved for life at our body temperature of around 37 degrees C., wild-type E. coli can be cultivated in the laboratory at temperatures up to but not beyond 44 to 46 degrees C. Pushing the upper temperature at which *E. coli* could grow to 48.5 degrees C. does not approach the level of heat resistance found in thermophile species, but what this experiment required was a distinct and significant redefinition of "extreme" for *E. coli*.

To achieve that, Dr. Jeannette Winter and colleagues at the Technische Universitaet Muenchen (TUM) founded three lines of *E. coli* bacteria from a common ancestor and propagated them under heat stress for hundreds of generations. The step-wise process they designed created conditions under which a combination of normal genomic instability and natural selection would be likely to produce adaptations for growth at extreme temperatures. It took around two years to reach 48.5 degrees C, but after that, adaptation to this new extreme was inherited. The researchers propagated a control population, also descended from the common ancestor, at 37 degrees C.

Technische Universität München   Corporate Communications Center   80290 München   www.tum.de

Dr. Ulrich Marsch	Head of Corporate Communications	+49.89.289.22779	marsch@zv.tum.de
Patrick Regan	International Public Relations	+49.89.289.10515	regan@zv.tum.de

Exhaustive analysis of cell physiology, protein expression, and genome sequences revealed a number of significant changes. Compared with the control group, the adapted lines of *E. coli* showed a clearly enhanced capability for living under conditions of heat stress. This was accompanied by reduced growth rates, showing that survival came at a cost in terms of overall fitness, a typical indicator of genomic mutations. One of the most striking changes measured was a 16-fold increase in GroE levels, more than five times what a normal heat shock response in *E. coli* would be expected to produce. Further analyses of heat shock genes and proteins ruled out other mechanisms – beyond the role of GroE alone – as being critical for evolution for life at 48.5 degrees C.

GroE chaperones are known to play an active role in assisting the folding process of other proteins, especially in cases where mutations that could cause improper folding threaten the survival of the cell. This experiment shows that they likely play a uniquely important role – by mitigating the potentially damaging effects of accumulating mutations on protein folding – in the evolution of heat resistance in *E. coli*.

"The correlation between genetic changes and chaperones has been shown not only in bacteria, but also in eukaryotes such as yeast, fruit flies, and fungi," says Dr. Jeannette Winter, a researcher in the TUM Department of Chemistry and a member of the Center for Integrated Protein Science Munich. Beyond yielding insights into evolutionary history, Winter says, further research on these highly conserved mechanisms could shed light on how organisms evolve in response to climate-related stresses in the future. "Better understanding of chaperones might also open the way to targeted generation of organisms for specific purposes -- enhancing their ability, for example, to live under stressful conditions, to break down harmful pollutants, or to produce specific, biotechnologically relevant proteins."

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Dr. Ulrich Marsch	Head of Corporate Communications	+49.89.289.22779	marsch@zv.tum.de
Patrick Regan	International Public Relations	+49.89.289.10515	regan@zv.tum.de

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Contact:

Dr. Jeannette Winter
Department of Chemistry
Technische Universitaet Muenchen
Lichtenbergstrasse 4
85747 Garching, Germany
Tel: +49 89 289 13191
Fax: +49 89 289 13345
jeannette.winter@ch.tum.de

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Film illustrating protein folding through chaperones (© MPI for Biochemistry):
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