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Scientists solve mystery of arsenic compound

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Scientists have solved an important mystery about why an arsenic compound, called arsenite, can kill us, and yet function as an effective therapeutic agent against disease and infections.

According to new research published in the October 2010 issue of *Genetics* scientists from Johns Hopkins, Baylor and Stanford discovered that arsenite, a common water contaminant in many parts of the world, affects a special protein folding machine in yeast, called TCP, also present in humans. This information not only opens the doors to developing safer therapeutic alternatives to arsenite-based medicines, but it may allow researchers counter the negative effects of arsenite poisoning.

"By better understanding arsenite, we might be able to protect humans from its hazards in the future," said Jef D. Boeke, Ph.D., co-author of the study from the Department of Molecular Biology and Genetics and The High Throughput Biology Center at The Johns Hopkins University School of Medicine in Baltimore. "Arsenite also has beneficial effects, and by focusing on these, we might be able to find safer ways to reap the beneficial effects without the inherent risks involved in using a compound derived from arsenic."

To make this discovery, scientists used advanced genomic tools and biochemical experiments to show that arsenic disturbs functions of the machinery (chaperonin complex) required for proper folding and maturation of several proteins and protein complexes within yeast cells. This mechanism of action by arsenic is not unique to yeast, as it has been

shown to exist in a range of organisms from bacteria to mammals.

"As the human population grows, freshwater supplies become increasingly precious, but unfortunately some of this water has been contaminated with arsenite," said Mark Johnston, Editor-in-Chief of the journal *Genetics*. "The more we learn about how this compound affects our bodies, the more we'll eventually be able to counter its deadly effects. In addition, we know that under certain controlled doses, arsenite has therapeutic value. This research hopefully gets us closer to a new generation of drugs that achieve maximum benefit with minimum risk."

More information: Xuewen Pan, Stefanie Reissman, Nick R. Douglas, Zhiwei Huang, Daniel S. Yuan, Xiaoling Wang, J. Michael McCaffery, Judith Frydman, and Jef D. Boeke. Trivalent Arsenic Inhibits the Functions of Chaperonin Complex. *Genetics* 2010 186: 725-734. www.genetics.org/

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