

Adverse Effects of Arsenic on the Immune Response of the Lungs to Pseudomonas Infection

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October 31, 2016



Outline

- Sources of arsenic exposure
- Arsenic and human health
- Innate immune function of the lung in response to *Pseudomonas* infection
- Arsenic suppresses the innate immune function of lung epithelial cells and professional immune cells (macrophages)

ATSDR list of substances that pose the most threat to public health

The ATSDR 2015 Substance Priority List

2015 RANK	SUBSTANCE NAME	TOTAL POINTS	2013 RANK	CAS RN
1	ARSENIC	1671.6	1	007440-38-2
2	LEAD	1529.4	2	007439-92-1
3	MERCURY	1458.6	3	007439-97-6



<https://www.atsdr.cdc.gov/spl/>
Google images

Sources of arsenic exposure



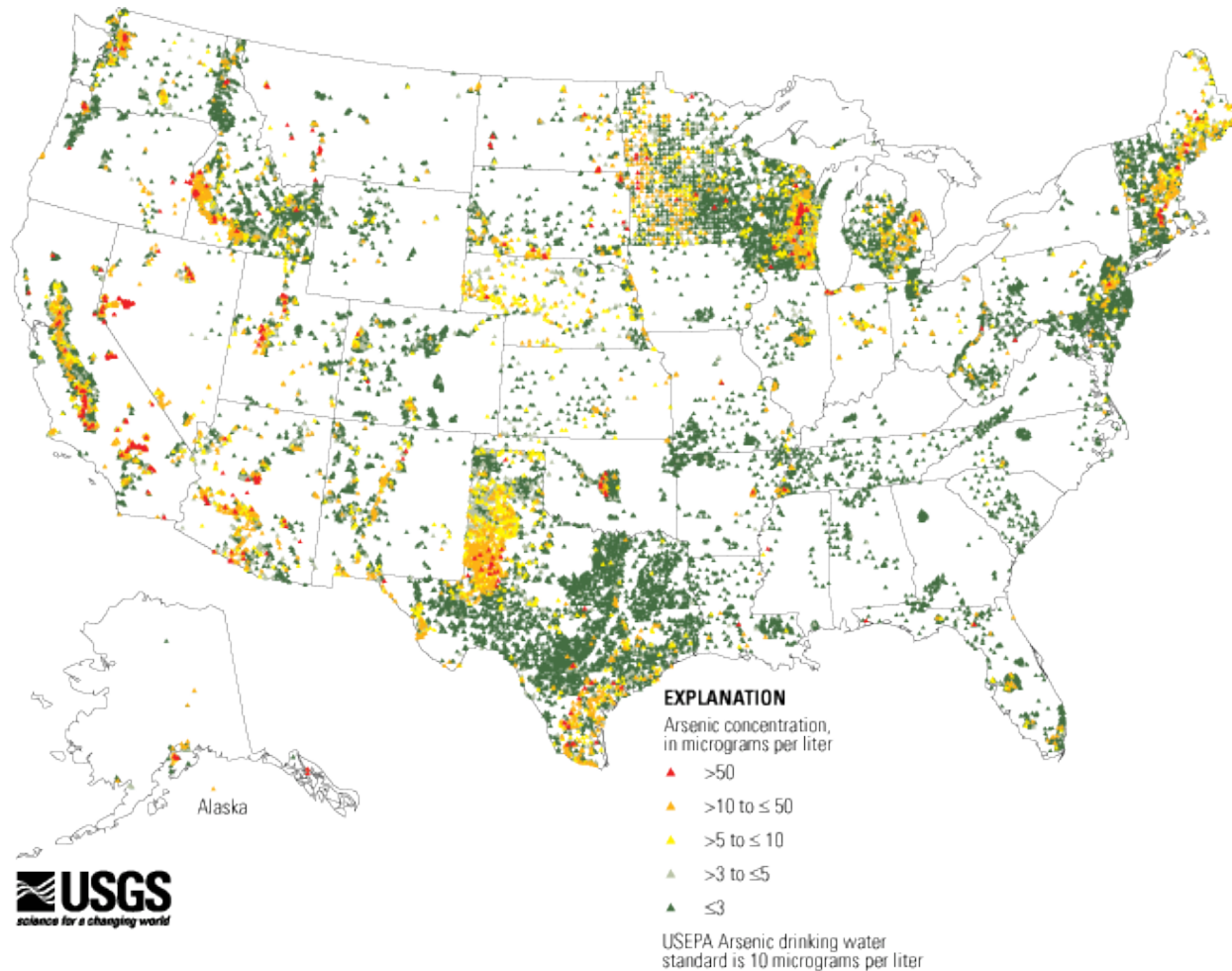
Arsenic exposure in the US

- Total arsenic consumption in the US from water, rice and rice based products is 10-25 ppb/day per person.
- This is equal to drinking 1 to 2.5 liters of water/day containing 10 ppb of arsenic (EPA limit).

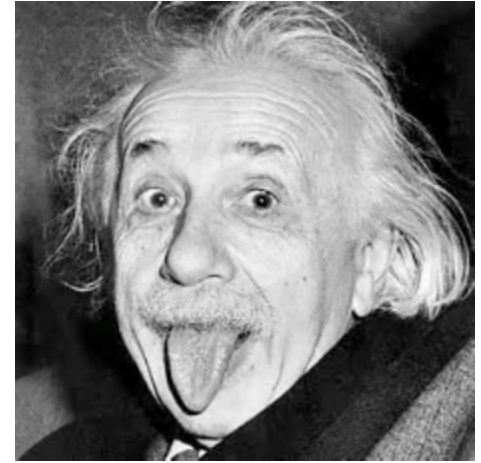


Arsenic in well water.

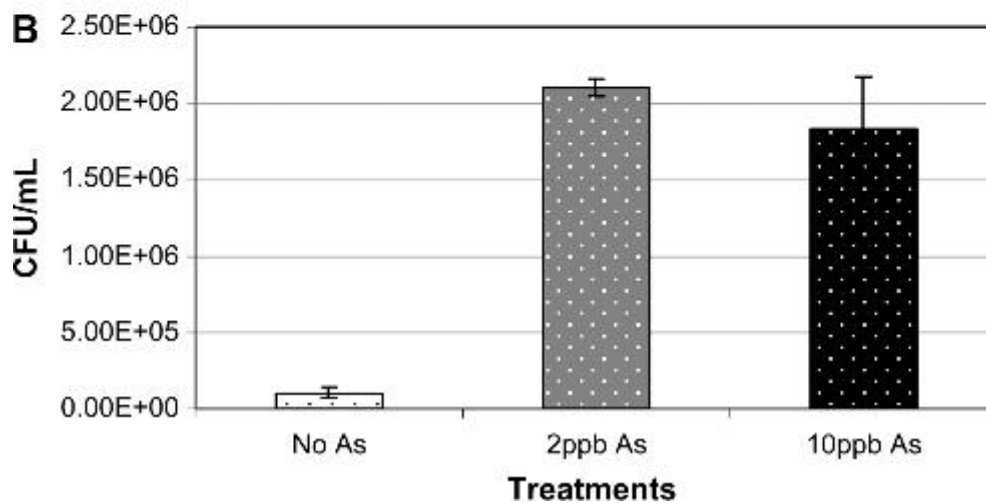
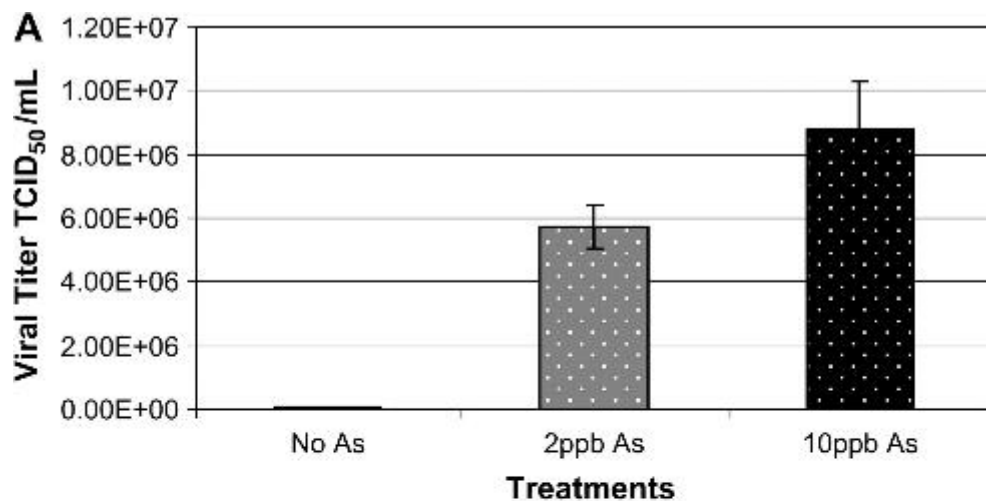
~3 million drink well water > 10 ppb



Arsenic and human disease



Arsenic enhances viral and bacterial infections in zebrafish



Prenatal exposure to iAs is associated with dysregulated fetal immune gene and protein expression

ORIGINAL RESEARCH

A Systems Toxicology-based Approach Reveals Biological Pathways Dysregulated by Prenatal Arsenic Exposure



Jessica E. Laine, MS, Rebecca C. Fry, PhD
Chapel Hill, NC

Arsenic enhances lung infections in infants

Research | Children's Health

A Section 508–conformant HTML version of this article is available at <http://dx.doi.org/10.1289/ehp.1409282>.

Infant Infections and Respiratory Symptoms in Relation to *in Utero* Arsenic Exposure in a U.S. Cohort

Shohreh F. Farzan,^{1,2} Zhigang Li,^{1,2} Susan A. Korrick,^{3,4} Donna Spiegelman,^{5,6} Richard Enelow,^{1,7} Kari Nadeau,⁸ Emily Baker,⁹ and Margaret R. Karagas^{1,2}

In utero arsenic exposure increases the risk of infections and respiratory symptoms in infants

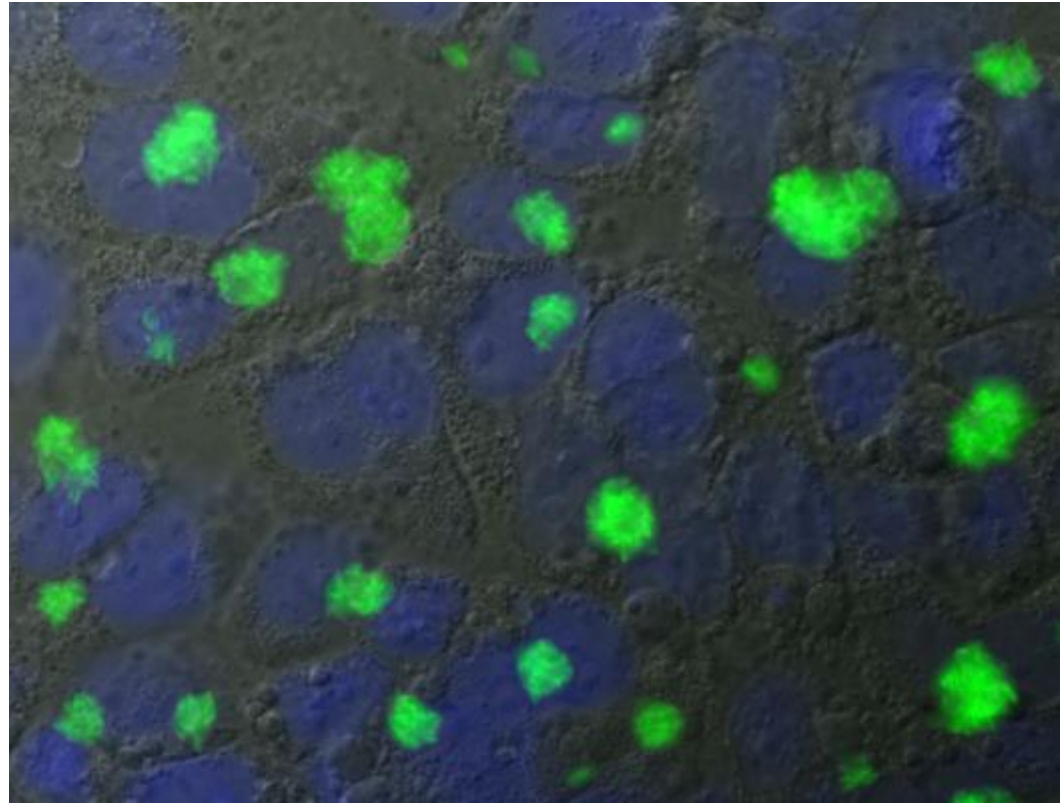
**How does low-dose arsenic
increase *Pseudomonas
aeruginosa* lung infections?**

What is the mechanism?

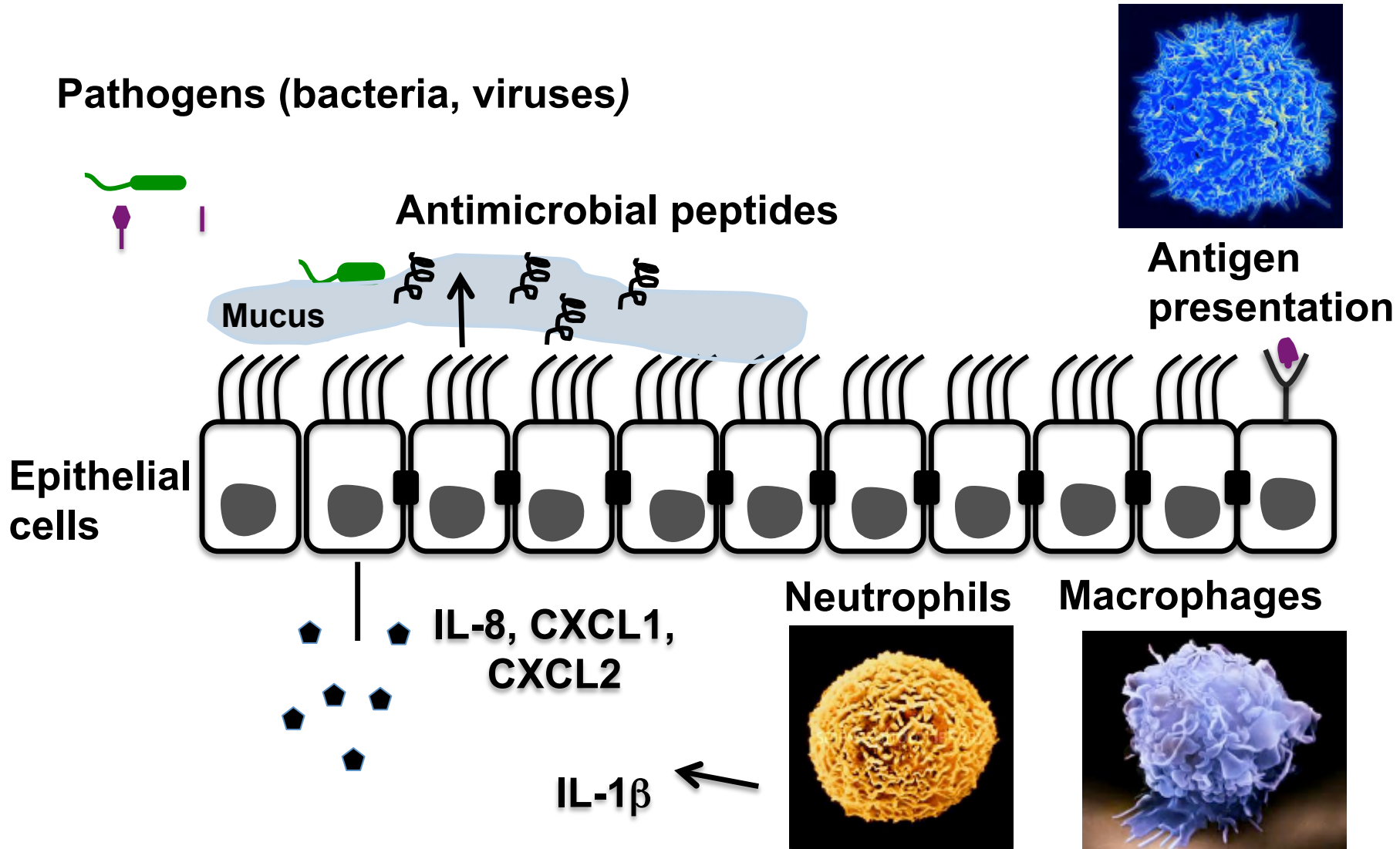


Pseudomonas aeruginosa (*Pa*)

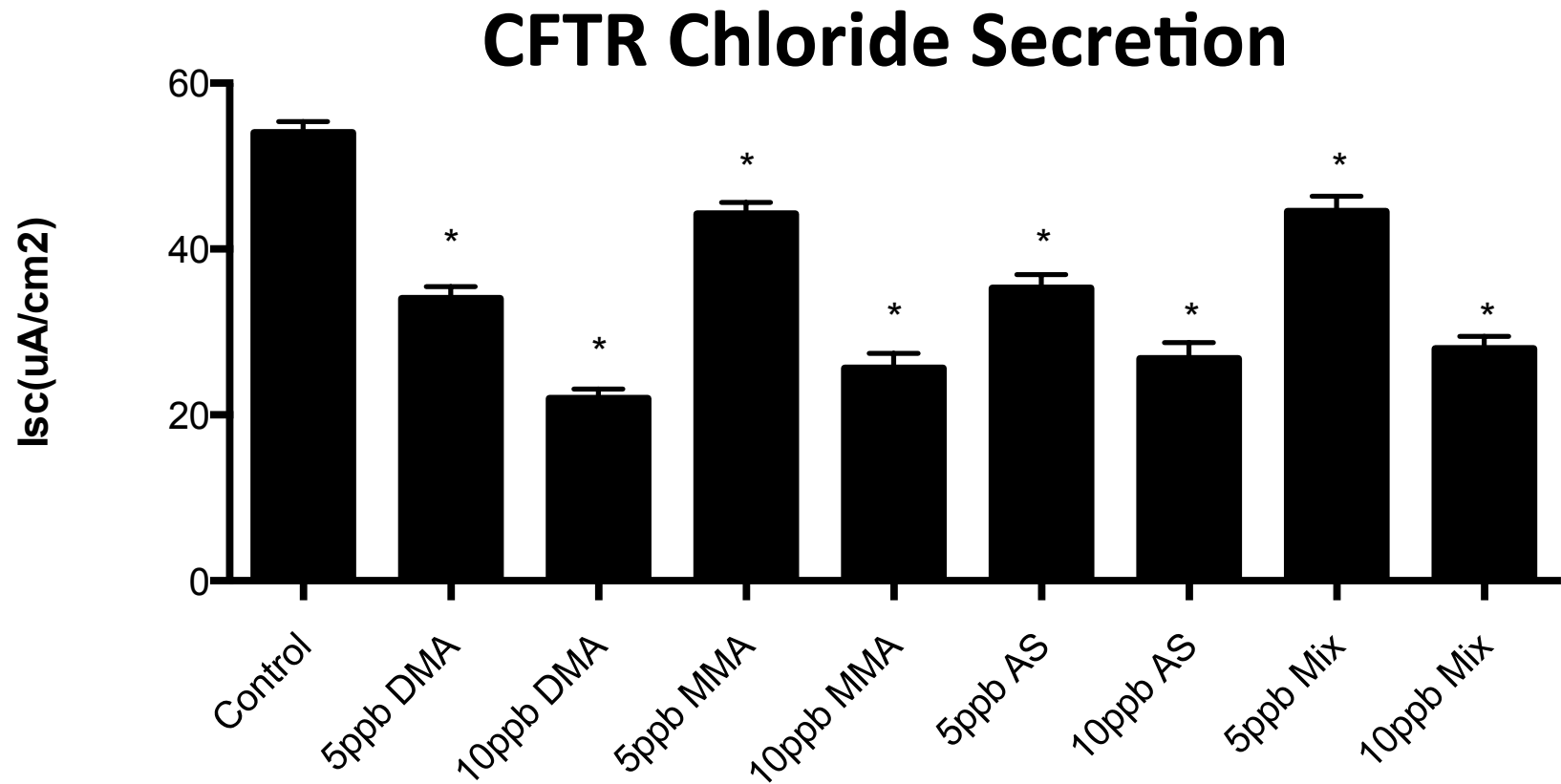
- *Pa* is a ubiquitous, opportunistic pathogen that is found in burn wounds, UTIs, and lungs in patients with COPD and CF
- *Pa* develops drug resistant biofilms



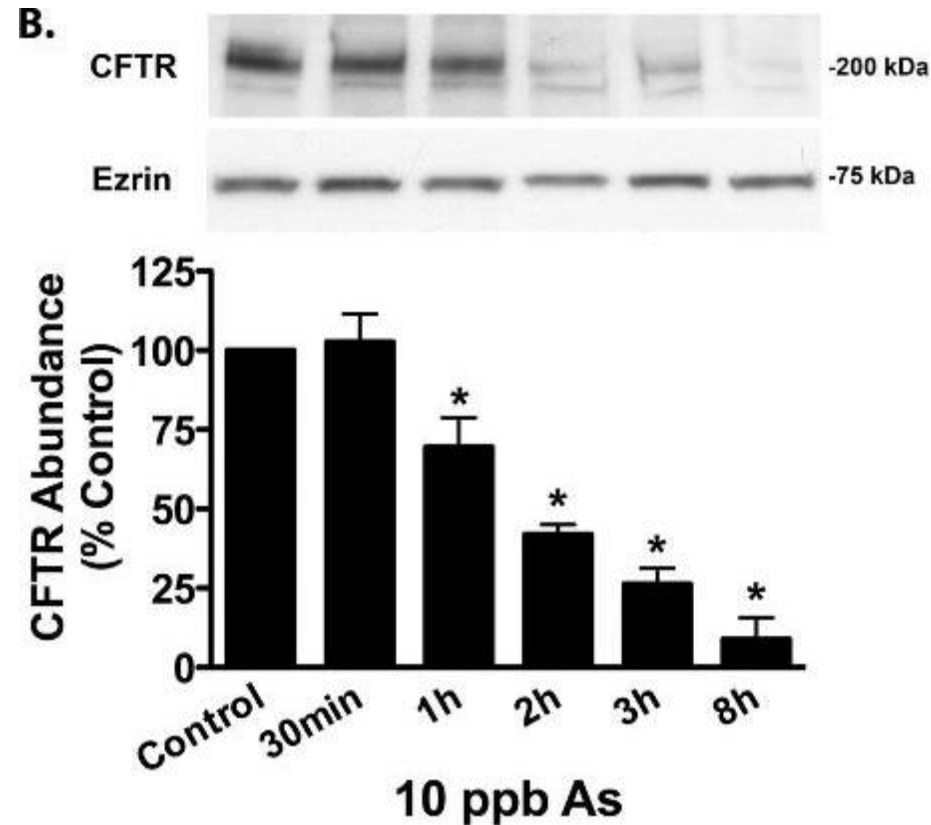
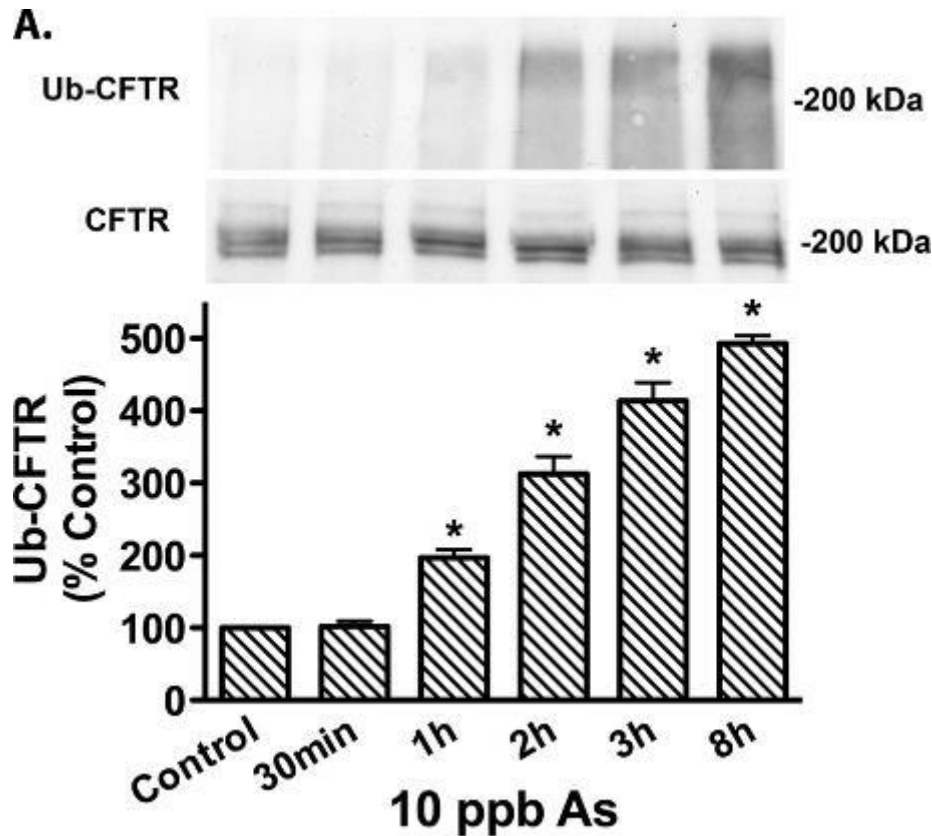
Innate immunity in the lung



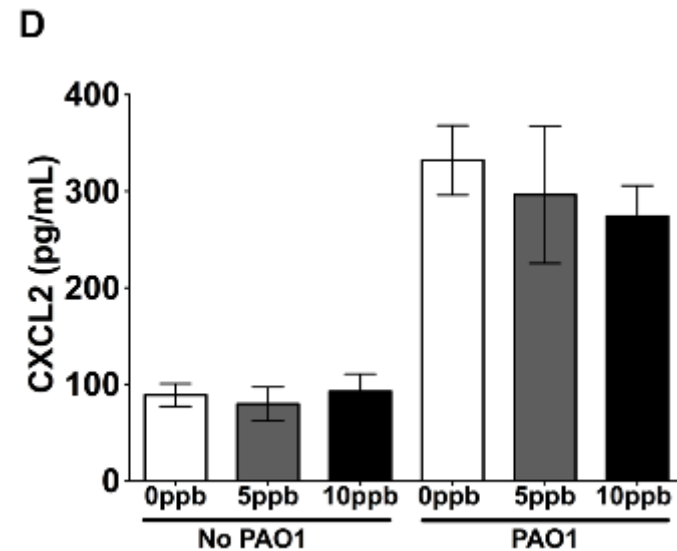
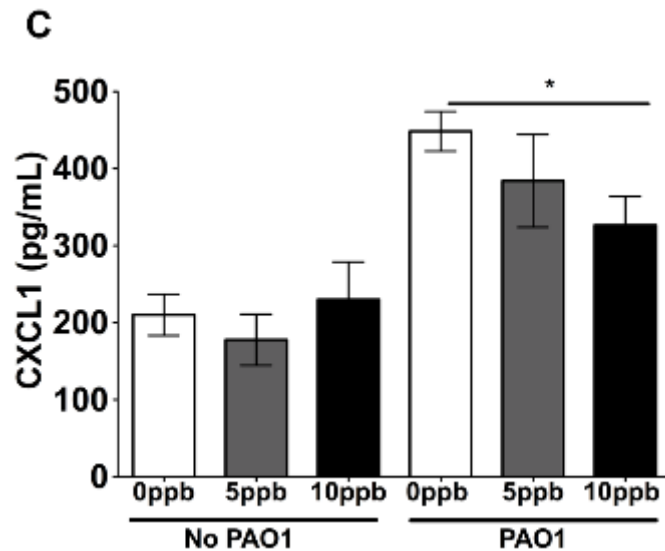
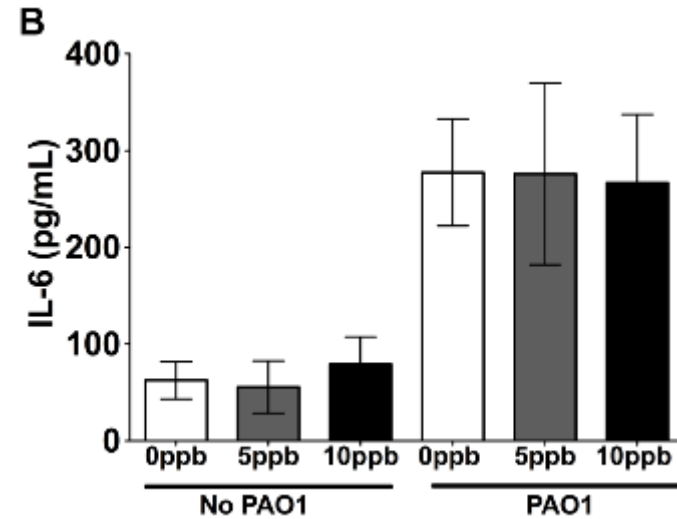
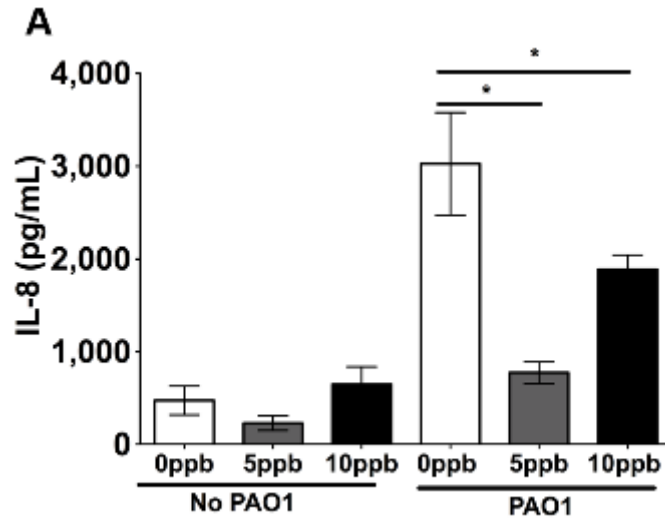
Arsenic reduces chloride secretion by lung epithelial cells



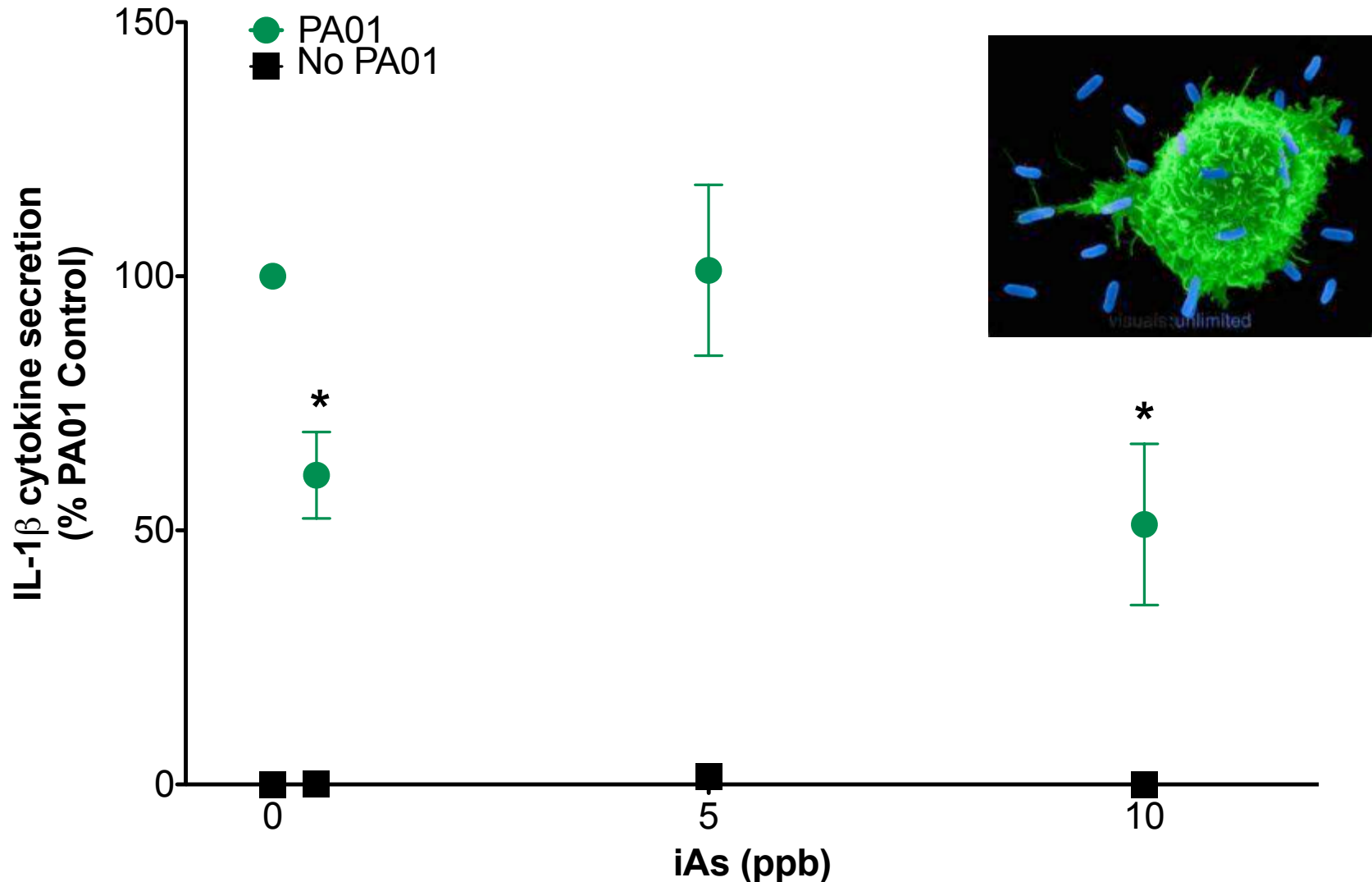
Arsenic increases the ubiquitination and proteasomal degradation of CFTR



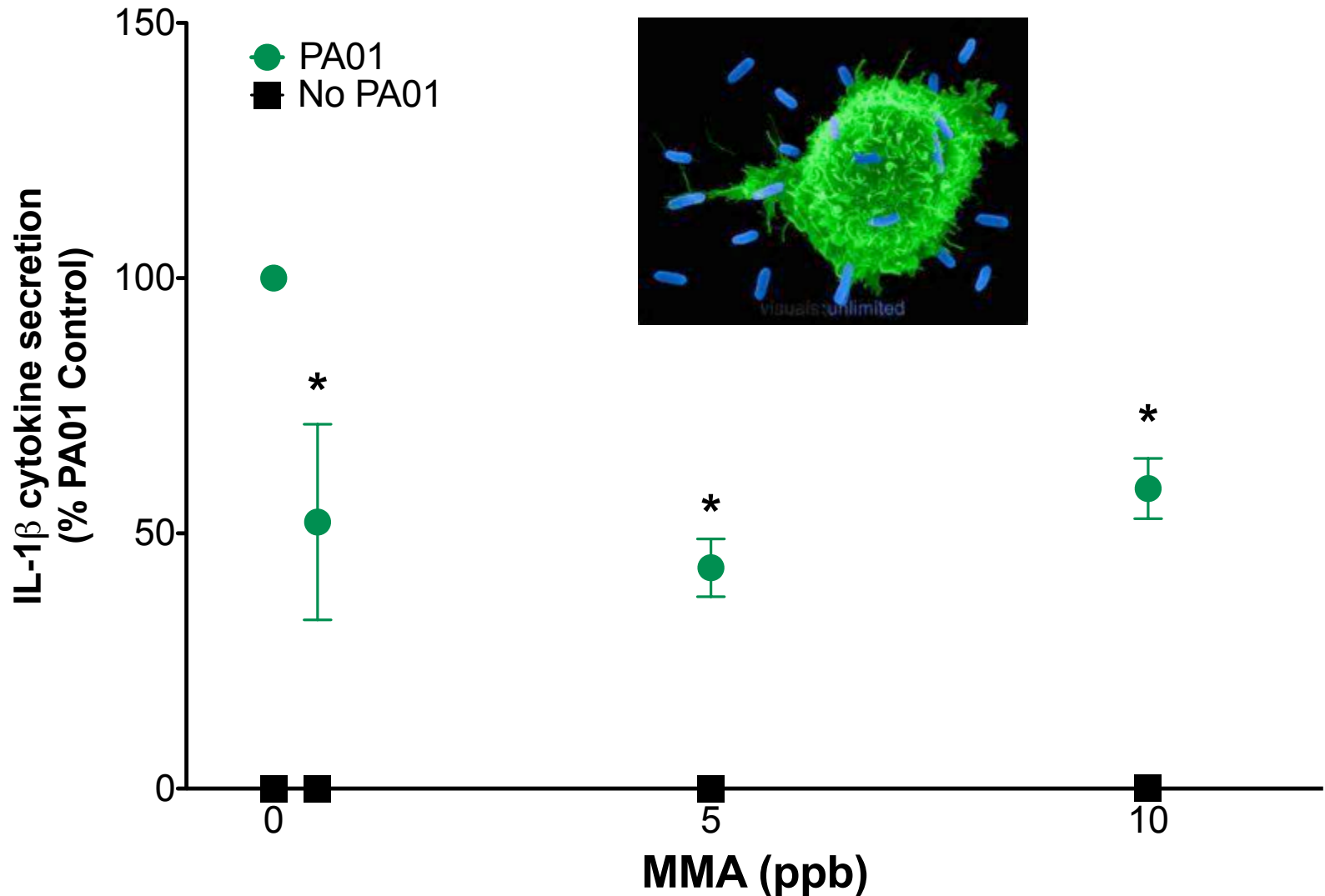
iArsenic reduces *Pa* stimulated IL-8 and CXCL1 secretion by lung epithelial cells



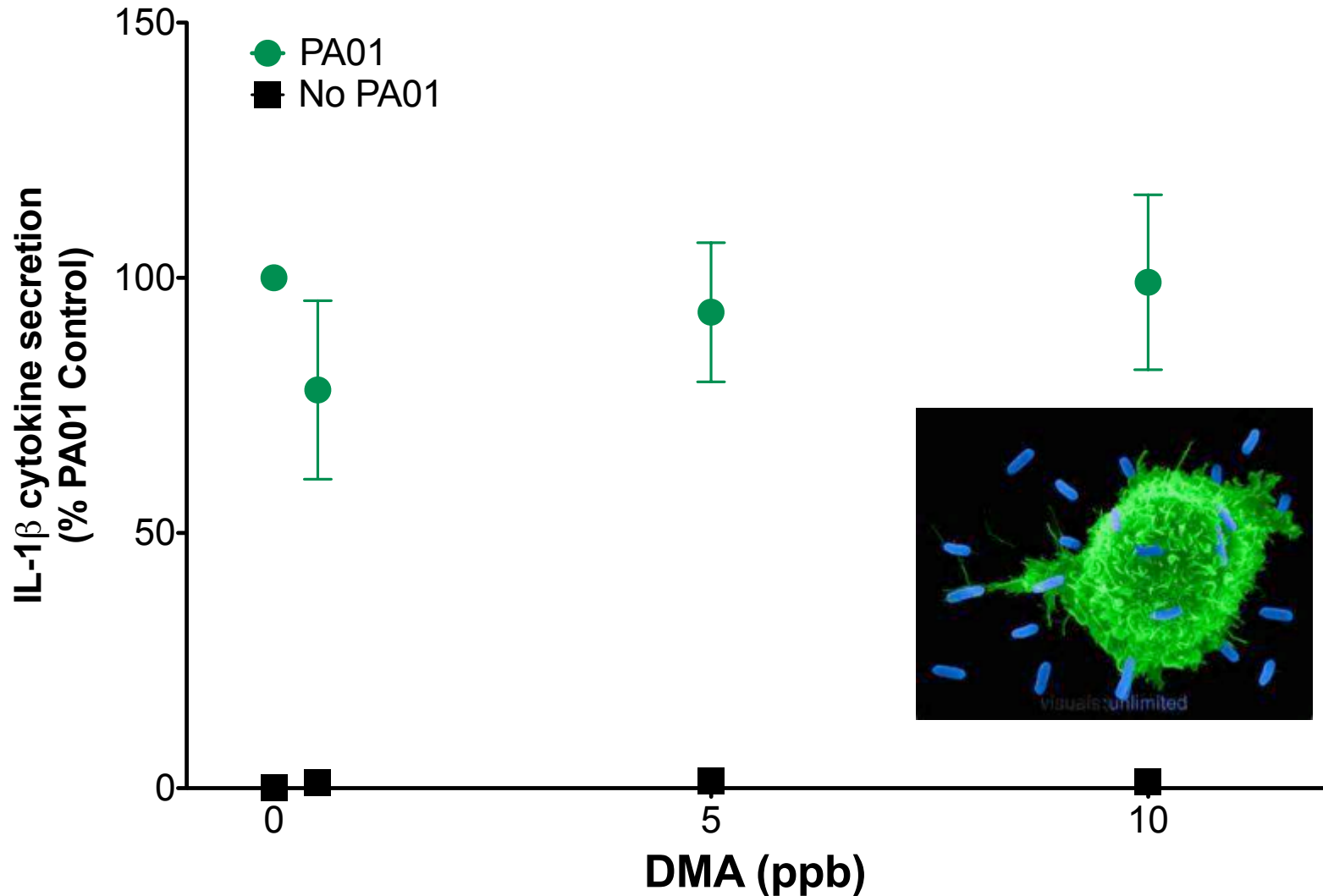
iArsenic reduces *Pa* stimulated IL-1 β secretion by human macrophages



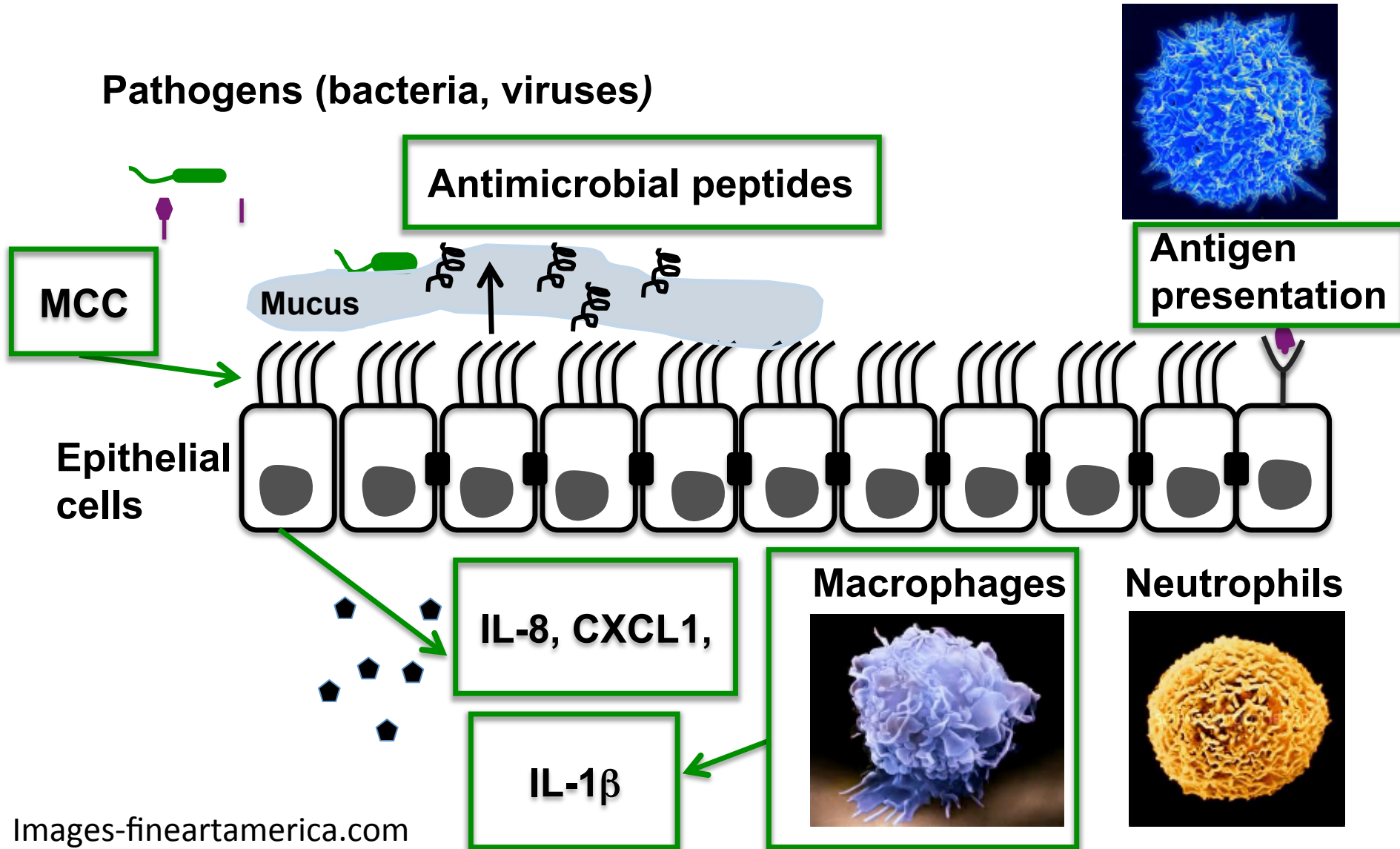
MMA reduces *Pa* stimulated IL-1 β secretion by macrophages



DMA has no effect on *Pa* stimulated IL-1 β secretion by macrophages

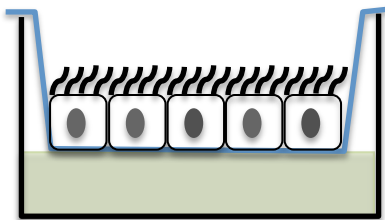


Arsenic reduces MCC and cytokine secretion and thereby enhances bacterial infection

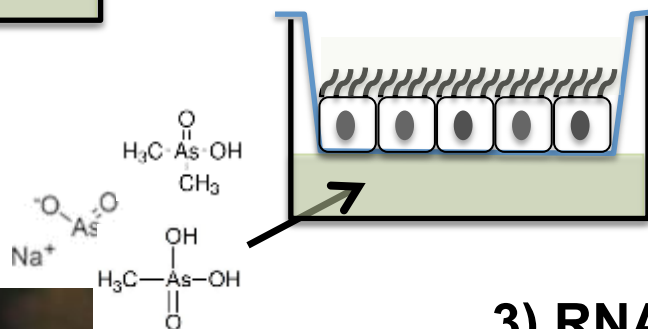


RNAseq to identify novel genes and pathways affected by arsenic

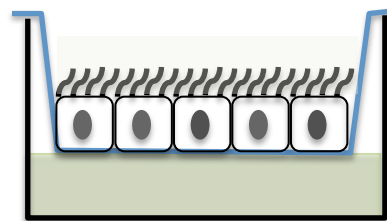
1) Human lung cells in cell culture (6 donors)



2) Exposed cells to 0, 5, 10 or 50 ppb As (25% iAs, 25% MMA, 50% DMA) for 6 days



3) RNA seq analysis of gene expression

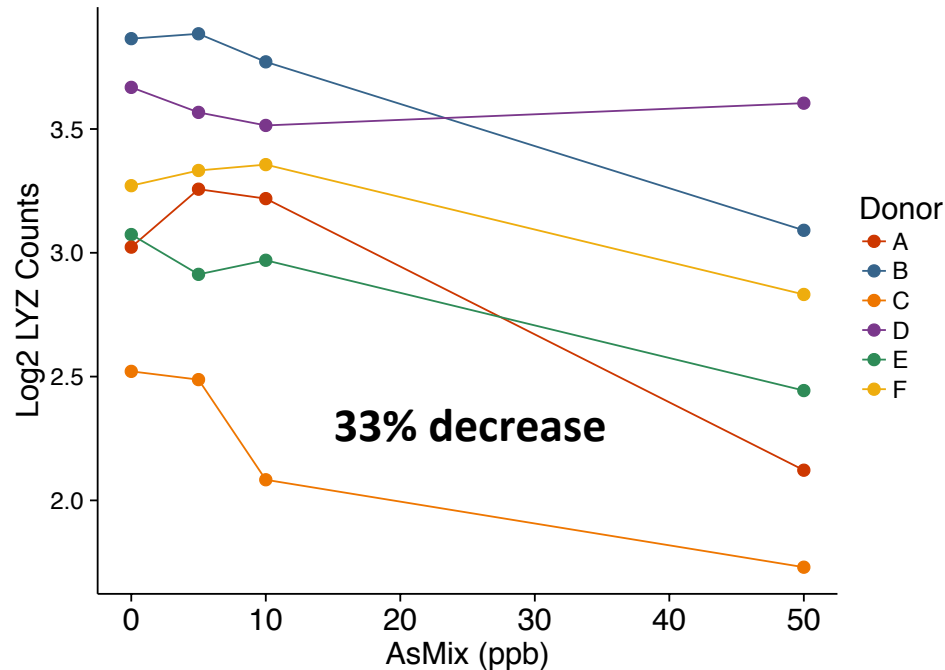


4) Media collected for cytokine analysis

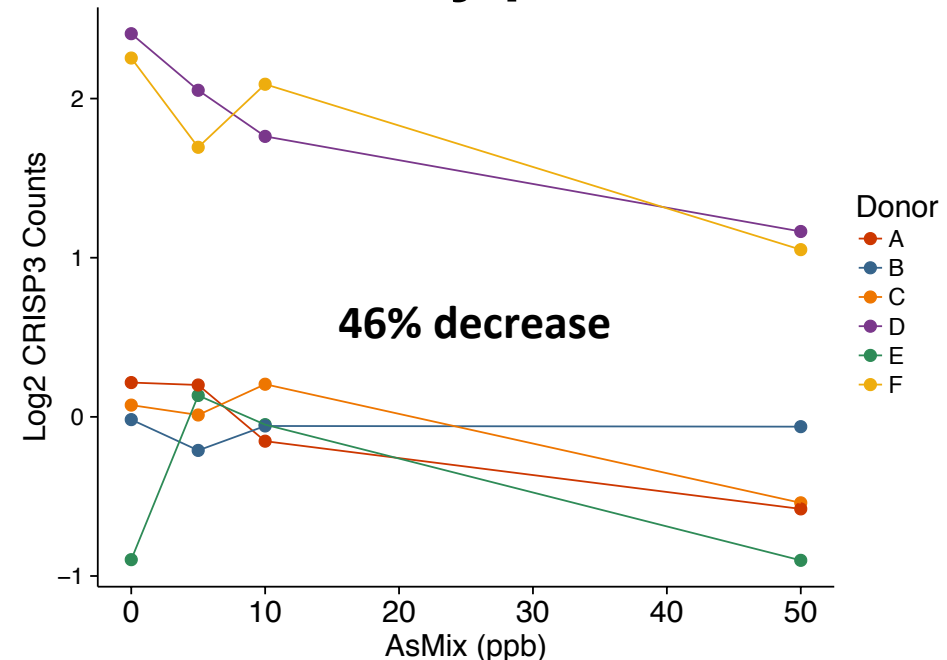


Arsenic decreases antimicrobial peptide gene expression

Lysozyme

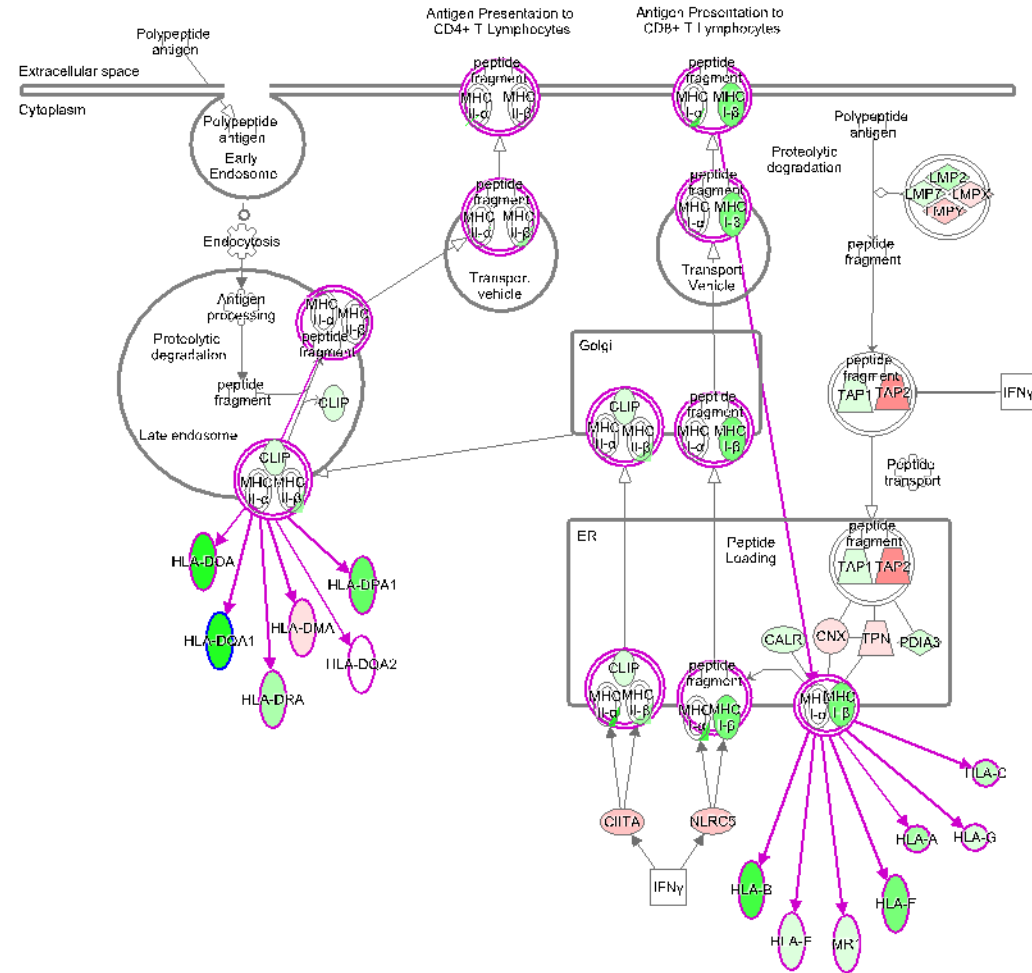


Cysteine-rich secretory protein 3



Arsenic decreases antigen presentation pathway gene expression

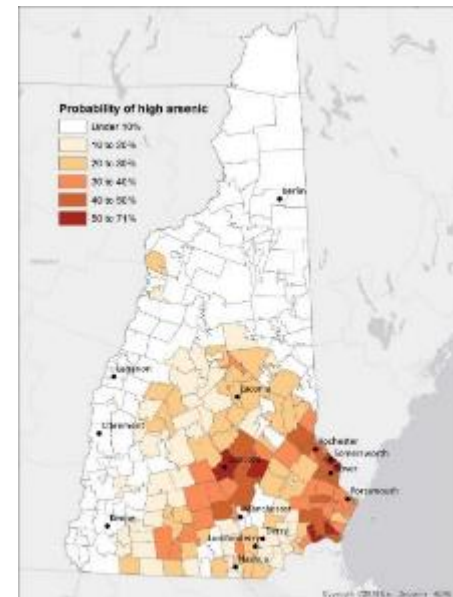
Antigen Presentation Pathway-As Overlay



**Dartmouth Superfund Program
Educational/Outreach Activities to Reduce
Exposure to Arsenic in the US**

EPA environmental educational program

Building school and
community collaborations to
eliminate arsenic from
drinking water in Maine
and New Hampshire: A model
for the US



EPA environmental education grant

- All About Arsenic website (<http://www.allaboutarsenic.org/>)
- Creation of classroom arsenic curriculum with a focus on watershed and home well testing
- Partnership with community partners to expand work on private wells



Encouraging/facilitating well water testing for arsenic

Arsenic in Your Well Water

What to do if your well has too much arsenic.



Switch to bottled water.

Finding out your well water has too much arsenic in it may cause you to worry. There are things you can do to protect your family from arsenic. The first thing to do is switch to bottled water for drinking and for making drinks such as coffee, tea, juice, and infant formula.

You can use this tipsheet to help you decide what to do next. Call the Maine CDC at 866-292-3474, tollfree in Maine, or 207-287-4311 to speak to an expert about arsenic in your well water.



<http://www.dartmouth.edu/~toxmetal/>

**Well Water Community
Action Toolkit**

Ask Well: Should You Filter Your Water?

By RONI CARYN RABIN DECEMBER 31, 2015 5:45 AM 84

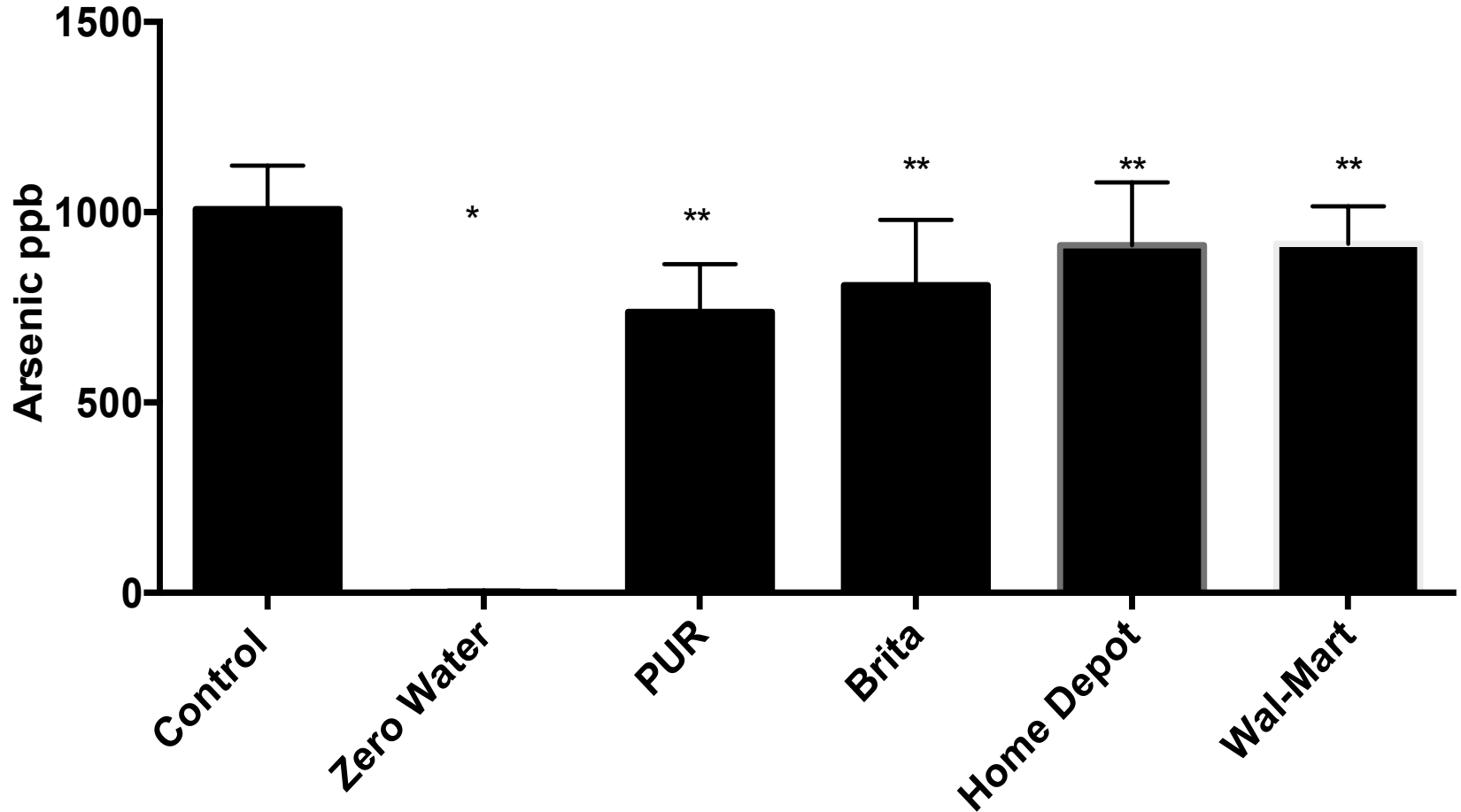


iStock

Yes, EPA rules may be too lenient. Some filters reduce lead, pesticides, chlorine, arsenic, antibiotics and hormones found in regulated public water supplies.

New York Times

Zero Water filters remove arsenic from drinking water



Stanton et al, 2016

I have no financial stake or anything financial or other wise to gain from promoting the use of ZERO WATER filters

Dartmouth Toxic Metals Superfund Research Program



**Research supported by P42ES007373 from the
National Institute of Environmental Health Sciences.**



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