

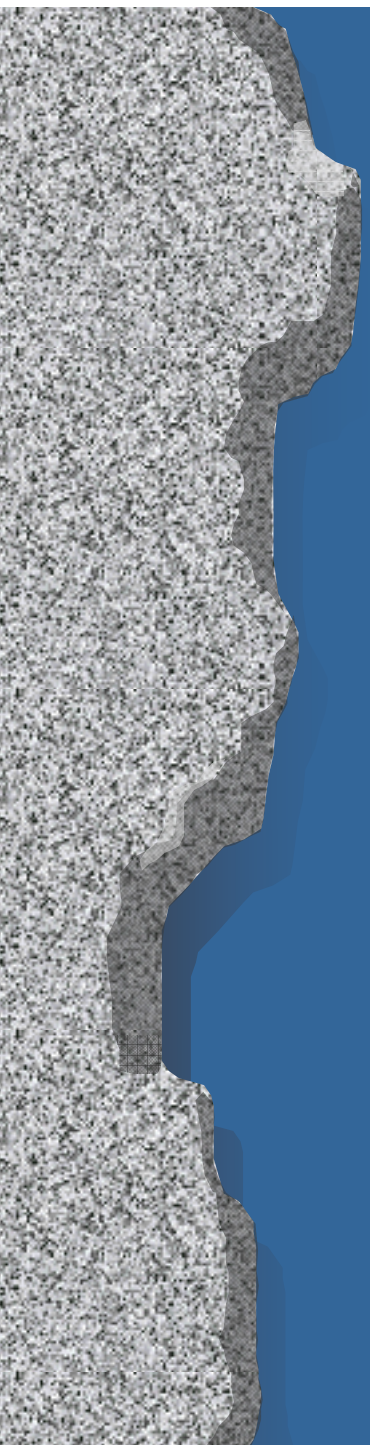


# Health Effects of Uranium Mining: New Research Findings

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### URANIUM 238 (U238) RADIOACTIVE DECAY

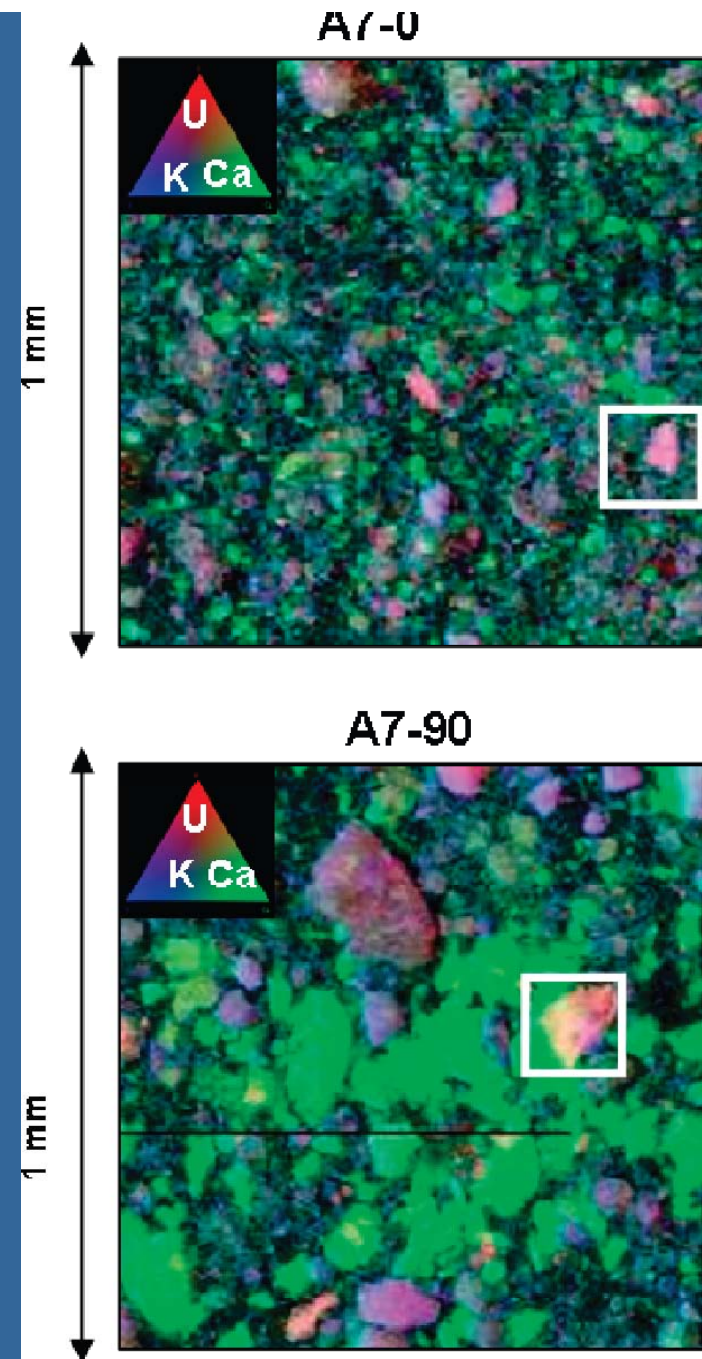
type of radiation	nuclide	half-life
	uranium—238	$4.5 \times 10^9$ years
$\alpha$	↓	
	thorium—234	24.5 days
$\beta$	↓	
	protactinium—234	1.14 minutes
$\beta$	↓	
	uranium—234	$2.33 \times 10^5$ years
$\alpha$	↓	
	thorium—230	$8.3 \times 10^4$ years
$\alpha$	↓	
	radium—226	1590 years
$\alpha$	↓	
	radon—222	3.825 days
$\alpha$	↓	
	polonium—218	3.05 minutes
$\alpha$	↓	
	lead—214	26.8 minutes
$\beta$	↓	
	bismuth—214	19.7 minutes
$\beta$	↓	
	polonium—214	$1.5 \times 10^{-4}$ seconds
$\alpha$	↓	
	lead—210	22 years
$\beta$	↓	
	bismuth—210	5 days
$\beta$	↓	
	polonium—210	140 days
$\alpha$	↓	
	lead—206	stable

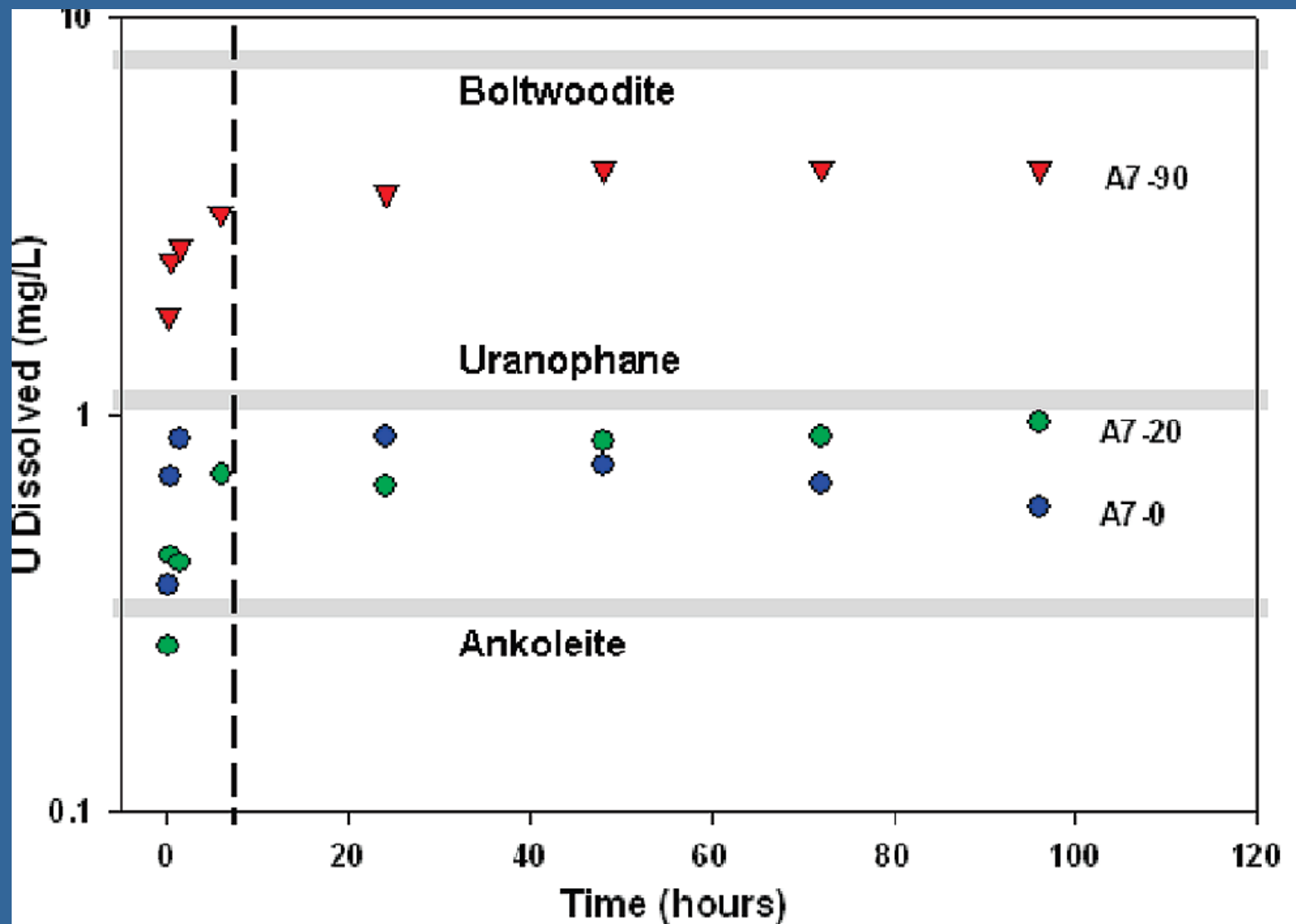


**Radon  
Daughters**

**FIGURE 4. (Left) Tricolor X-ray fluorescence plots of U, Ca, and K in A7-0 and A7-90. Purple color represents the association between U and K. White boxes represent uranium “hot spots”. Green represents Ca.**

deLemos et al. VOL. 42, NO. 11, 2008 / ENVIRONMENTAL SCIENCE & TECHNOLOGY





deLemos et al. VOL. 42, NO. 11, 2008 / ENVIRONMENTAL SCIENCE & TECHNOLOGY



Anne Raup, New York Times, Published: March 28, 2007



# Health Effects

# Radon (WLM) Doubling of Risk for non-smokers

Age at disease	Years since last radon exposure		
	<10	10-19	>20
<50	2	3	13
50-59	5	11	45
60-69	24	52	209
>70	36	77	309

From DOJ, July, 1996



RECA: **6,020** uranium workers compensated by January 31, 2008 for **\$601 million**.

<http://www.usdoj.gov/civil/torts/const/reca/index.htm>



# Problems with Radon Standard

NIOSH recommended in 1987 that the exposure standard for underground mine workers, covered by MSHA, be reduced from 4 WLM to 1 WLM, which has never been done.

## Health Effects 2

- 2) **Radium** causes bone cancer, cancer of the nasal sinuses and mastoid air cells and leukemia
- 3) **Thorium...**
- 4) **Arsenic** causes lung and skin cancer, neurological harm, hyper-pigmentation and hyperkeratosis of the skin
- **Ionizing radiation** causes cancer, birth defects, genetic damage

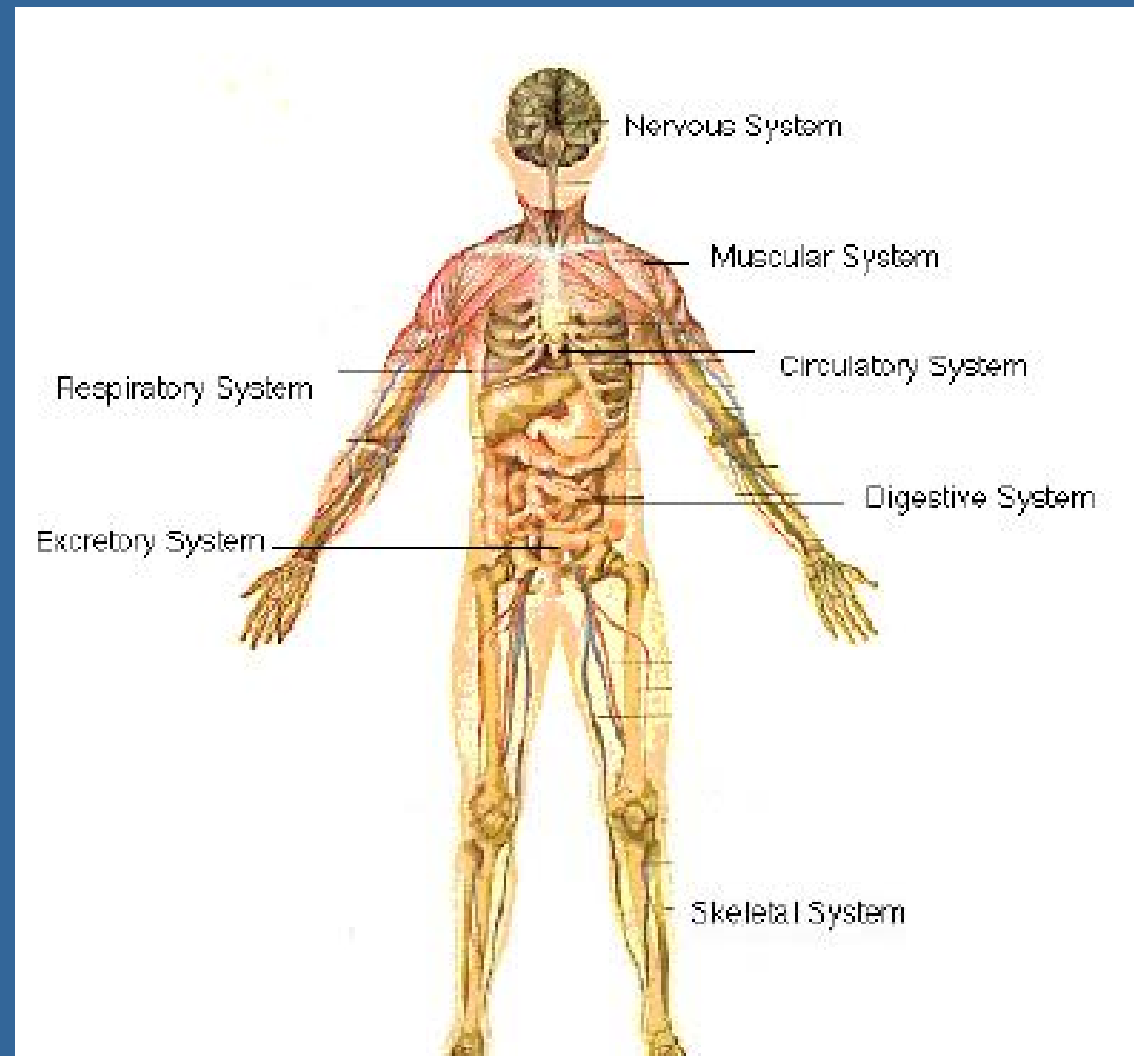
# Uranium: Routes of Entry

**Inhalation**

**Ingestion**

**Skin  
absorption**

**Penetration**





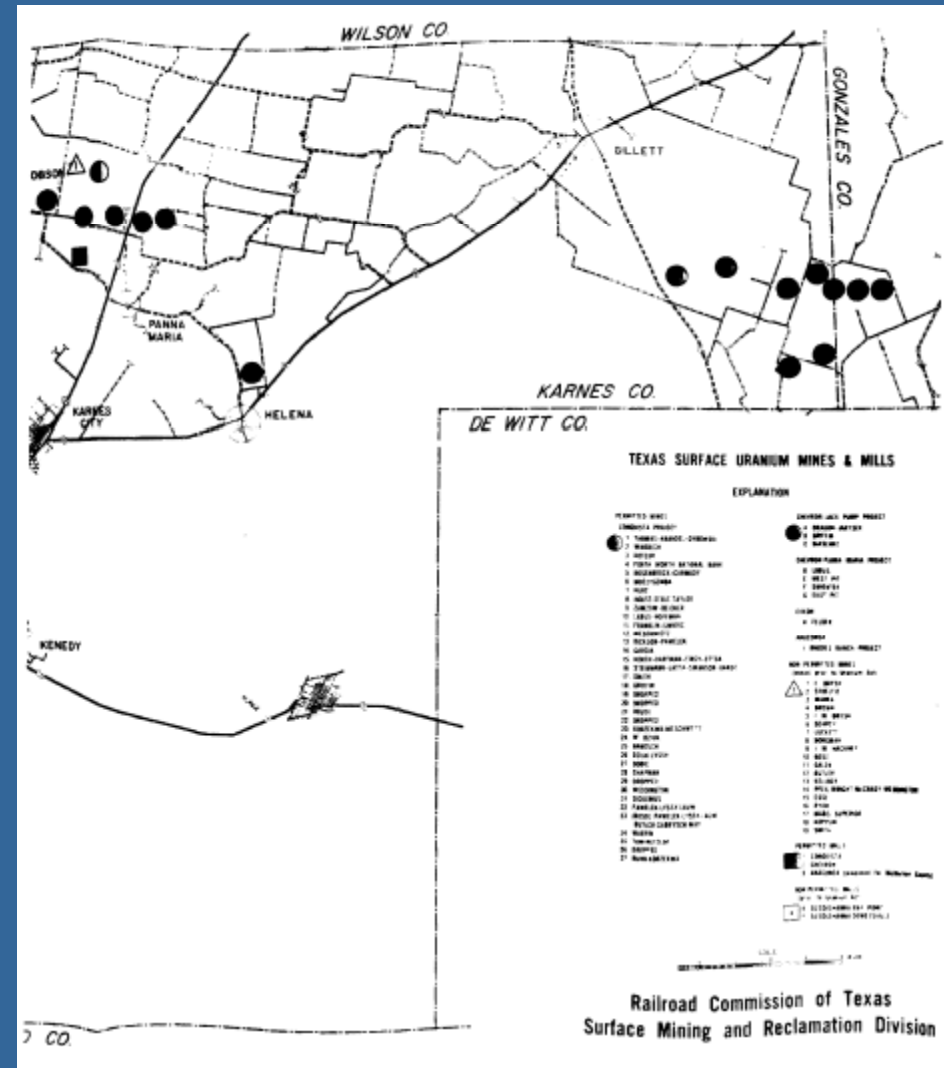
# Uranium: Well Established Health Effects

- Kidney damage in animals
  - Reviewed in ATSDR, 1999
- Developmental defects in animals
  - Domingo et al., 2001
  - Paternain et al., 1989
  - Llobet et al, 1991

# Karnes County, Texas, Susquehanna mine

Falls City Mill Site

Karnes County, Texas



[http://www.eia.doe.gov/cneaf/nuclear/page/umtra/falls\\_city\\_title1.html](http://www.eia.doe.gov/cneaf/nuclear/page/umtra/falls_city_title1.html)

<http://www.rrc.state.tx.us/forms/publications/smr/d/statisticalfactsonmining.pdf>

# Au et al., 1995

Articles • Au et al.

## Biomarker Monitoring of a Population Residing near Uranium Mining Activities

William W. Au,<sup>1</sup> Richard G. Lane,<sup>2</sup> Marvin S. Legator,<sup>1</sup> Elbert B. Whorton,<sup>1</sup> Gregg S. Wilkinson,<sup>1</sup> and Gary J. Gabehart<sup>1</sup>

<sup>1</sup>Department of Preventive Medicine and Community Health and <sup>2</sup>Department of Radiation Therapy, The University of Texas Medical Branch, Galveston, TX 77555-1110 USA

We investigated whether residents residing near uranium mining operations (target population), who are potentially exposed to toxicants from mining waste, have increased genotoxic effects compared with people residing elsewhere (reference population). Population surveys were conducted, and 24 target and 24 reference residents were selected. The selected subjects and controls were matched on age and gender and they were nonsmokers. Blood samples were collected for laboratory studies. The standard cytogenetic assay was used to determine chromosome aberration frequencies, and the challenge assay was used to investigate DNA repair responses. We found that individuals who resided near uranium mining operations had a higher mean frequency of cells with chromosome aberrations and higher deletion frequency but lower dicentric frequency than the reference group, although the difference was not statistically significant. After cells were challenged by exposure

Pana Maria, Texas. Populations residing near tailings and mining activities may be exposed to a variety of hazardous materials which may cause them to have increased risk for health problems. We conducted a cross-sectional study of a population residing adjacent to uranium mining activities and a population residing in an area free of uranium mining operations, using biomarkers to measure differences in chromosome aberrations and in DNA repair response after their lymphocytes are challenged *in vitro* with  $\gamma$ -rays.

### Methods

**Identification of mining sites and target residents.** Active mine/mill operations, unreclaimed mine/mill sites, and sites that have been closed for less than 3 years in Karnes County, Texas, were identified, confirmed by site visits, and marked on a

map. Areas were similar to those areas inhabited by our target population. From our survey of the reference area, 137 dwellings were located. Residents were interviewed using procedures described earlier.

**Selection of subjects.** Enrollment in this study was restricted to nonsmokers who had never worked in the uranium industry, had not been exposed to radiographic procedures to soft tissues such as brain and abdominal scans, and had not undergone radiotherapy or chemotherapy with potent cytotoxic drugs. Inclusion in the target group was restricted to individuals who had resided in the uranium mining target area for 10 or more years. Inclusion in the reference group was restricted to individuals who had never resided in any of the uranium mining areas that we were able to identify. We also eliminated heavy drinkers from both the target and reference populations (daily consumption of more than two shots of hard liquor or four cans of beer) and matched reference and target subjects on age ( $\pm 7$  years) and gender.

We selected 154 residents (73 targets and 81 references) for interview. Among the target subjects, 10 refused to participate and 30 were ineligible based on our selection criteria. This left 33 qualified target individuals for our laboratory study.

- “...target residents have a higher spontaneous frequency of abnormal cells and cells with chromosome deletions than reference residents.”
- “With the challenge assay, the frequencies of aberrant cells, deletions, and dicentrics in lymphocytes from the target residents are consistently higher than those from the controls...”

Environmental Health  
Perspectives, Volume 103, Number  
5, May 1995



# Some Recent Research Findings

# Stearns et al., 2005

“Data suggest that uranium could be chemically genotoxic and mutagenic through the formation of strand breaks and covalent U–DNA adducts. Thus the health risks for uranium exposure could go beyond those for radiation exposure.”



photo by Jerry Foreman

# Stearns et al., 2005

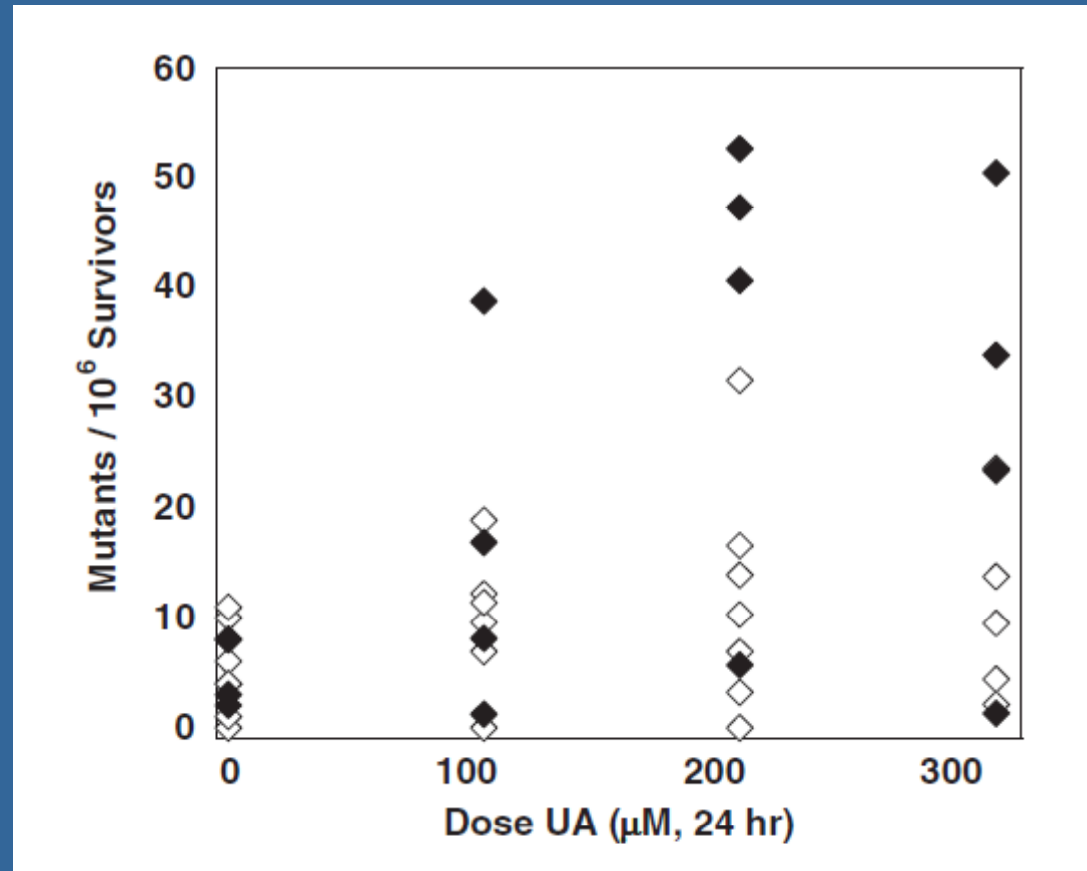
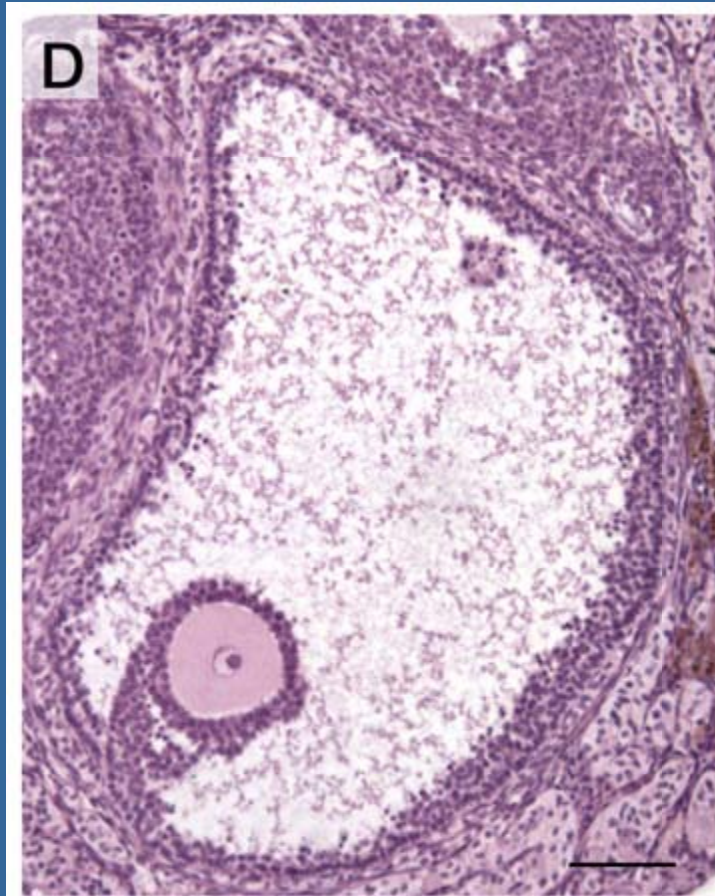


Fig. 2. 6-Thioguanine-resistant cells obtained after 24 h exposure of CHO-AA8 (open diamonds) and CHO-EM9 (closed diamonds) cells to UA. Methods are described in the text. Each data point refers to an individual experiment. *Mutagenesis* vol. 20 no. 6 pp. 417–423, 2005

# What is an oocyte?



“(D) follicles... with an oocyte...”

“An oocyte...is a female gametocyte or germ cell involved in reproduction. In other words, it is an immature ovum, or egg cell. An oocyte is produced in the ovary...”

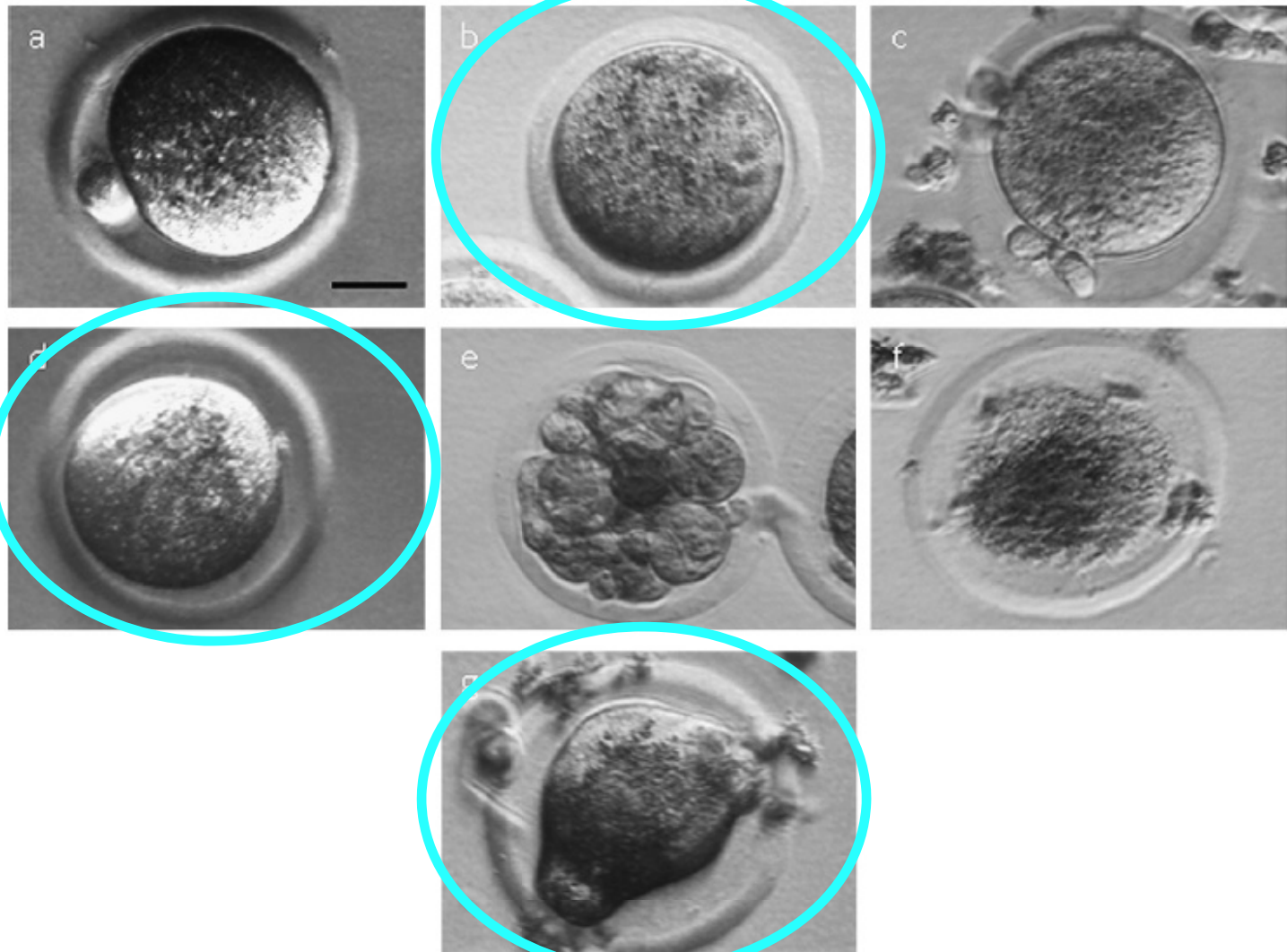
<http://en.wikipedia.org/wiki/Oocyte>

Arnault et al, 2008, Toxicology 247 (2008)  
80–87

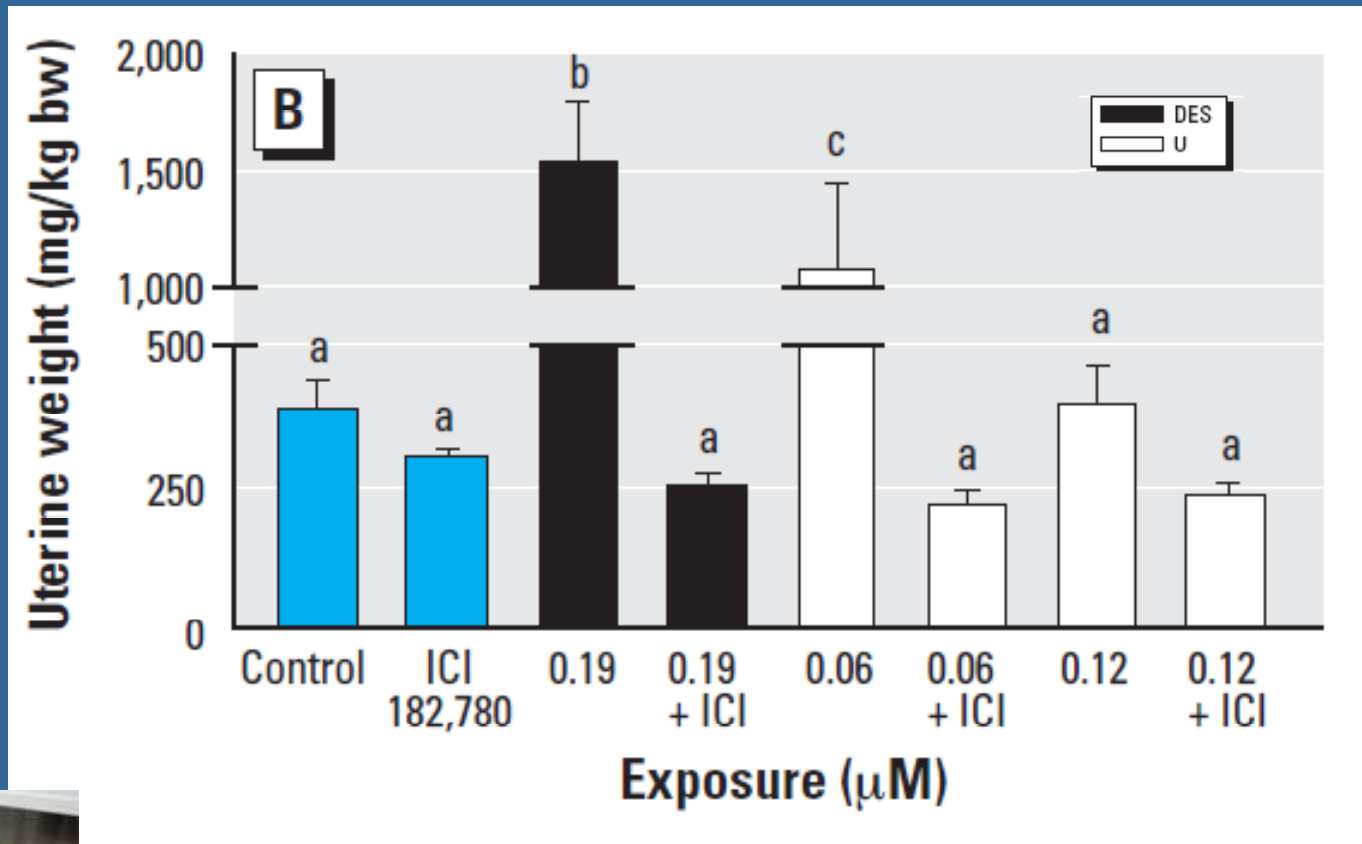
# Mouse oocyte studies: High doses

Study	Finding
Kundt et al., 2009	Found no threshold at 2.5 mgU/kg/d for quality of oocytes, and abnormalities in chromatin organization and nuclear integrity. Below current NOAEL.
★ Arnault et al., 2008	Uranium induces changes in folliculogenesis and oocyte maturation.
★ Feugier et al., 2008	Reduced the proportion of healthy oocytes by half at 20 mgU/L (see next slide)

# Feugier et al., 2008



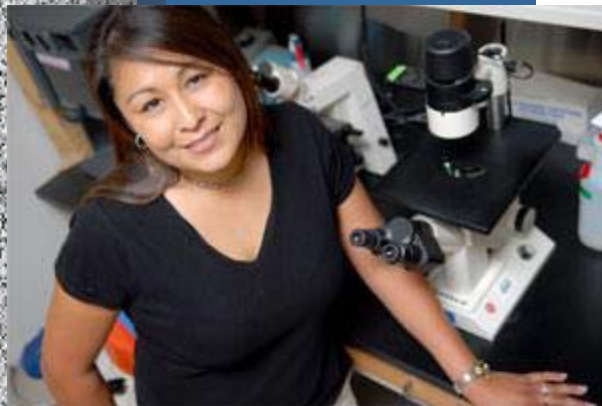
# Raymond-Whish et al., 2007



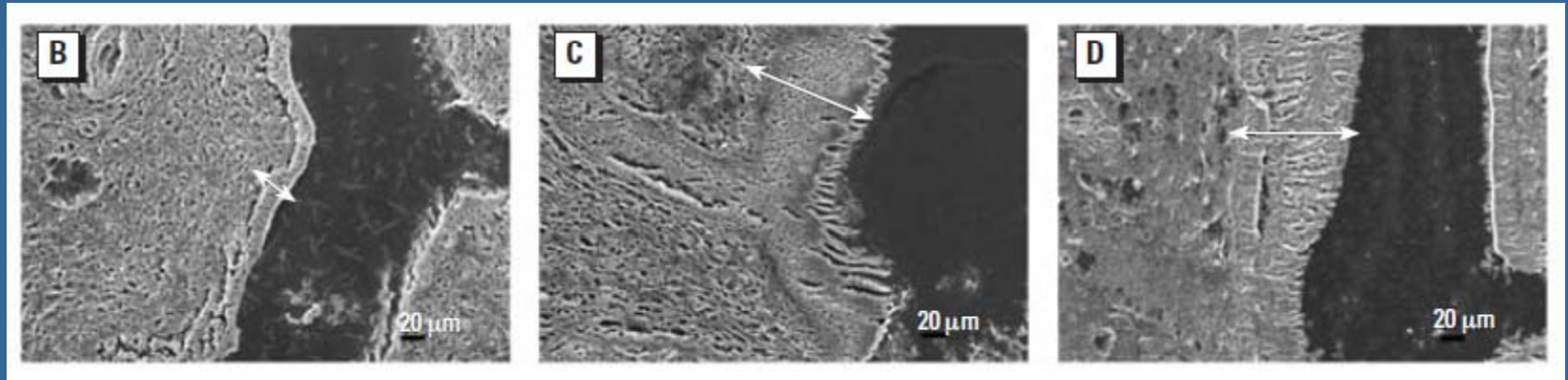
**Figure 2.** Effect of UN or DES alone and in combination with ICI 182,780 on uterine weight in ovariectomized C57Bl/6J mice.

Environmental Health Perspectives • VOLUME 115 | NUMBER 12 | December 2007

Jake Bacon/Arizona Daily Sun Stefanie Raymond-Whish stands in a lab at Northern Arizona University.  
<http://photos.azdailysun.com>

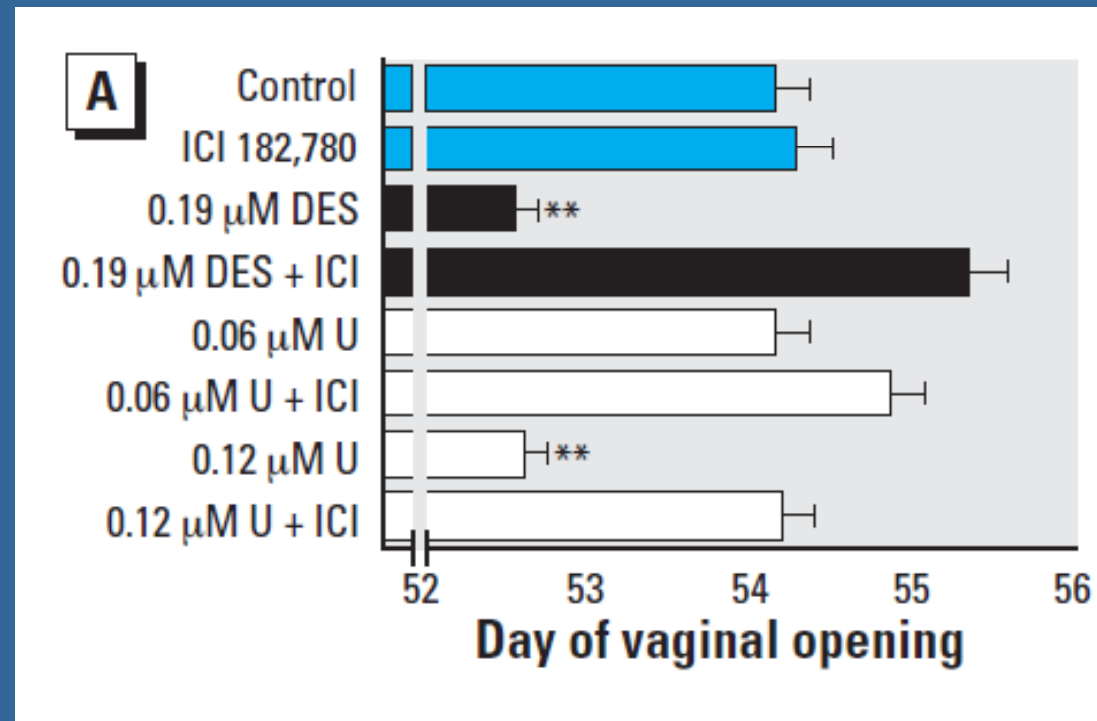


# Raymond-Whish et al., 2007 (continued)



**Figure 3.** Uterine luminal epithelial cell growth in ovariectomized C57Bl/6J mice stimulated by UN or DES in drinking water for 30 days. Representative scanning electron microscopy images at the same magnification of uterine epithelial cell layers from tap water control (B), 0.19  $\mu\text{M}$  DES (C), or 0.12  $\mu\text{M}$  U (D). Arrows highlight epithelial cell height in DES-exposed (C) and U-exposed (D) ovariectomized mice.

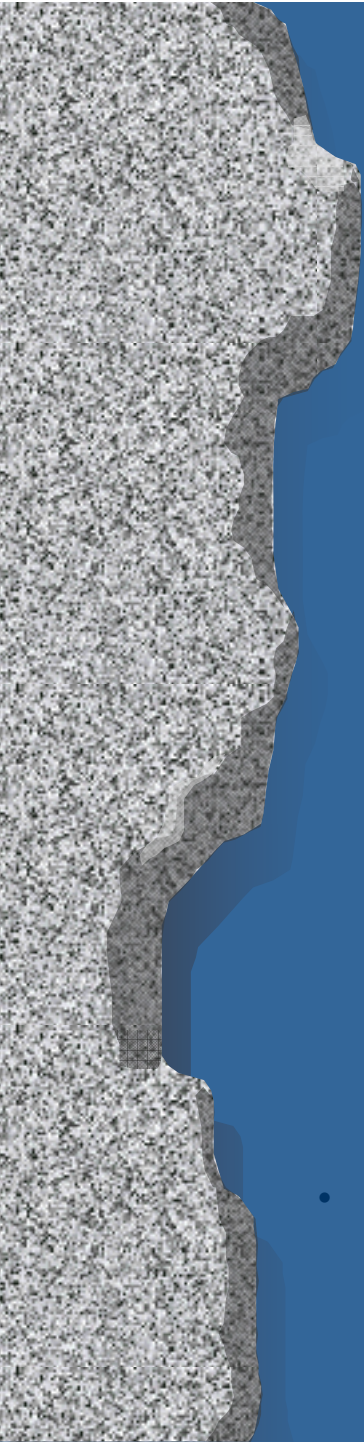
# Raymond-Whish et al., 2007 (continued)



**Figure 4.** Effect of UN in drinking water on VO. Ovariectomized C57Bl/6J mice (50 days of age) were exposed to control tap water, 0.19  $\mu$ M DES, or 0.06 or 0.12  $\mu$ M U for 10 days, or one of these doses plus vehicle or 500  $\mu$ g/kg ICI 182,780 in vehicle. (A) Mice were examined daily for VO from 50 days of age to the day of vaginal opening; values shown are mean day of VO  $\pm$  SE (n = 6–7).

# Uranium in drinking water in Humans

Study	Finding
Moss et al., 1983	Increases in B <sub>2</sub> -microglobulin in urine
Mao et al., 1995	Microalbuminuria
Zamora et al., 1998	Increased urinary glucose, alkaline phosphatase and B <sub>2</sub> -microglobulin
Kurttio et al, 2002	Increases of calcium and phosphate, but NOT B <sub>2</sub> -microglobulin or albumin
Kurttio et al, 2006	No evidence of nephrotoxicity
Selden et al., 2009	Little evidence of nephrotoxicity



# Uranium Legacy Impacts on Health of Residents: DiNEH Project Update

- Johnnye Lewis, Ph.D., DABT
  - *Director, Community Environmental Health Program,*
  - *Director, Novel Methodologies Research Component of the Clinical and Translational Science Center,*
    - *University of New Mexico-Health Science Center, College of Pharmacy*
  - *Principal Investigator (PI): DiNEH Project 's Navajo Uranium Assessment and Kidney Health Project*
    - *NIEHS/NIH funded Community-Based Participatory Research*
  - *Project Team: UNM: Mallery Downs,RN; Glenn Stark, Miranda Cajero, Bernadette Pacheco, Jeremy DeGroat,*
    - *Gabriel Huerta, Ph.D.*
  - *Southwest Research & Information Center: Chris Shuey, MPH (Co-PI), Sarah Henio-Adeky, Sandy Ramone, Teddy Nez*
    - *University of Texas,Houston: Don Molony, MD*
  - *(independent research in this presentation funded by NIEHS P30 ES-012072, R25 ES013208, & R01 ES014565*
    - *and M01-RR-00997)*



**Figure 1. a. Navajo family hauling water from a windmill.; b. new home under construction within 1200' of mine waste pile; c. children playing near partially reclaimed waste pile; d. cattle grazing on contaminated soil adjacent to mine waste. (Photo credit, J. deLemos, C. Shuey, and C. George). From delemos et al., in preparation.**

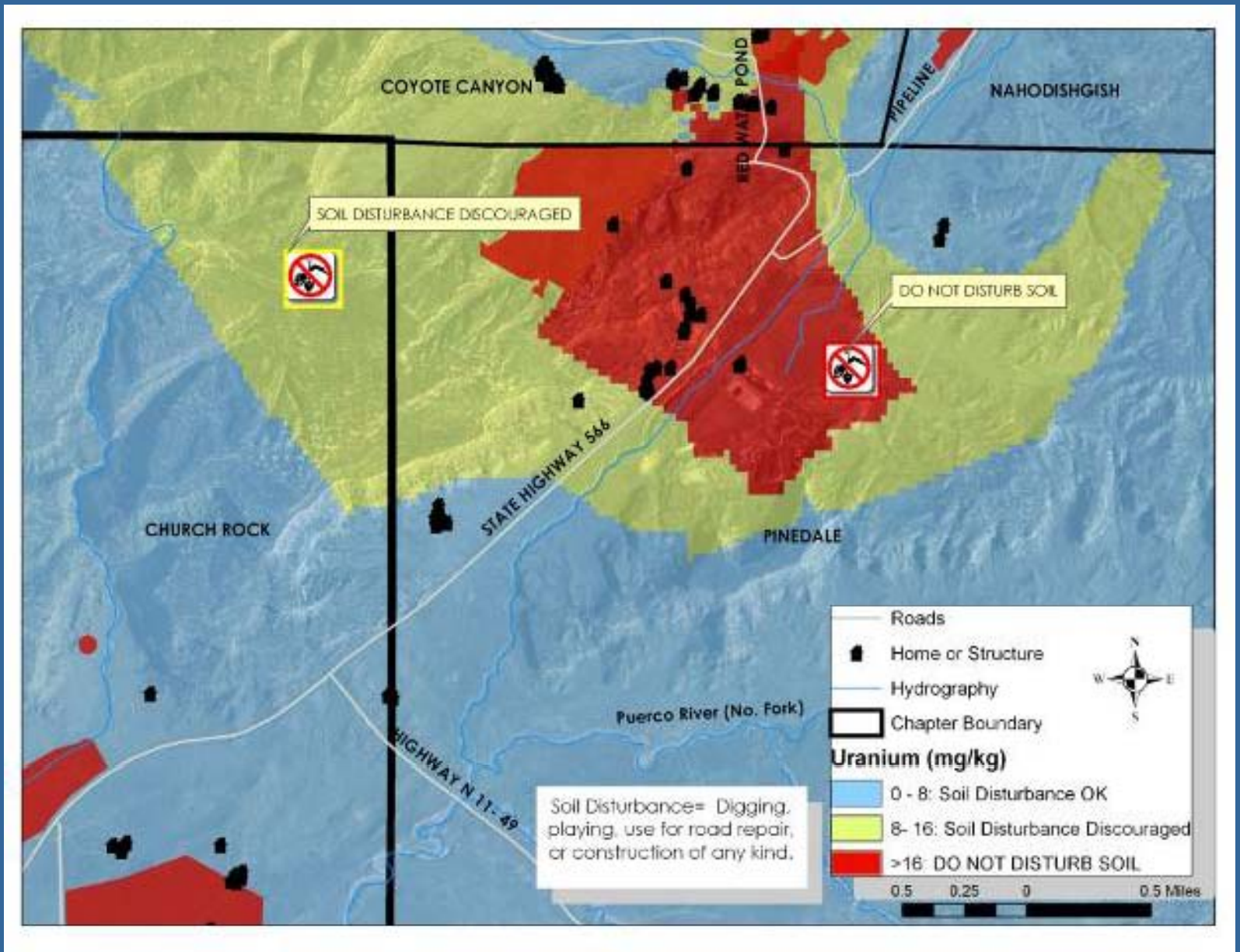
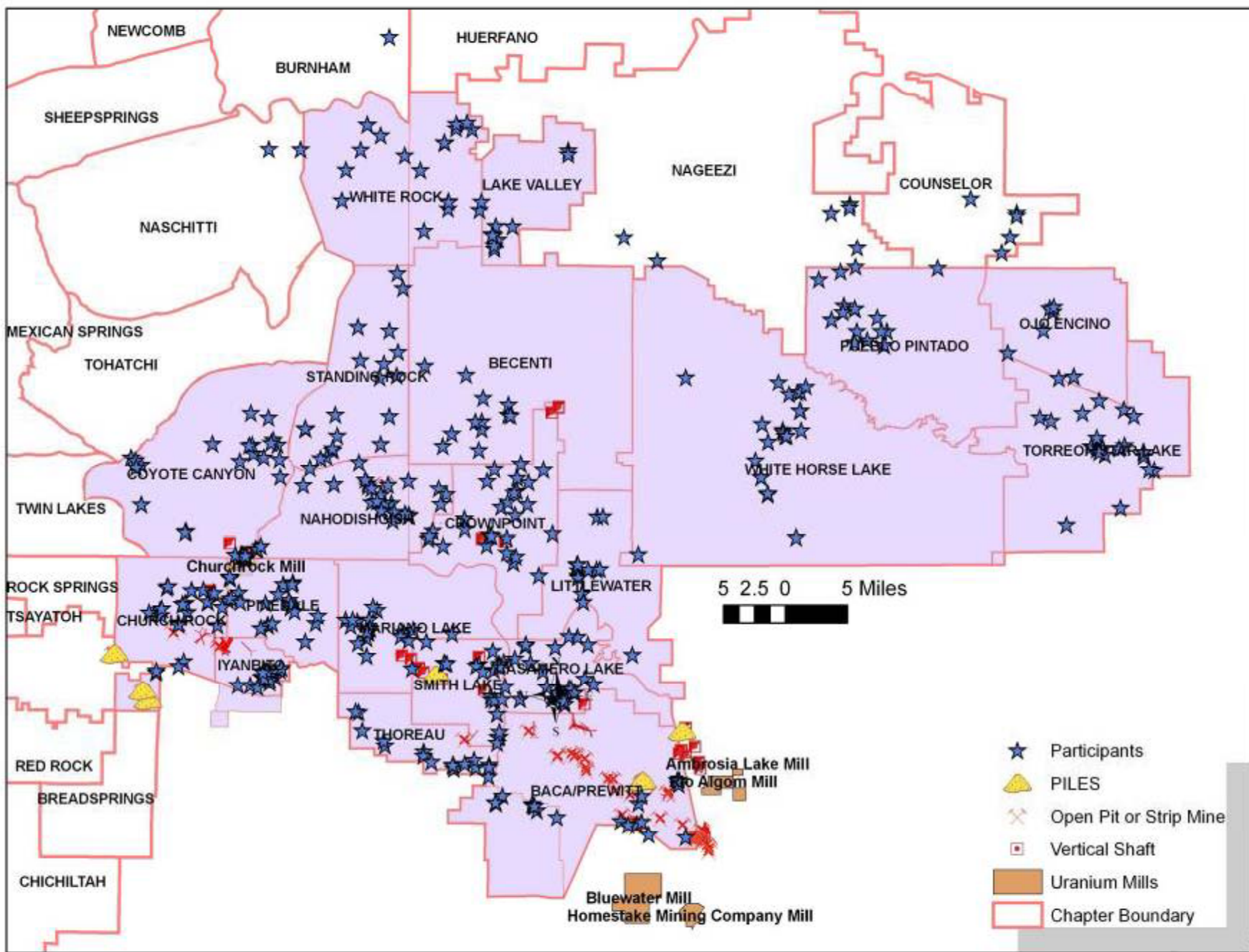


Figure 5: Soil restriction recommendation map.

deLemos et al., in preparation.



# Gene expression and uranium exposure

Study	Organism	Finding
Prat et al., 2010	Cultured human kidney and pulmonary cells	In kidney cells 70 genes over-expressed and 112 under-expressed involved in cell signaling, cell defense and apoptosis.
Wan et al., 2006	Mouse immune cells	Altered gene expression, possibly involved in cancer, autoimmune and other processes.
Ondrias et al., 2008	Mouse kidney cells	Affected a specific calcium receptor.
Lebebours et al., 2009	Zebra fish	Lots of changes in gene expression, mostly related to detoxification and oxidative stress.

# Canu et al., 2010

- 2,709 workers at the ARENA NC Pierrelatte plant in France.
- SMR = 1.49 for lymphatic cancer (N=9)
- SMR = 2.85 for pleural cancer (N=5)



# Bone and vitamin D

- Kurttio et al., 2005: Evidence that uranium in drinking water in Finland affects bone in men, but not women.
- Tissandie et al., 2007: Evidence that depleted uranium exposure in rates affects vitamin D metabolism, including through changes in gene expression.

# Problems with Uranium Standards

- EPA = 30 ug/L in water
- WHO = 2 ug/L in water (based on LOAEL)
- OSHA = 50 ug/m<sup>3</sup> in air (at LOAEL)
- DOE = 1.5 ug/L in urine (radiation only)

# UNM Book: 2006

