COLLEGE OF PHARMACY
METAL EXPOSURE AND TOXICITY ASSESSMENT ON TRIBAL LANDS IN THE SOUTHWEST

Overview of Community-partnered Research to Assess Health Effects of Environmental Exposures to Uranium in Tribal Communities

New Mexico Public Health Association Annual Meeting
May 19-20, 2022

Chris Shuey, MPH, Community Engagement Core Lead
Jose Cerrato, Ph.D., Mineralogy and Toxicity of Mine Wastes
Eliane El Hayek, Soil and Plant Uptake in Agricultural Areas Near Mines
Esther Erdei, Ph.D., DiNEH Project Methods and Findings
Debra MacKenzie, Ph.D., Navajo Birth Cohort Study-ECHO+
Sarah Henio-Adeky, BA, Navajo Translation of Thinking Zinc Clinical Trial

Funding: NIH/NIEHS P42 ES025589 (UNM METALS)

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HEALTH SCIENCES

Stanford University

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Contributors, Funding, Disclosures, Disclaimer, Approvals

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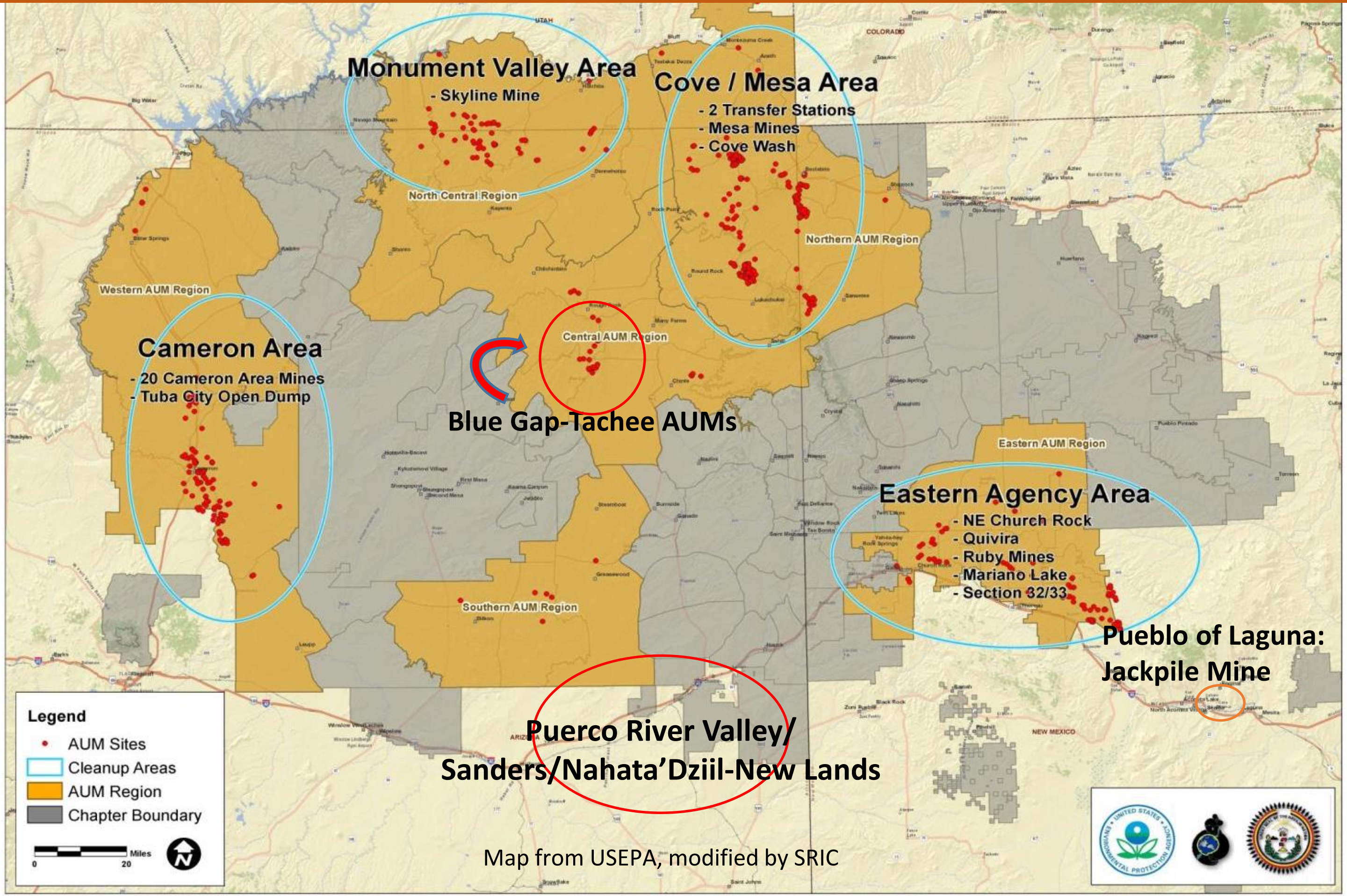
Approvals:

Human research is monitored and approved by UNM Human Research Protections Office (HRPO), the Navajo Nation Human Research Review Board (NNHRRB) and the New Mexico Cancer Care Alliance, as required by federal, state and Tribal law.

The Problem: U Mine Wastes Pervasive on Navajo, Laguna

The Numbers:

- 524 AUMs on Navajo Nation
- >10,400 AUMs in Western U.S.
- Jackpile Mine at Laguna – once largest open-pit U mine in world
- All AUMs fall under federal Superfund law for assessment, remediation



Map from USEPA, modified by SRIC

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Community Engagement: Overarching Questions

- How did Native communities impacted by uranium mining help inform 25+ years of UNM's environmental health research?
- How have impacted Native communities participated in EH research?
- What are the roles of citizen and indigenous science in EH research?
- What have we learned from these community-based collaborations?

L-R: Cameron Farm assessment, 2019; Chris Nez at Claim 28 "Prius Rock", 2014;
Red Water Pond Road Community, 2007; soil and plant sampling, Pueblo of Laguna, 2020

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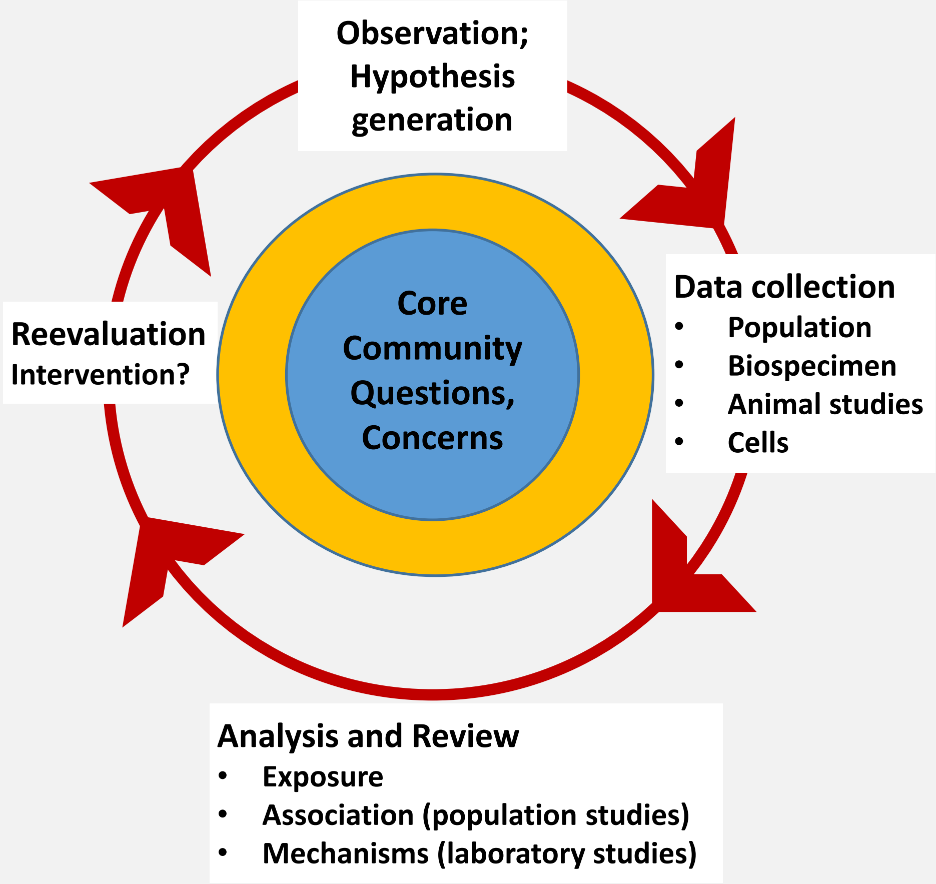
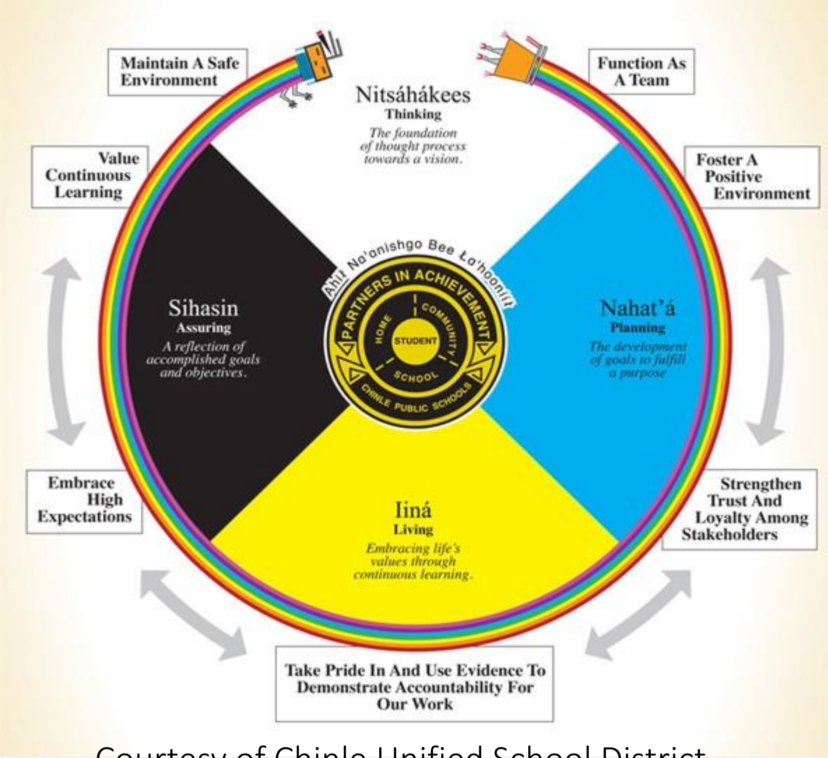
Models underlyng our community-partnered research: Western and Indigenous Commonalities





Courtesy of Chinle Unified School District

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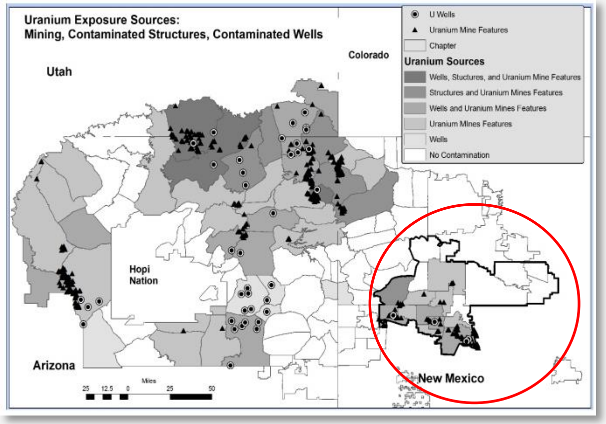
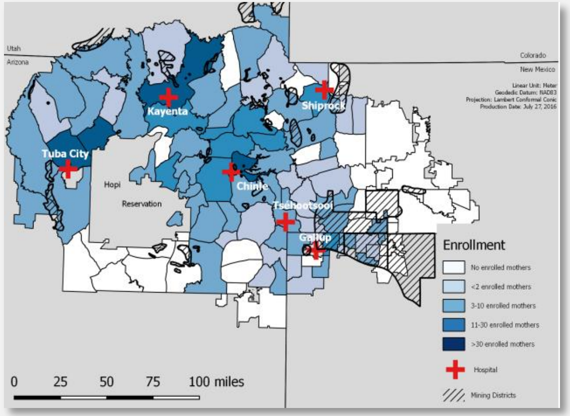
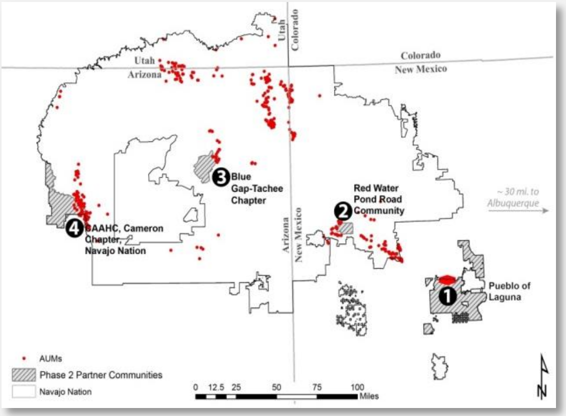
Major Community-Partnered Environmental Health Research Studies of the UNM Community Environmental Health Program (J. Lewis, director) and Southwest Research and Information Center (C. Shuey)

DiNEH Project (RO1) (2001 – 2012)	First research to examine community impacts on health in partnership with and at request of 20 chapters in and adjacent to Eastern Agency of Navajo Nation (NIEHS)
NBCS & NBCS/ECHO (2010 – ongoing)	Responsive to congressional mandate to community concerns from DiNEH Project: "What is exposure doing to the health of future generations?" (CDC, NIH-OD)
Center for Native Environmental Health Research Equity (2015 – ongoing)	Comparative community partnered study with Navajo, Sioux, and Apsalóoke to examine ecosystem and health effects in tribes from distinct language groups and cultures impacted by mine waste, combined effects of microplastics and organic emissions from waste combustion. (NIEHS, USEPA, NIMHD)
UNM METALS Superfund Research and Training Center (2017-2022, 2022-2027)	Multidisciplinary and transdisciplinary team science research partnership with Navajo and Pueblo communities to examine environmental and health risks from mine waste to communities and design interventions to reduce and reverse impacts (NIEHS)

Community questions about exposures have driven UNM environmental health research







DiNEH Project, 2002-2012

- Does U in drinking water increase risk of kidney disease?
- Do multi-pathway exposures to metals in mine wastes increase risks of chronic disease?
- **Population:** 1,304 in 20 chapters; 267 in biomonitoring

Navajo Birth Cohort Study, 2010-present

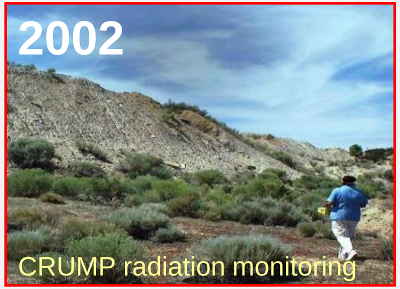
- Do exposures to U mine waste affect child health, development?
- Do exposures to metals in mine wastes increase chronic disease?
- **Population:** >1,000 families totaling ~1,800 mothers, fathers, children; ongoing

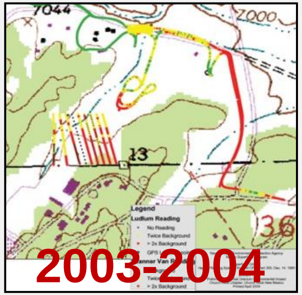
METALS SRP, 2014-present

- Do mixed-metal U mine wastes contribute to air, water and farmland contamination?
- Do exposures to U wastes result in immunologic, cardiovascular, pulmonary effects?
- **Populations:** Diné, Laguna across four communities

How have impacted tribal communities participated in EH research?

Red Water Pond Road residents played active role in CRUMP (2002-’07), DiNEH Project (2006-2007) and EPA removal actions (2007-’12)





RWPRC residents helped measure gamma radiation rates and collect soil samples around homes next to the Northeast Church Rock Mine, leading to a USEPA-mandated RSE in 2006-2007 and three removal actions (below).

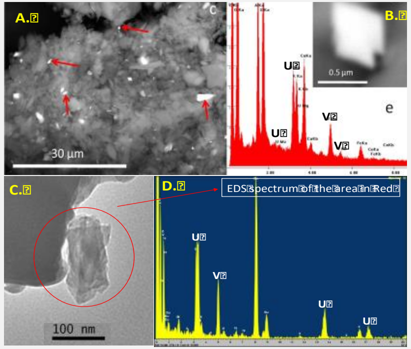
Three USEPA-ordered “interim removal actions” removed 18” to 25’ of radium- and uranium-contaminated soils (~136,000 cy) from around homes, mine-water arroyo. Residents were “relocated” to hotels in Gallup for 3 to 7 months each time.

Blue Gap-Tachee residents joined field studies on effects of exposure to mine dusts

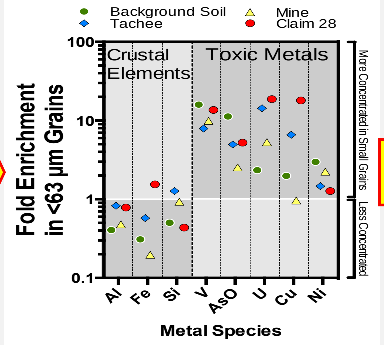
1. Some residences close to mine wastes

2. C. Nez identifies U ore, Claim 28

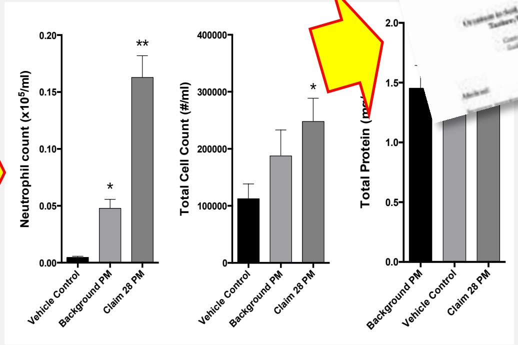
3. T. Shirley operates PM sampler



4. Microscopy identifies U-V complex (C) in sub-micron particles



5. Most toxic metals in smaller particle sizes



6. Mouse aspiration of mine-dust in solution indicate toxicity to lungs, autoimmune response

7. 2014 Metals Monograph 1; 2015 Blake ES&T paper; 2018 Zychowski SOT

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How have Diné communities participated in EH research?

Cameron residents collaborated with METALS to assess contaminants in soils, plants on farmlands near AUMS

"Crustal Average" concentrations: the "normal" amount throughout the world

Example of UNM laboratory results for soils, roots and plants collected in a uranium-mining impacted community on the Navajo Nation (2019)

Farm Soil, Roots and Plant Grab Samples: Analtyical Results Reported by UNM Center for Water and the Environment (E. El Hayek, Ph.D.), Aug. 2, 2019

Analytes

		Site 1 – Plant 1				Site 1 – Plant 2			Site 2 – Plant 3			Site 2 – Plant 4			
Element mg/kg dry weight of sample	Crustal Ave.*	Soil 0-8 (inches)	Soil 10-12 (inches)	Roots	Shoots	Soil 0-8 (inches)	Roots	Shoots	Soil 0-6 (inches)	Roots	Shoots	Soil 0-6 (inches)	Soil 6-10 (inches)	Roots	Shoots
Al	82,300	8580.5±1329	7960.8±4539	613.5±335	15±5	10851.7±1366	869.4±380	50.1±3	12391.9±2055	143.7±39	2.3±1	12215.9±1935	11086.3±439	353.3±86	-
Fe	56,300	6463.1±197	6362.7±157	286.2±201	-	7022.1±170	405.6±215	-	6873±159	41.5±15	-	6709.6±51	6959.9±205	186.4±55	-
Ca	41,500	9847.9±8549	11771.8±4506	13977.8±474	9007.8±686	10435.[illegible]±1356	14970.6±2255	76[illegible]±568	11936.6±1919	8727.5±2572	8237.1±211	13777.5±1358	13113.3±194	9348.9±2235	5364.4±196
Na	23,600	1801±171	2116.4±362	2748.5±143	6336.8±570	1837.6±296	2806.5±51	4453.5±310	1779.6±265	2915.4±247	12053.6±197	2095.4±255	2061.5±21	2841.3±822	8893.4±329
Mg	23,300	954±67	746.4±339	1214.3±192	1392.7±129	854.5±89	1373.9±239	1445.1±25	933±91	884.4±105	3252.4±75	973.4±76	938±10	1150.1±261	2088.3±84
K	20,900	4341.6±273	4874.9±276	5578.5±1306	7312.7±297	4476.2±501	4824.2±1051	3341.8±158	4444.8±502	5977±351	8422.3±211	4912.5±622	4736.2±23	2992.6±884	9676.9±372
P	1,050	268±22	283.2±3	735.5±110	1690.1±86	251.6±11	339.8±44	786.8±203	260.8±7	429.3±62	1695.5±78	296.5±19	258.8±7	331.03±86	1749.5±97
S	350	372.3±4	327.9±101.2	1551±89	4411.5±496.5	[illegible]37.9±30.5	1536±180	2441.3±6[illegible]	322.7±39	1331.6±232.6	5788.1±301.5	504.7±42	603.3±5.4	1411.2±278	4286.6±264.1
Mn	950	334.8±17	347.8±5	24.9±20	-	36[illegible]±12	40.5±25		353.4±13	-	-	345.4±4	377±10	-	-
Zn	70	25.1±1.3	28.2±1.5	-	-	31.7±0.[illegible]	-	-	35±0.8	-	-	31±0.5	32.3±1	-	-
Cr	102	6.5±0.3	6.7±0.4	-	-	6.4±0.4	[illegible]	-	7.7±0.5	-	-	7.5±0.1	7.2±0.5	-	-
Cu	60	18.4±1.5	21±1.3	-	-	24.4±0.3	[illegible]	-	30±0.5	-	-	22.1±0.6	24.2±0.9	-	-
Co	25	2.1±0.4	2.9±1.1	-	-	2.9±0.2	-	-	2.8±0.3	-	-	2.4±0.2	2.9±0.3	-	-
Cd	0.15	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Pb	14	2.8±0.8	3.7±1.6	-	-	3.6±0.9	-	-	3.4±1.2	-	-	2.1±0.8	3.2±0.9	-	-
Ni	84	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Mo	1.2	-	-	-	-	-	-	-	-	-	-	-	-	-	-
As (ICP-MS)	1.8	2.4±0.3	3.2±0.5	0.7±0.2	0.4±0.1	2.5±0.7	0.7±0.[illegible]	0.4±0.3	2.1±0.6	0.4±0.1	0.4±0.1	2.5±0.4	2.9±0.1	1.5±1.6	0.7±0.4
Sr	370	164.05±10	169±22	524.6±96	326.4±24	189.1±7	467.5±1[illegible]3	270.4±21	169.1±8.4	430.4±134	334.3±15	164.6±4	180.4±1.3	394.3±101	167.5±8
V	120	22.8±1.5	25.5±1.6	-	-	28.8±0.6	-	-	29.6±0.8	-	-	28.2±0.2	29.2±1	-	-
U (ICP-MS)	2.7	1.9±0.3	2.6±0.4	0.7±0.4	0.6±0.1	2.4±0.6	0.7±0.2	1.2±0.2	1.8±0.5	0.5±0.1	0.3±0.1	2.2±0.1	2.3±0.1	0.6±0.1	0.7±0.3

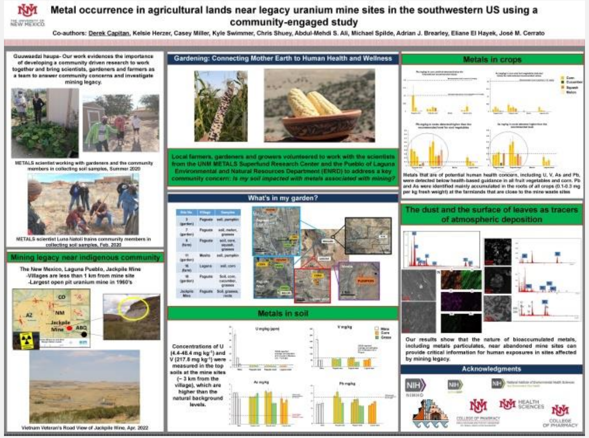
All concentrations in milligrams per kilogram dry wgt.
*Jefferson Lab 2007 reference.

Measured concentrations from ICP-OES and ICP-MS tests

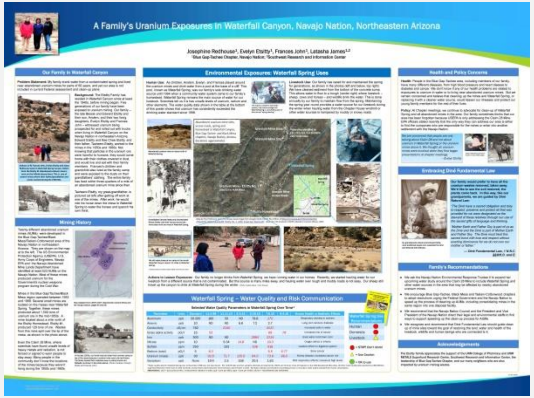
Preliminary findings: Most metals at or below crustal averages on farmlands; little uptate of toxic metals in Camelthorn; good uptake of key nutrients

Citizen and Indigenous Science: Community Action Posters Describe Impacts

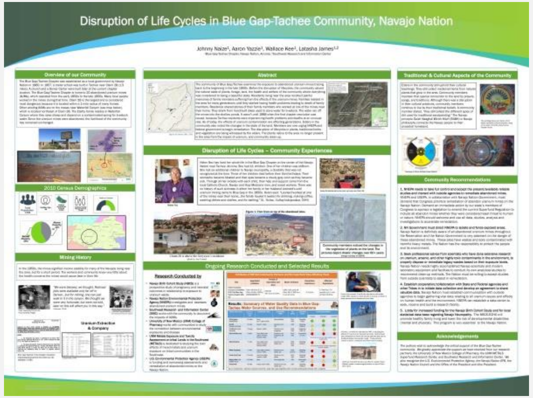
L: RWPRCA "Living with Uranium Wastes for 50 Years and Four Generations" (2018, 2020



R: Metals Assessments on Laguna Pueblo agricultural lands, 2022



A family's uranium exposures in Waterfall Spring, 2018



Blue Gap-Tachee Chapter: Disruption of Life Cycles, 2018

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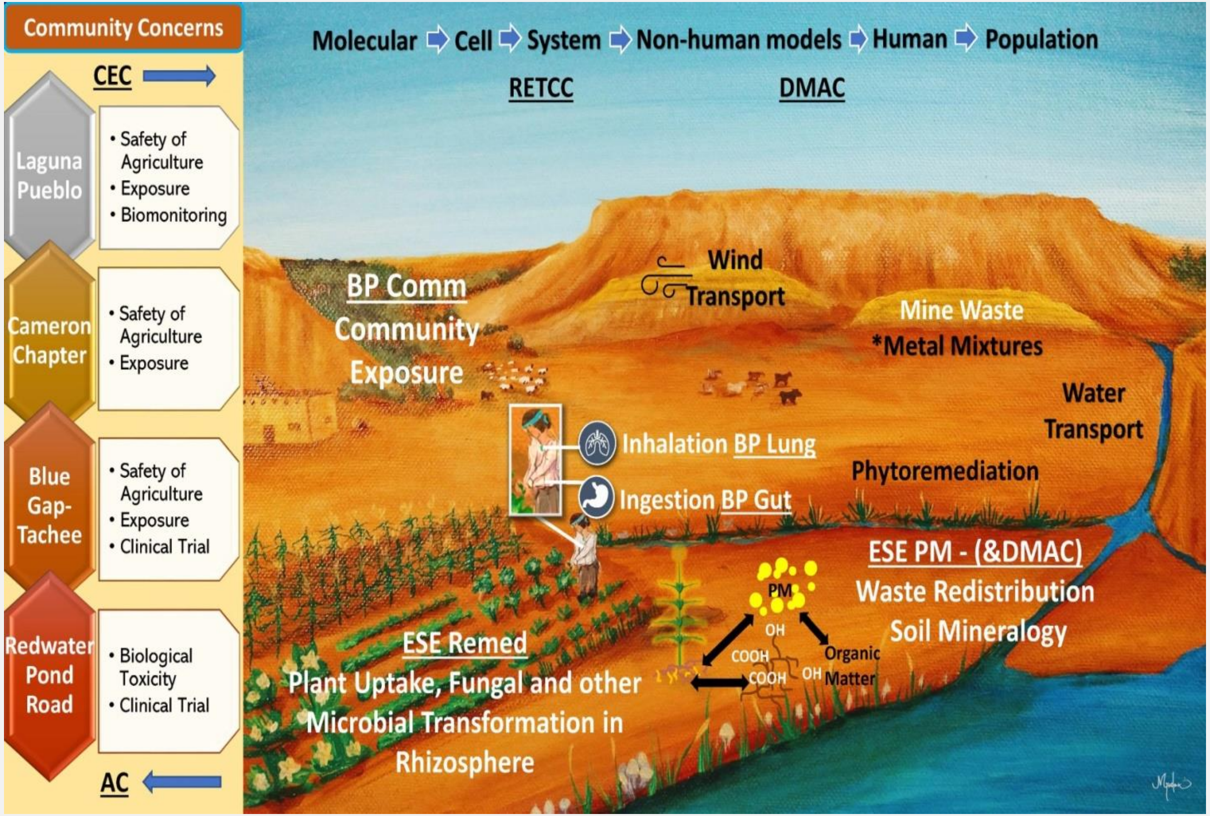
What have we learned from Community-engaged Research around uranium mining impacts?

- Community members:
  - field staff (25+)
  - study designers
  - participants in studies
  - leaders in policy initiatives
- Common toxic substances (U, V, As, Ra, Pb, etc.), common conditions across mines
- Collaborations can reduce health risks from mine wastes
- Citizen and indigenous science *is science*: validated, informed by traditional values, multidisciplinary
- Eager to engage their communities, join the next generation of scientists



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Mineralogic composition and nanoparticle matter in AUM wastes

José M. Cerrato

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Department of Civil, Construction & Environmental Engineering

October 4, 2021

Co-Authors: Melissa, Gonzales, Adrian Brearley, Joseph Galewsky, Carmen Velasco, Isabel Meza, Johanna Blake, Mehdi Ali, Sumant Avasarala, Adrian Brearley, Eliane El Hayek, Jorge Gonzalez, Juan Lezama

Funding: NIH/NIEHS P42 ES025589 (UNM METALS)

OVERARCHING QUESTIONS

- How do U and other metals occur and behave in mine waste sites?

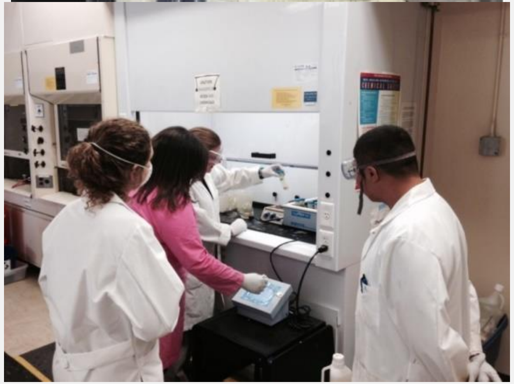
- What is the mineralogical composition and size of mine waste particles?

Funding: NIH/NIEHS P42 ES025589 (UNM METALS)

How do we answer this question? Analytical Facilities &Training

- Aqueous Chemistry Analyses:
  Inductively coupled plasma (ICP)
  a) Optical emission spectrometry (ICP-OES)
  b) Mass spectrometry (ICP-MS)
  c) Ion chromatography (IC)
- Solid Analyses

Postdoc, Graduate, Undergraduate, and High School Level Training!



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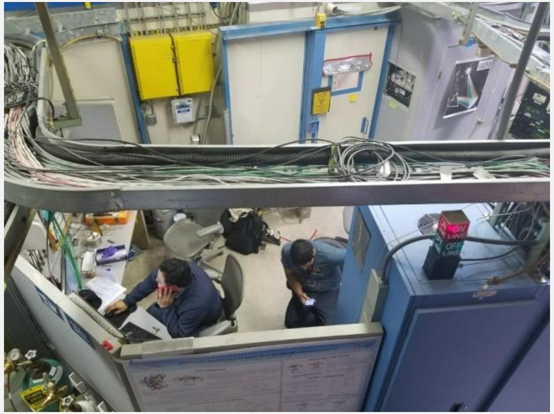
Use of Spectroscopy and Microscopy Methods



X-ray Spectroscopy

Electron Microscopy

RESULTS: Uranium, Arsenic, and pH in Water around Claim 28 Mine in Blue Gap

Sample	Parameter		
	U (µg/L)	As (µg/L)	pH
Blue Gap Tachee Spring	163.2	5.7	7.4
Blue Gap Tachee Seep	135.4	9.6	3.8
Blue Gap Tachee Well	2.1	36.7	8.7

Blake et al. 2015
Blake et al. 2019

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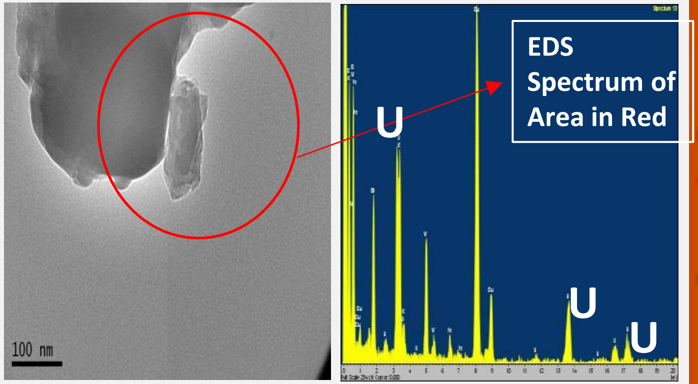
RESULTS: Solid Elemental Composition

Sample Name	Uranium (mg/kg)	Vanadium (mg/kg)	Arsenic (mg/kg)	Iron (mg/kg)
Blue Gap Tachee (Mine Waste 1)	3118	3082	30	4371
Blue Gap Tachee (Mine Waste 2)	7345	919	9	77006
BRS	BDL	BDL	BDL	24013

BRS – Baseline reference soil: control from Blue Gap Tachee (Navajo)

RESULTS

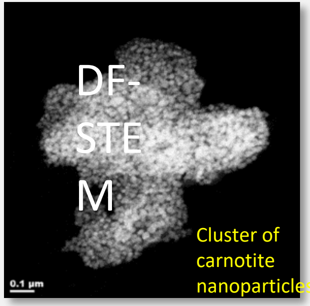
- Discovery of previously unrecognized nanoparticles of U-bearing minerals (metals mixtures) in:
  - AUM mine waste samples and associated soils.
  - Legacy accumulation of airborne dust in church attic (Laguna Pueblo).
  - Weathering products of U-bearing strata from Jackpile mine – Laguna Pueblo.
- U-V-bearing minerals in nanoparticles are exclusively in respirable PM 2.5 fraction.



- BGT mine waste samples exhibit high toxicity.

Zychowski et al. (2018) Toxicological Science.

Mine wastes



Electron microscopy shows that Blue Gap/Tachee Claim 28 mine waste contains clusters (<1 um) of carnotite ($K_2(UO_2)_2(VO_4)_2 \cdot 2H_2O$) nanoparticles that are dispersing into individual nanoparticles that adhere to surfaces of other mineral grains.

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HOW CAN YOU USE THESE FINDINGS?

- Knowledge of mineralogical composition provides insights about metal mobility for understanding risks to human health and identifying remediation strategies.
- Important to recognize exposure to hazardous metals mixtures carried by nanoparticles can occur by multiple pathways. Metals toxicity is key.
- Inhalation and ingestion of nanoparticulates are exposure pathways for humans and livestock.

Findings used to document community concerns; engage community members; bring community members into STEAM studies; apply indigenous values to air monitoring

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The role of biogeochemistry in metals bioavailability and cytotoxicity

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October 4, 2021

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Funding: NIH/NIEHS P42 ES025589 (UNM METALS)

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National Institute of Environmental Health Sciences
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OVERARCHING QUESTIONS

- **How water chemistry affects the bioavailability of metals in plants?**
- **Can fungi help enhancing metals (arsenic) uptake and bioaccumulation in plants?**
- **How cytotoxicity can change with respect to the chemical physical form of metal in the environment?**

How do we answer these questions?
Greenhouse experiments to study metals in plants

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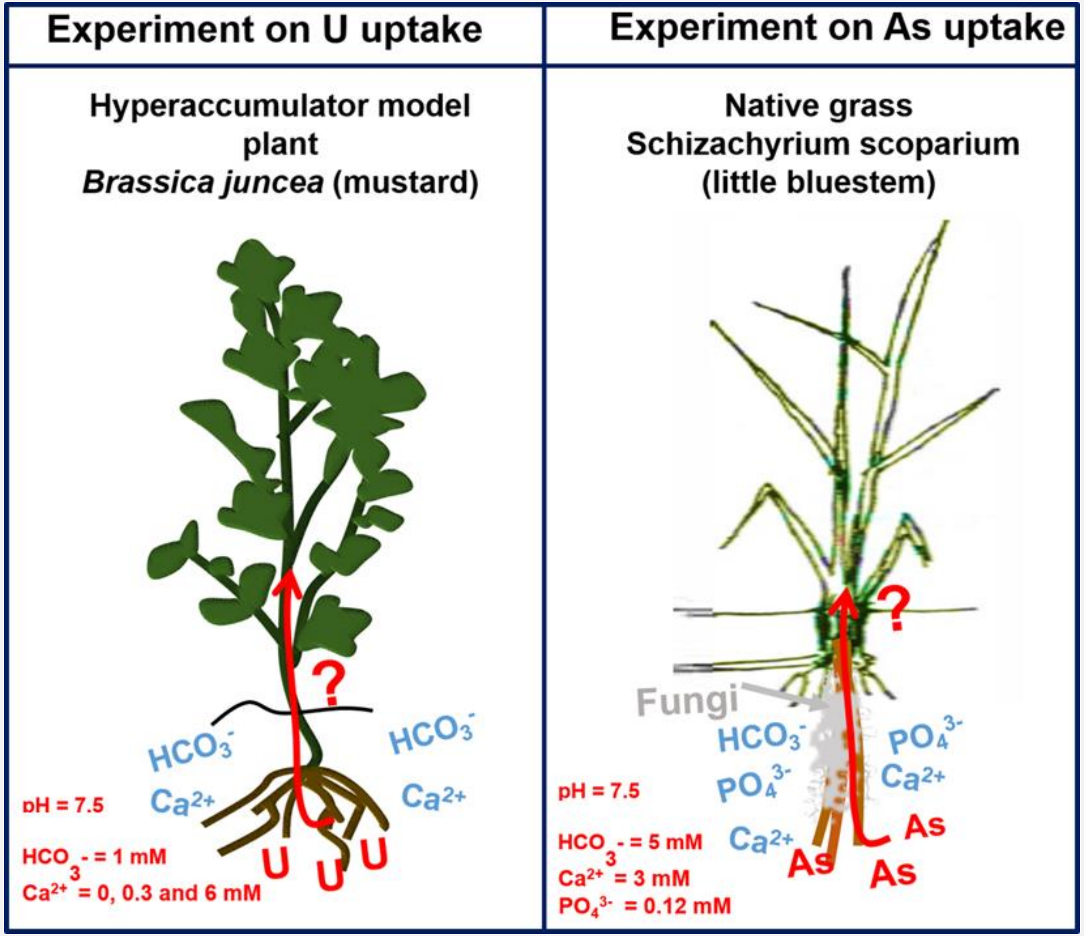
How do we answer these questions?
Greenhouse experiments to study metals in plants



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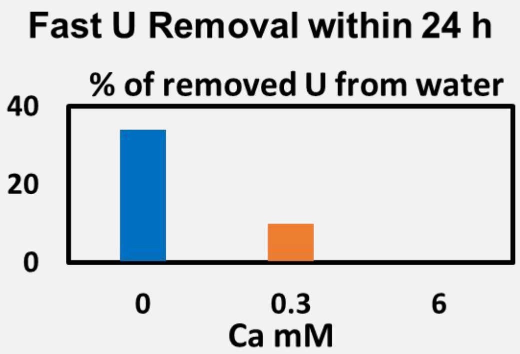
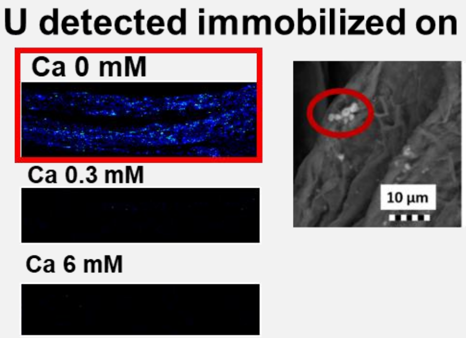
RESULTS: Water chemistry effects on U bioavailability

Plants exposed to U concentrations (30-700 µg/L) in carbonate solutions at circumneutral pH over a range of Ca concentrations:

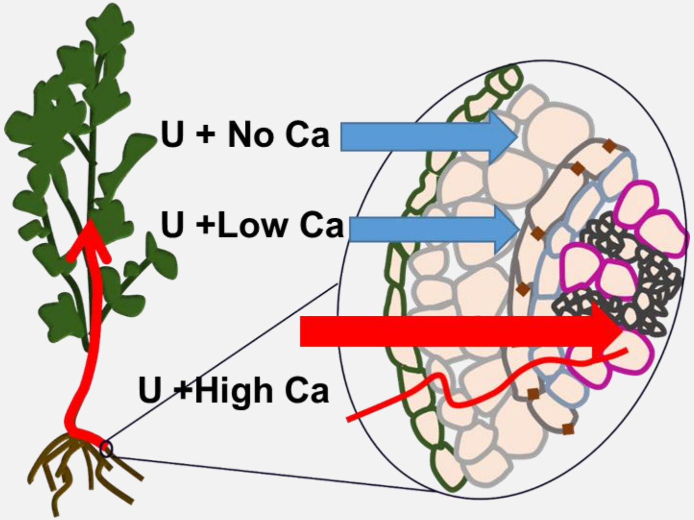




Plants exposed to high U concentrations (19.04 mg/L)

At low Ca (<0.3 mM), U can still be immobilized in the roots of the plant.

High Ca (6 mM) helps U enter deeply into root structures and go up to the stem and the leaves of the plant.



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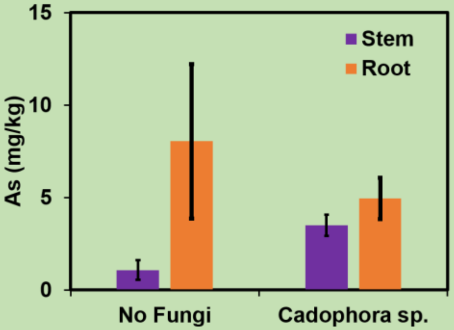
RESULTS: Water chemistry and fungi effects on As bioavailability and toxicity

Growth of plants in the presence of fungi

Plant without fungi	Plant inoculated with fungi
→	132% longer plant roots
→	71% longer plant stems
→	1800% larger plants

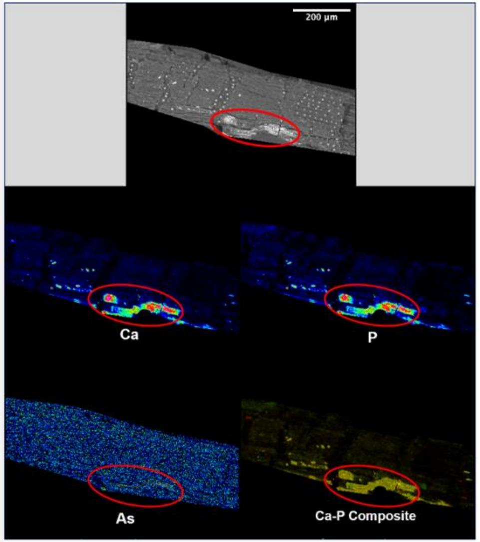
As content in the plants



Plant without fungi	Plant inoculated with fungi
→	Significant decrease in As accumulation in the roots (P<0.05)
→	Significant increase in As accumulation in the shoots (P<0.05)

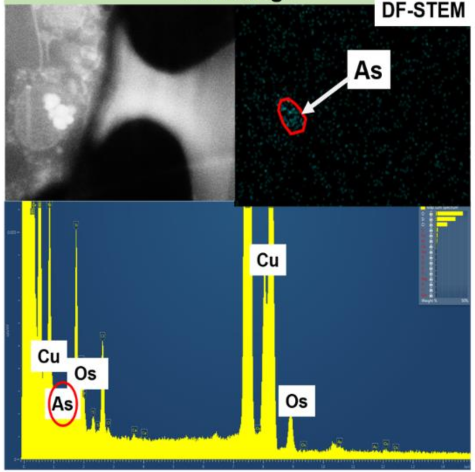
Integration of spectroscopy to identify sites of accumulation in the plant

Association Ca-P-As on root surface



Intracellular As accumulation in the presence of fungi

EDS/STEM X-Ray map of root inoculated with fungi



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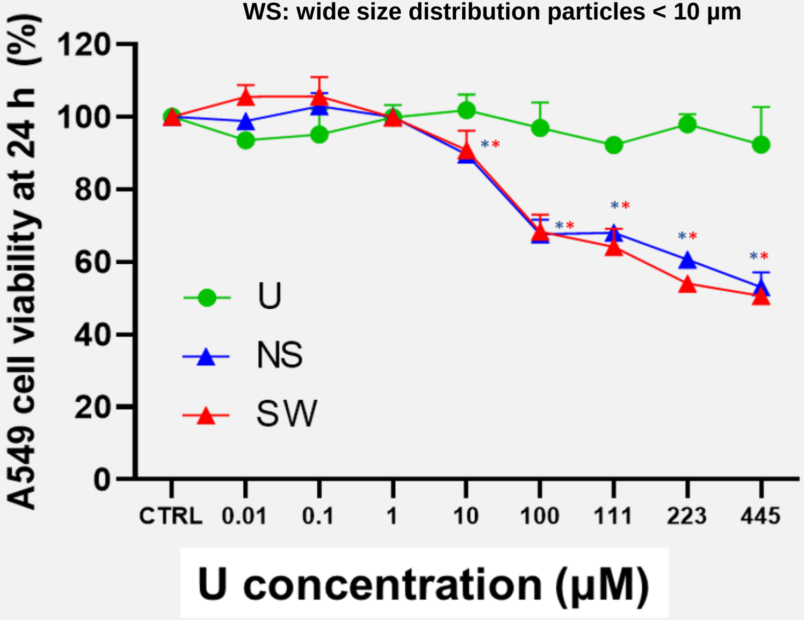
RESULTS: How the chemical physical form of metal affects its cytotoxicity?

The toxicity of Carbon-rich U-bearing particles were used as a solid particulate phase of U and compared to soluble U salts in airway epithelial cell model (A549)

U: aqueous uranium
NS: narrow size distribution particles < 1 µm
WS: wide size distribution particles < 10 µm



The particulate form of U in carbon-rich particles enhances its bioavailability and toxicity in comparison to aqueous uranium

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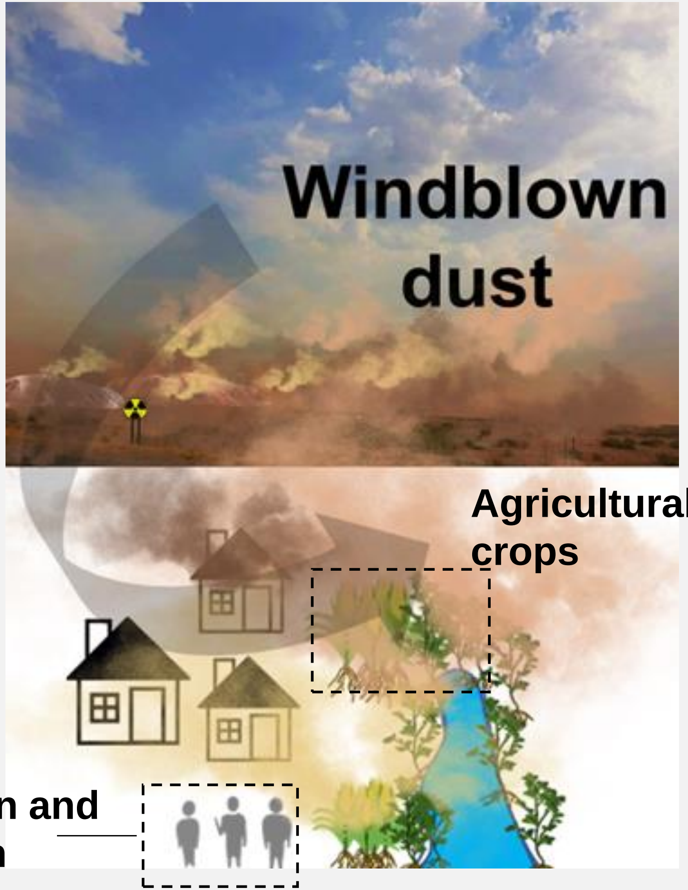
Effects of the chemical physical form of uranium on its cellular toxicity

Understanding environmental health risks needs understanding bioavailability and toxicity which depend not only on the level of metals concentration but also their chemical physical forms in their surrounding environment.



How we involved community members in the process?

Gardening: Connecting Mother Earth to Human Health and Wellness

A research partnership with gardeners and farmers on the Pueblo of Laguna to look for metals on agricultural lands near legacy uranium mine sites

What's in my garden?

Local farmers, gardeners and growers volunteered to work with the scientists from the UNM METALS Superfund Research Center and the Pueblo of Laguna Environmental and Natural Resources Department (ENRD) to address a key community concern: Is my soil impacted with metals associated with mining?

Vietnam Veteran's Road View of Jackpile Mine, Apr. 2022

METALS scientist working with the community members in collecting soil samples, Summer 2020

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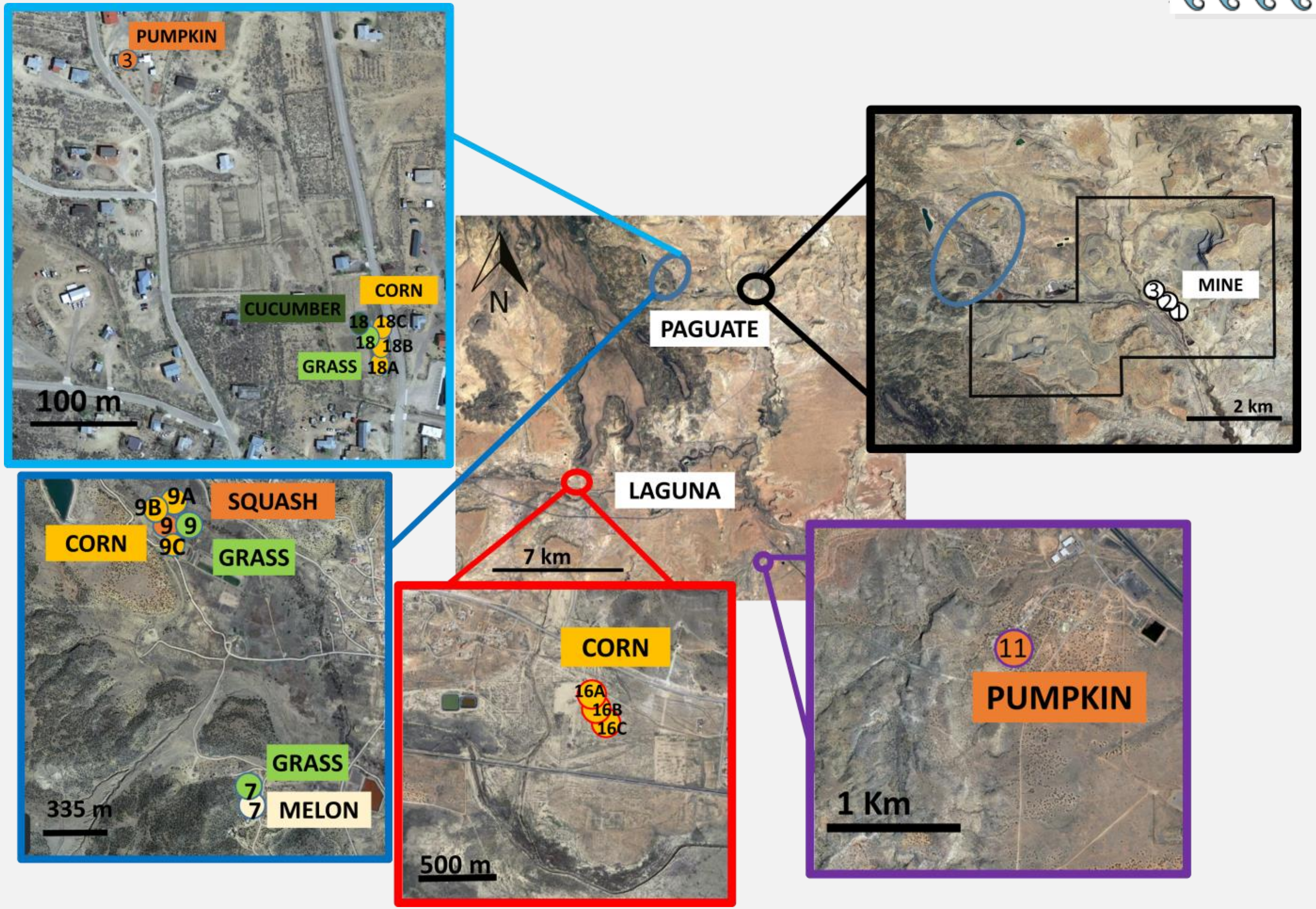
Sampling locations for data reported here

Site No.	Village	Samples
3 (garden)	Paguate	soil, pumpkin
7 (garden)	Paguate	soil, melon, grasses
9 (farm)	Paguate	soil, corn, squash, grasses
11 (garden)	Mesita	soil, pumpkin
16 (farm)	Laguna	soil, corn
18 (garden)	Paguate	Soil, corn, cucumber, grasses
Jackpile Mine	Paguate	Soil, grasses, roots



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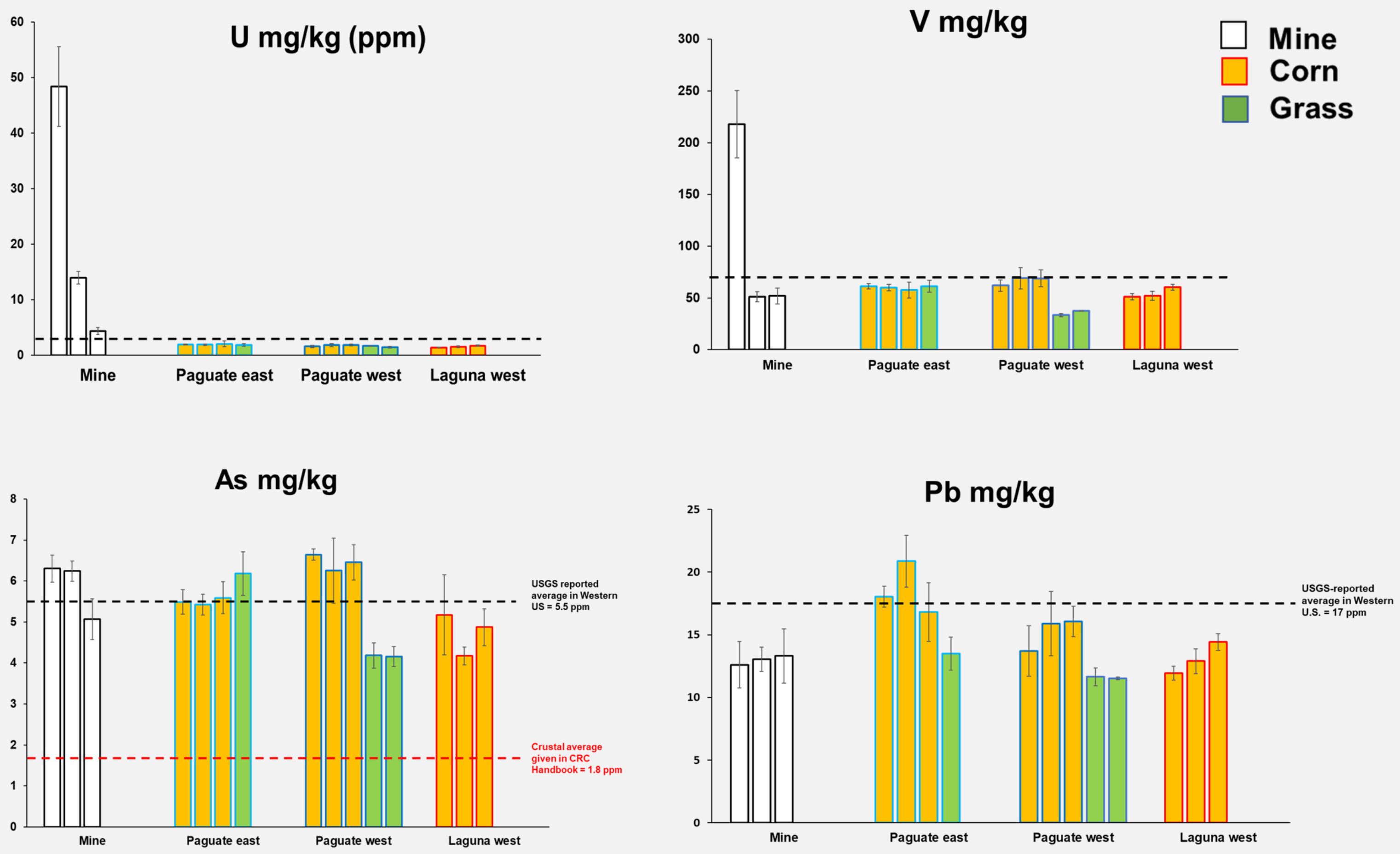
Metals in soil



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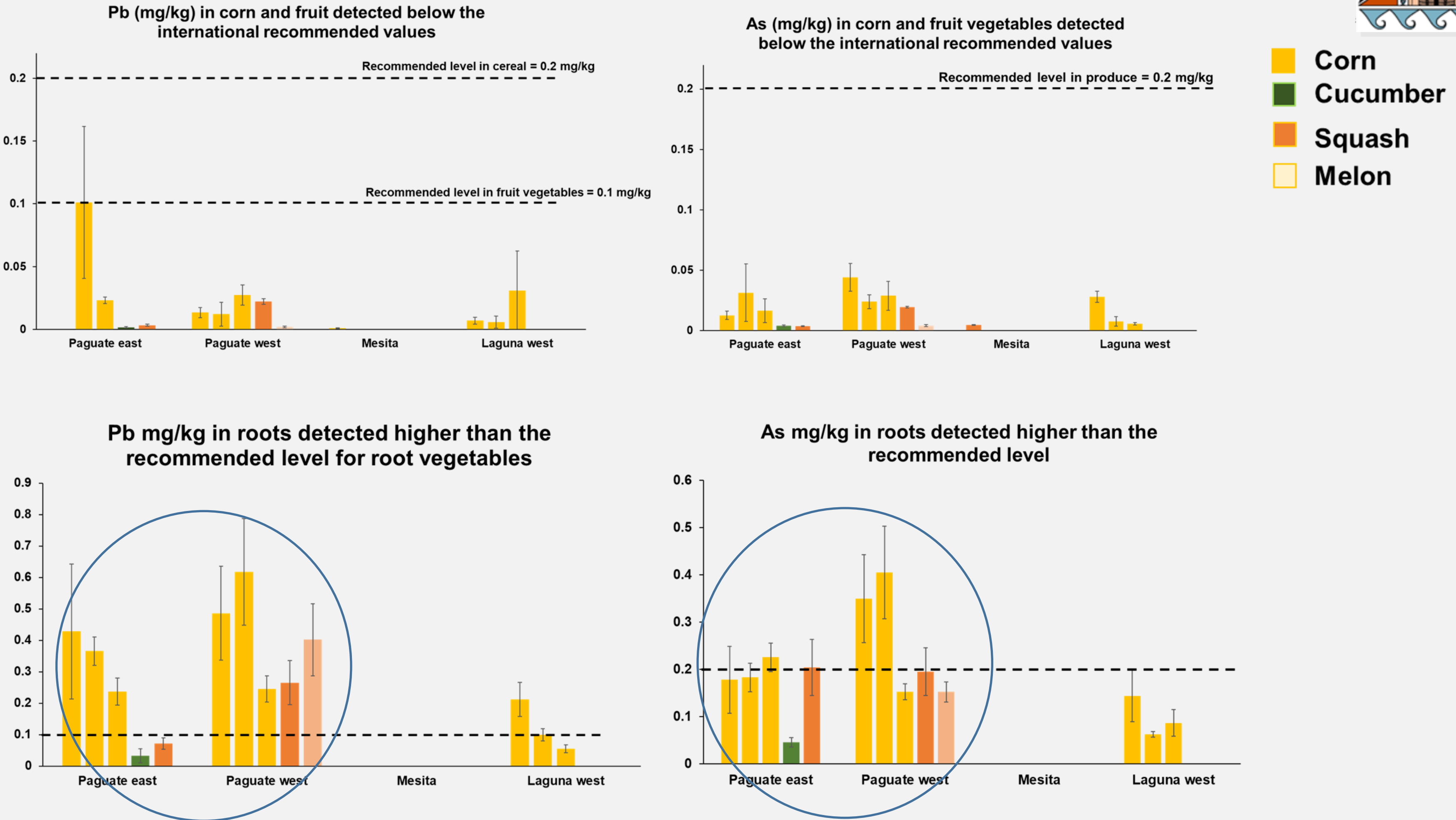
Metals in crops



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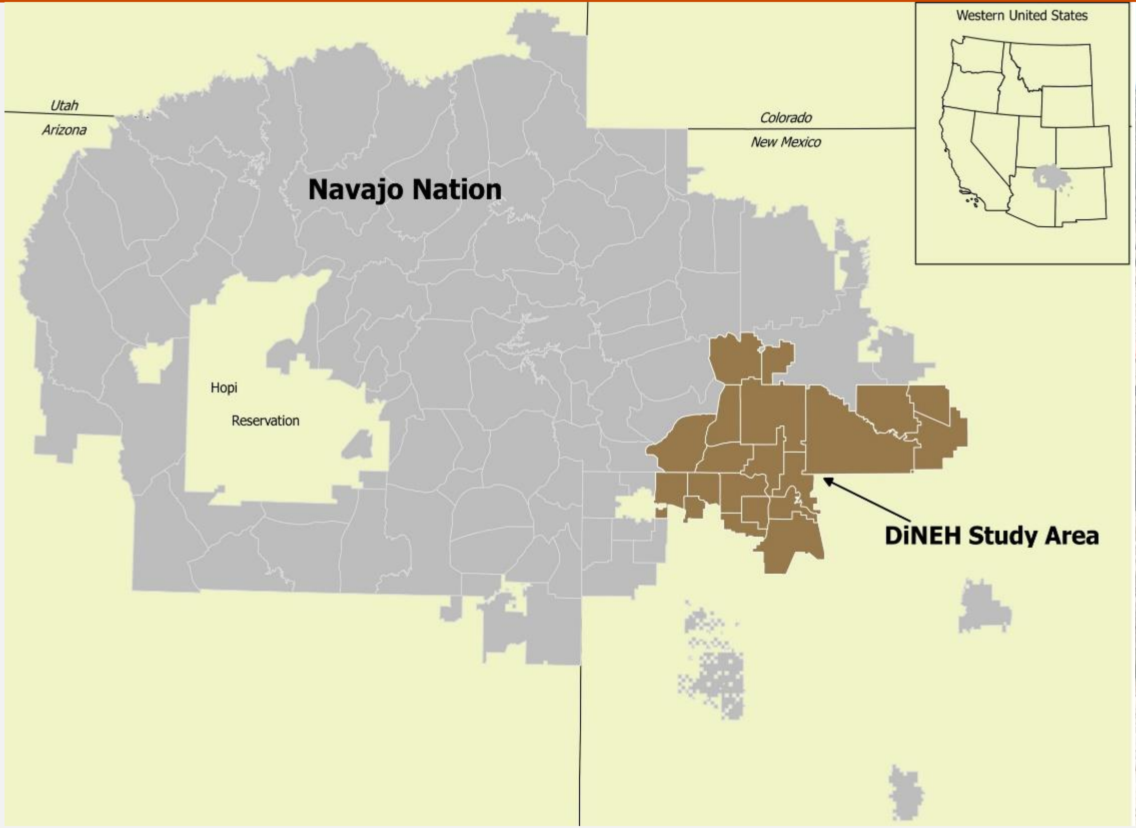
HOW CAN YOU USE THESE FINDINGS?

- **Plants a pathway of exposure but a major player in understanding environmental chemistry and creating solutions**
- **Chemical parameters in the rhizosphere can enhance or decrease metals bioavailability and plants uptake; e.g., high U and Ca levels at circumneutral pH can increase U uptake to the shoots of the plant**
- **Studying bioavailability and toxicity is important to understand environmental health risks which depend not only on the level of metals concentration, but also on their chemical physical forms in their surrounding environment.**
- **Uranium and vanadium exceeding background were found ONLY in topsoil samples collected from the Jackpile Mine.**
- **Metals that are of potential human health concern, including U, V, As and Pb, were detected below health-based guidance in all fruit, vegetables and corn.**
- **Although the impact of mining legacy was not detectable in our sampling sites, we should note that these tests are limited to a certain number of locations; further studies are needed to understand the mobility of dust around the mine site.**

Diné Network for Environmental Health (DiNEH) Project:

Documenting exposures to legacy uranium mining wastes on the Navajo Nation

Esther Erdei, Ph.D.



Call for action to protect water sources

- Violation of Human Rights (UN 1948)
- Respect toward traditional knowledge, practices; support sustainability of all interactions w/ nature & non-human life
- Water is Life movement - Water is Life Blood of Mother Nature – human body is 73% H_2O
- Lack of USEPA risk assessment methodology for Tribal use – Animas River U contamination from CO, UNM CEHP & UoA collaboration
- Rural areas reviews – own works, 2 publications (Nov 2018 & Apr 2019) in *Current Epidemiology Reviews*
- Environmental justice, environmental racism, environmental privilege

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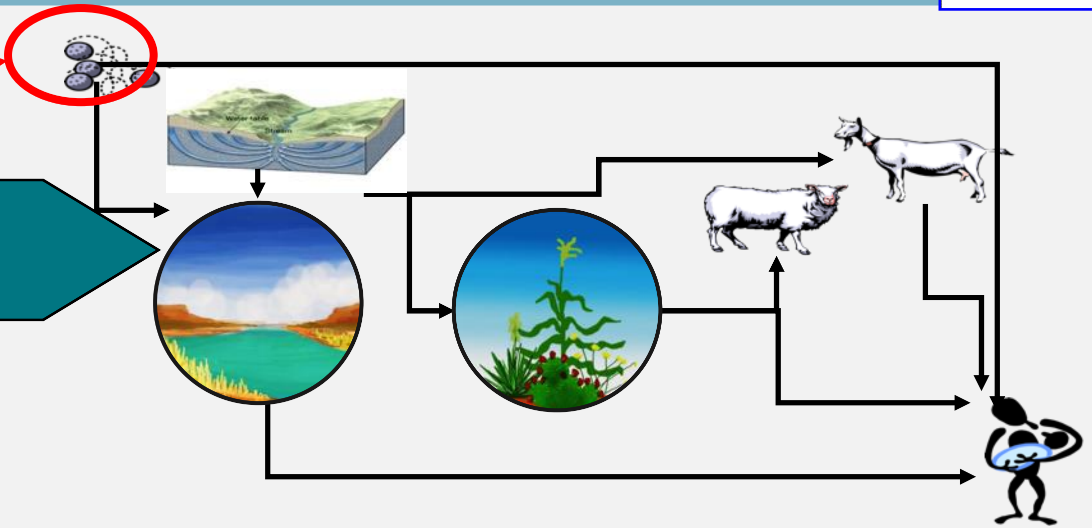
Identifying Exposures: Pathways, Routes

SOURCES: Potentially harmful contaminants in the environment



Exposure Pathways

Air, water, plants, animals

(can be very simple or quite complex)

Exposure Routes:

How contaminants enter the body

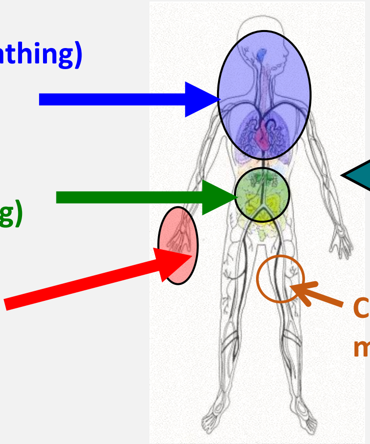
Fetal Exposure Route:

Placental transfer

Inhalation (Breathing)

Ingestion (Eating, Drinking)

Absorption (Skin Contact)



Circulation: mother→placenta→baby

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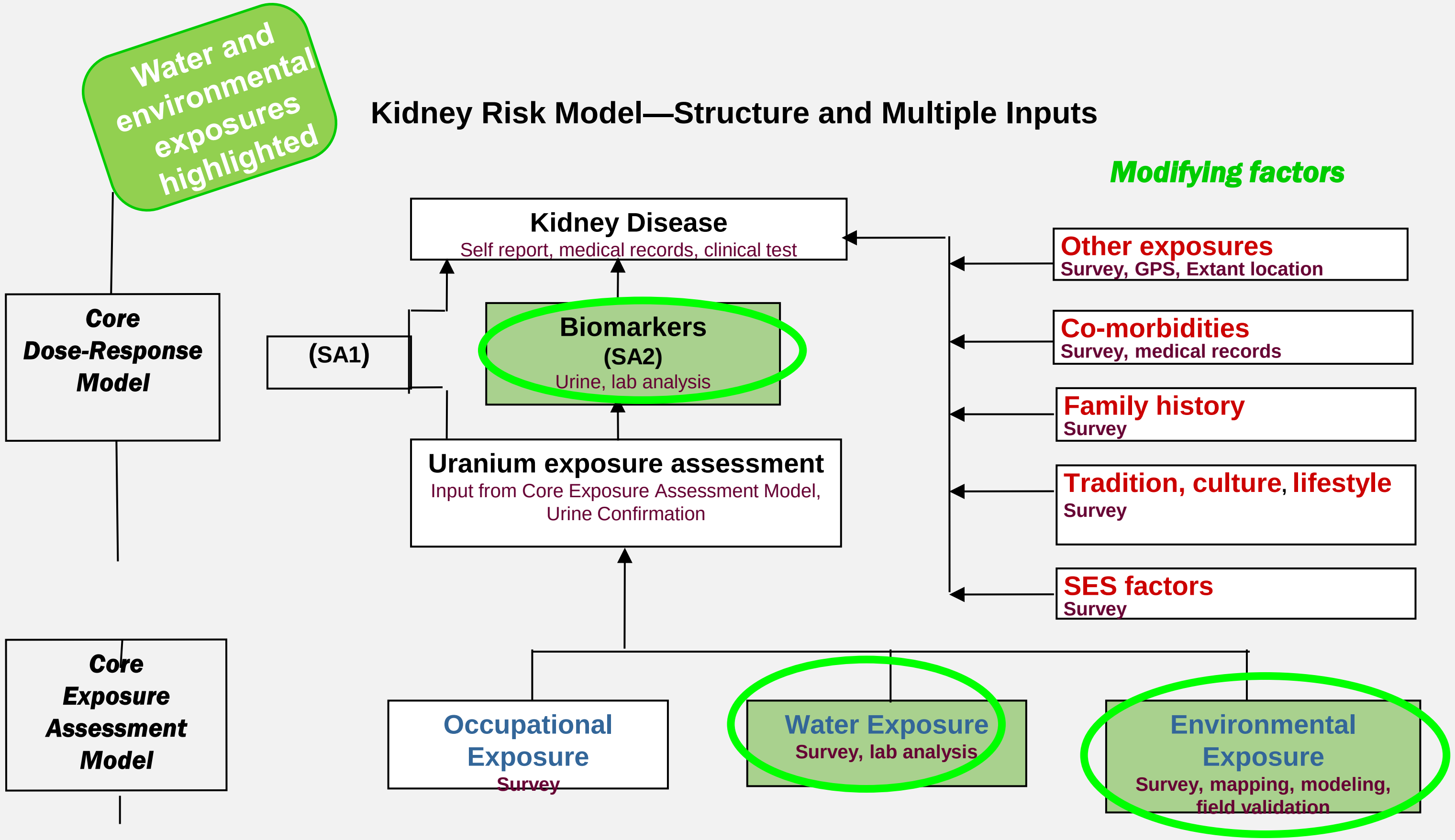
DiNEH Project Risk Model

Sources of inputs to estimate each participant's total exposure



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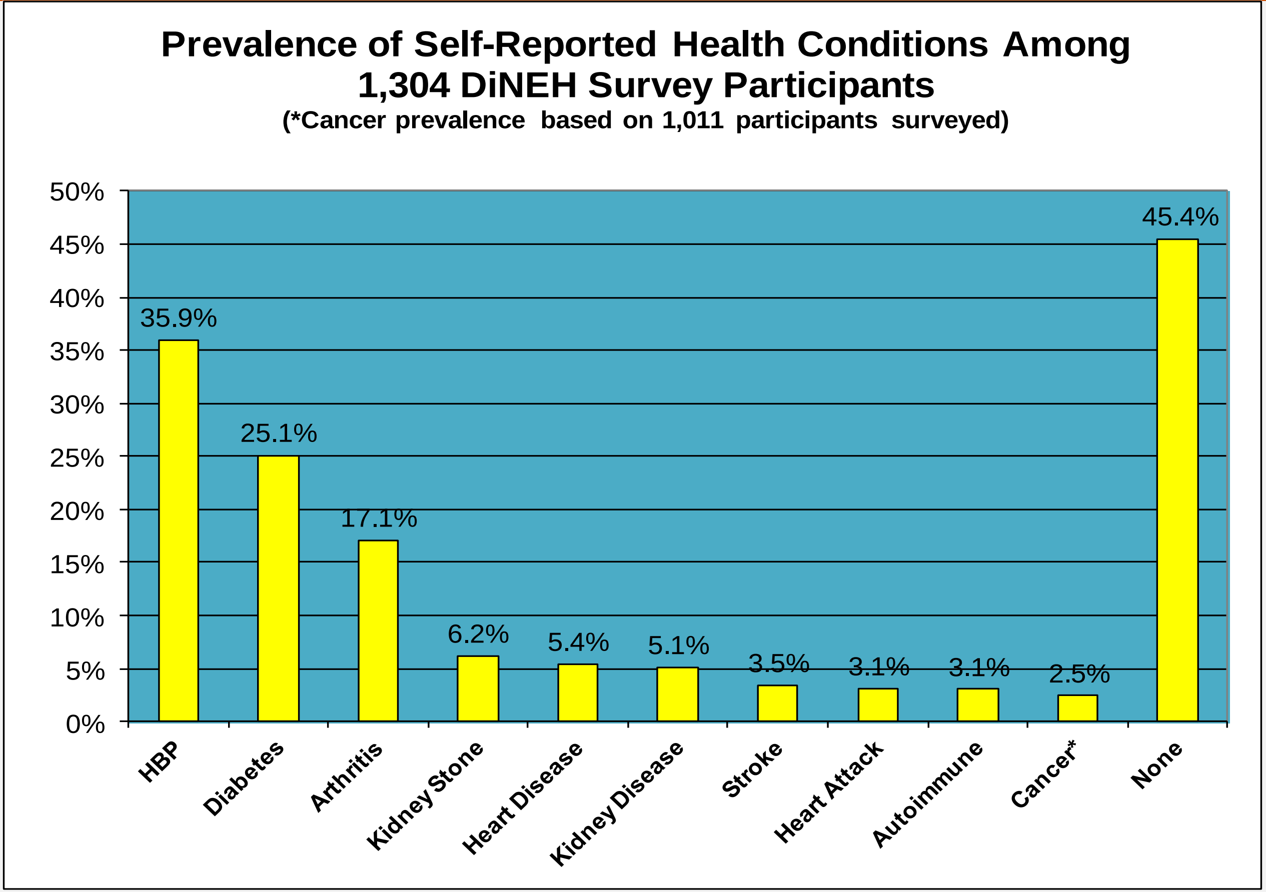
DiNEH Survey Responses – Phase I



- High prevalence of cardiovascular disease and diabetes in DiNEH participants
- Do chronic exposures to U mine wastes exacerbate existing disparities in metabolic diseases?

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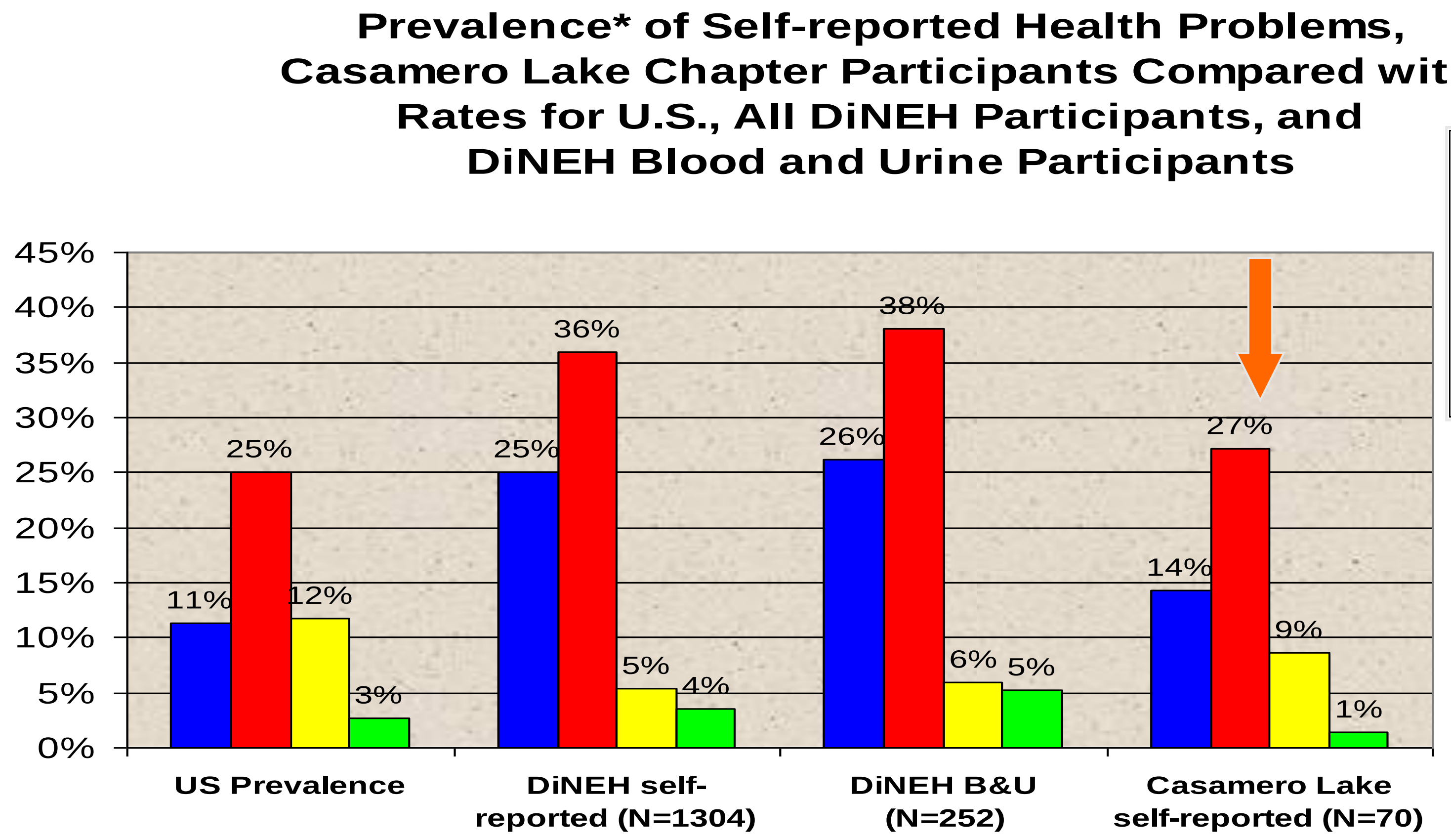
DiNEH Survey Results for Casamero Lake Chapter:
Health Problems



For further comparison: Navajo diabetes prevalence, 1991-1993 = 22% (all ages), 40% (≥ 40 yrs) (Navajo Nutrition Study, 1997).

*Prevalence = percentage of the population having a particular disease or condition at any given time

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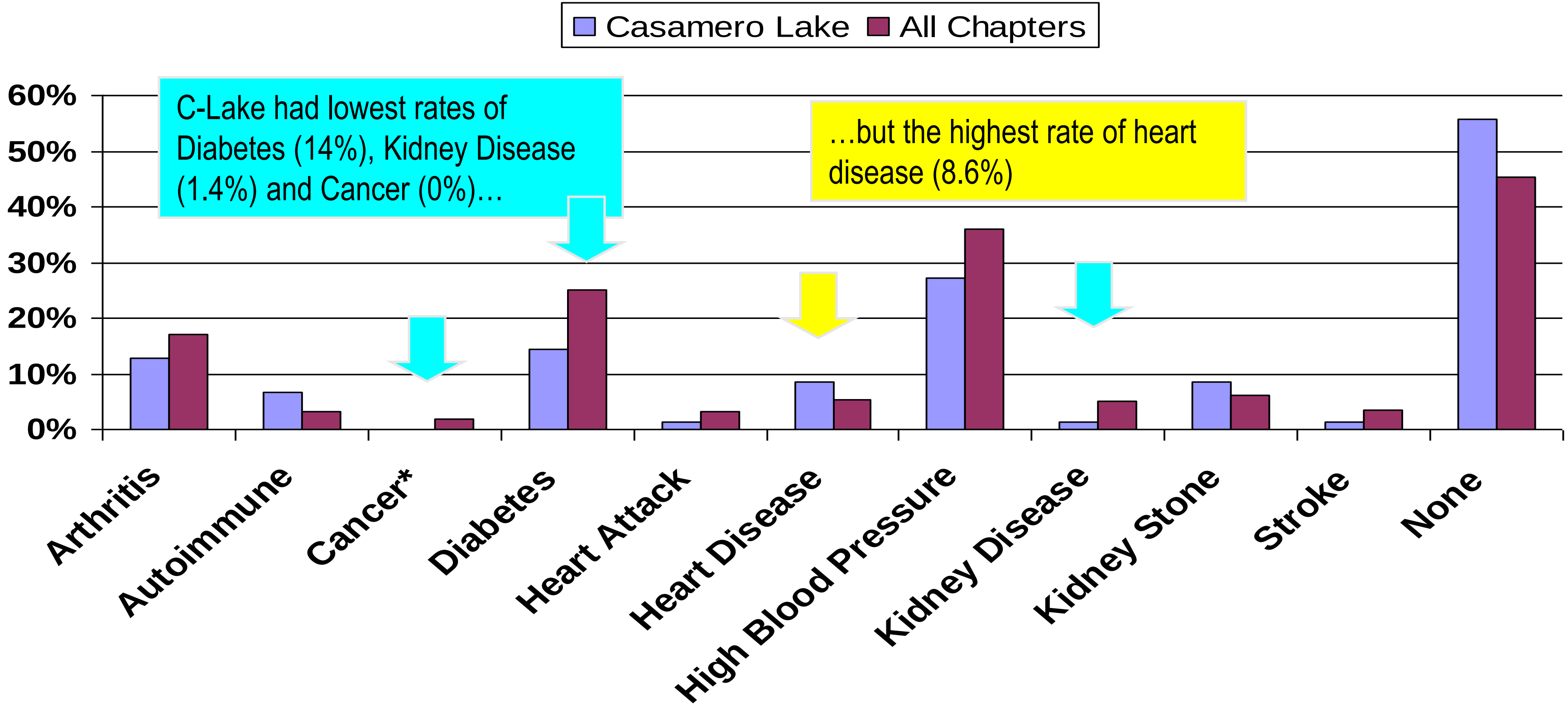
All Health Problems Reported by Casamero Lake Residents v. All Chapters



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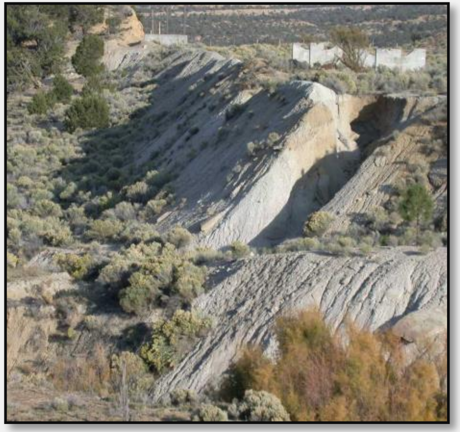
Goal of the DiNEH Phase II sub-study

- Direct response to community members' requests for research on immune system function during the capacity building and environmental risk evaluation work
- Address possible pathways within the human body in association with environmental uranium and other heavy metal (V, Pb, Hg, Ni, Cu, and As) exposures
- Find early indicators of health effects from legacy exposures



DiNEH Project Phase II
Biological sample collection

- Samples collected from 267 individuals, evenly distributed across 20 chapters (chart)
- 14 community-based collection events
- IHS collaboration through CUE-JTH Program
- Early markers, showing alterations in immune cell distribution and activity
- Biomonitoring to determine urinary metals/metalloids – U, total As, Ni, Cu, V

Chapter	# DiNEH Survey Participants (1,304)	# DiNEH Participants in B&U Collections (267)
Baca-Prewitt	96	32
Becenti	60	22
Casamero Lake	70	14
Church Rock	69	13
Coyote Canyon	65	18
Crownpoint	71	20
Iyanbito	**61**	**17**
Lake Valley	61	9
Littlewater	65	11
Mariano Lake	69	19
Nahodishgish	60	15
Ojo Encino	65	2
Pinedale	64	5
Pueblo Pintado	65	9
Smith Lake	69	19
Standing Rock	72	17
Thoreau	66	18
Torreon	67	0
White Rock	26	1
Whitehorse Lake	63	6

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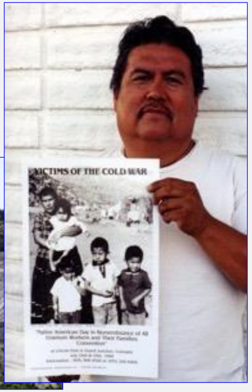
DINEH PROJECT RESULTS
(AVERAGE AGE 55)

ACTIVE-MINING ERA EXPOSURES (WORKERS* AND FAMILIES) → INCREASED KIDNEY DISEASE, ADD TO OTHER KNOWN RISKS

* *Many workers had already died from lung cancer, more family members than workers*










ONGOING ENVIRONMENTAL LEGACY EXPOSURES → INCREASED RISK FOR HYPERTENSION, AUTOIMMUNITY, AND MULTIPLE CHRONIC DISEASES

Based on proximity to waste and self-reported activities creating contact with waste

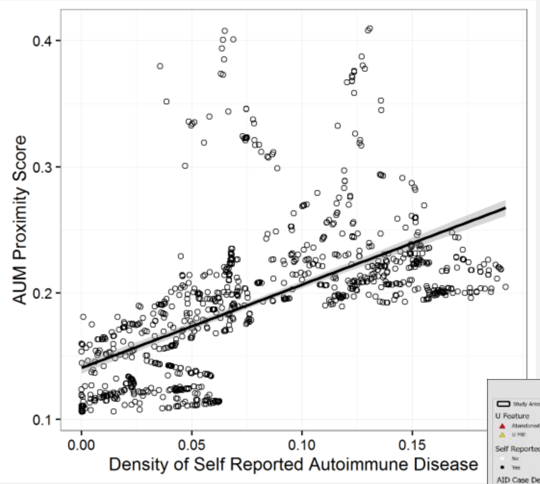
Autoimmunity also linked to uranium in drinking water

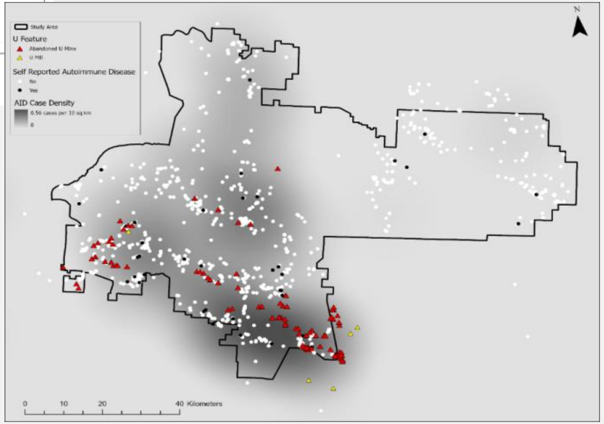
Hund et al., 2015, Journal of Royal Statistical Society, Series A, Statistics in Society

Erdei et al., 2019, Journal of Autoimmunity

Evidence of immune dysregulation in Diné adults – uranium associated increase in autoantibodies

- Self-reported autoimmune disease diagnosis -- associated with proximity to AUM (n=1,304).
- Prevalence = 3.1% in both phases, lower than published national rates (3.0%-7.5%)
- Aggregation of AID cases – increased in Chapter with abandoned U mines/milling sites (map)





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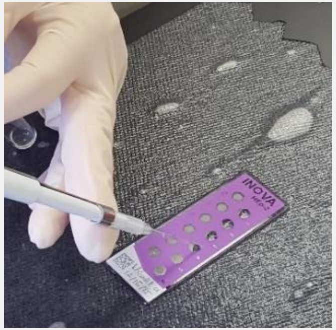
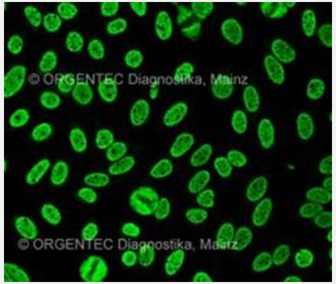
Autoantibody production and detection

- 239 samples analyzed at IHS LabCorp in Phoenix, AZ
  - (CLIA certified clinical diagnostic laboratory)
- Antinuclear antibody (ANA) testing using flow cytometry-based microbead assay
- Fluorescence staining and microscopy (traditional method; figure, top right) vs. new faster technique by IHS LabCorp
- Microbeads – special panel of autoantigens tested; positive response to specific autoantibodies may indicate connective tissue disease, Sjögren's syndrome, all clinically relevant.
- ~27.2% of individuals (n=239; average age 55 ± 14 yrs) had detectable anti-nuclear antibodies
- ANA positivity associated with proximity to waste sites, certain metals in drinking water





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Disruption of immune function → autoantibodies seen through the lens of a Native artist

Healthy immune cell – protections in place

Immune cell dysfunction – protections fighting each other

Paintings by Mallery Quetawki, Zuni Pueblo

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Navajo Birth Cohort Study initiated in 2010 to address the impacts of uranium exposure on child health outcomes

Birth Outcomes, Child Development

- **Home Environmental Assessment**
  - **Locations of nearly 600 homes**
  - **Indoor dust**
  - Radon
  - Gamma survey indoors and outdoors
  - **Drinking water**
- **Enrollment Survey**
  - Occupational history
  - Activity Survey
  - Family history of exposures
- **Biomonitoring (mom, baby)**
  - **Urine metals (36-element panel)**
  - **Whole blood (Pb, Cd, total Hg)**
  - **Serum (Cu, Se, Zn)**

Assess birth outcomes and child development from birth to age 9.

NBCS→ECHO+

NBCS (2010-2018)

Enrolled 780 women during pregnancy, exposure assessment, assessment of child development through 1 year of age

NBCS/ECHO

Enrolled 481 (179 pregnant mothers and 302 children from NBCS

NBCS-ECHO Plus – 2019-2024

- Continue enrollment to 1200 (345 children and 60 new pregnant mothers)
- Add common elements developed by ECHO consortium (allows us to compare exposures/outcomes with national sample
- Assessment continues through the age of 9

ECHO (Environmental influences on Child Health Outcomes) Funded by NIH Office of the Director

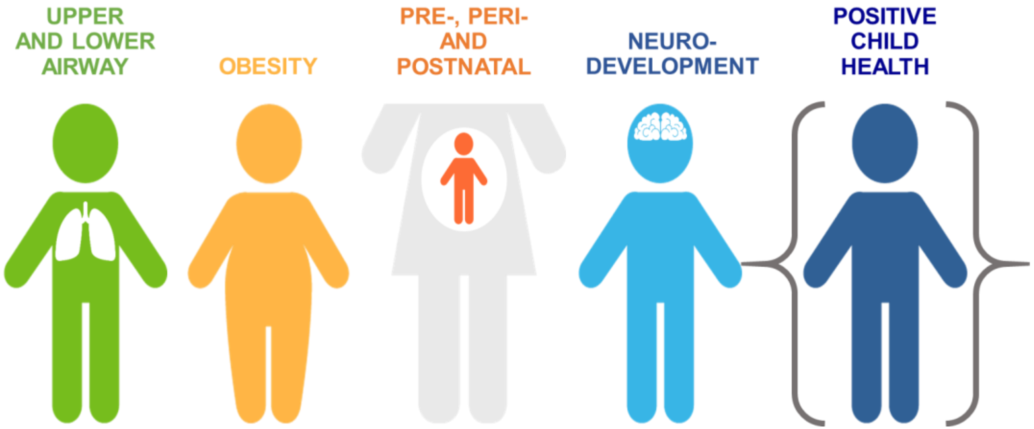
MISSION:
To enhance the health of children for generations to come

VISION:
To become one of our nation's pre-eminent research programs in child health

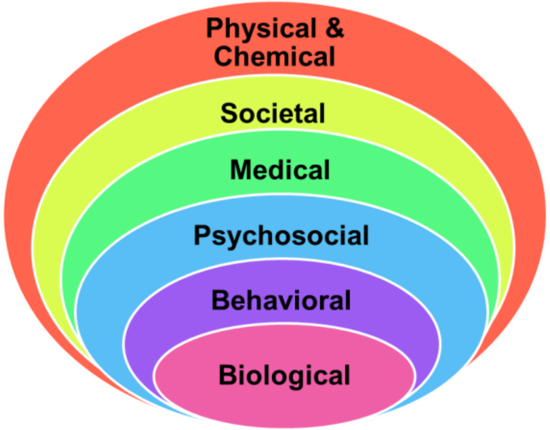
LONG-TERM GOALS:
Scientific: To inform high-impact programs, policies, and practices that improve child health

Strategic: To establish best practices for how to conduct Team Science in the 21st century

Focus on key pediatric outcomes



Data Collection



Pregnancy
- Surveys and questionnaires
- Blood and urine for metals

At delivery:
- Collect blood and urine for metals

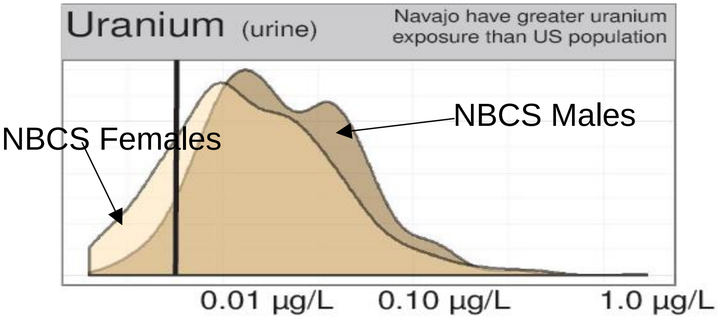
From birth through 9 years of age:
- Collect data from surveys and questionnaires
- Collect biospecimens every year
- Annual ASQ assessment
- Between the ages of 3-5 and again between the ages of 6-8 we conduct physical and neurodevelopmental assessments.

Art by Mallery Quetawki

Exposures seen from biomonitoring of key metals

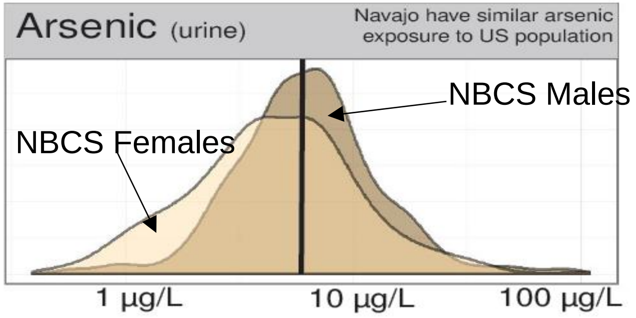
Uranium (kidney toxicity; estrogen mimicker)

- Black vertical line represents the 50th percentile for US population
- NBCS median urinary uranium concentrations exceed the US median (36% of men and 26% of women have urine uranium above national norms

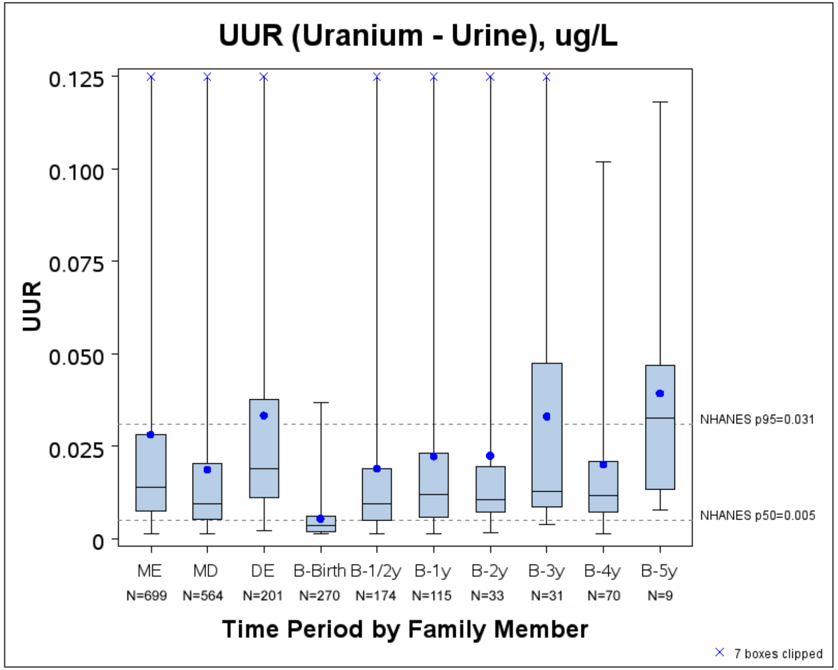


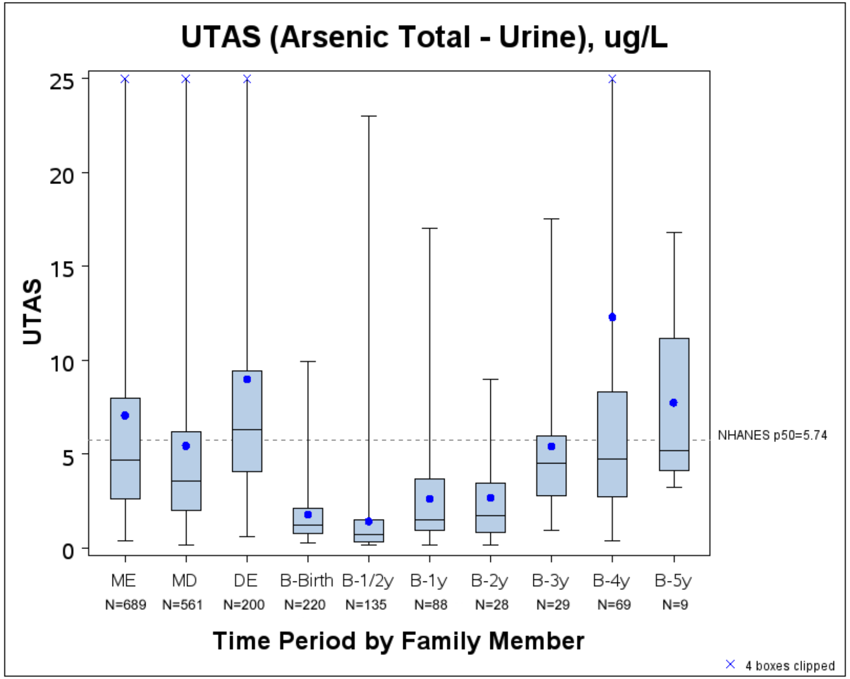
Arsenic (cancer, immunotoxicity)

- Distribution of urine total arsenic in NBCS females and males
- NBCS median urinary total arsenic concentrations are similar to the US median
- Exposure sources very different – in US, population exposures primarily seafood, rice



NBCS/ECHO: Exposures begin in childhood
By age 4, children are reaching adult concentrations



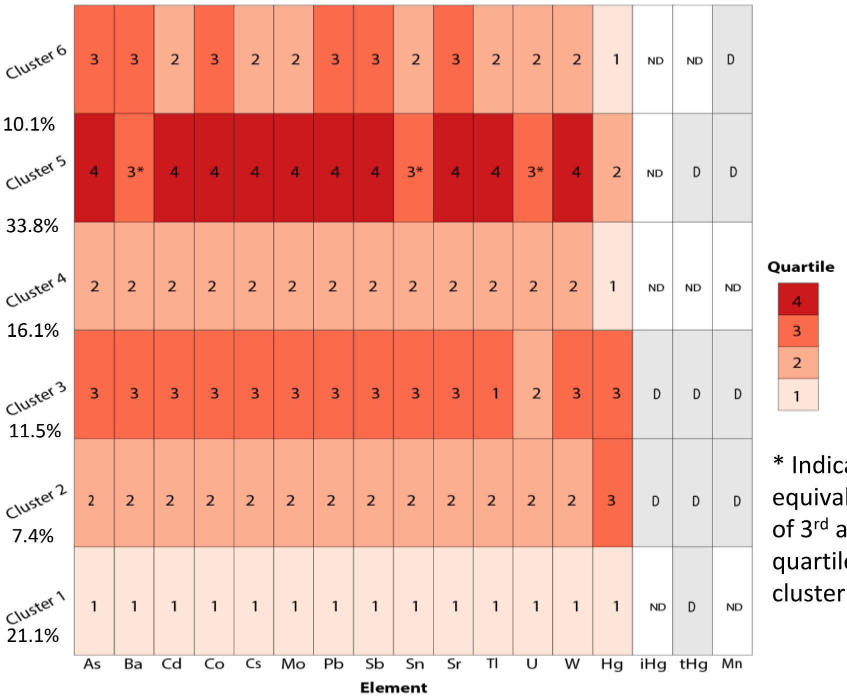


- Median concentration for urine uranium in the US ***adult*** population from NHANES (2015-16) = (0.005 µg/L)
- NBCS children birth to age 4 = 0.0035 – 0.013 µg/L

- Median concentration for total arsenic in urine in the US ***adult*** population from NHANES (2015-16) = (5.41 µg/L)
- NBCS children birth to age 4 = 1.2 – 4.5 µg/L

Exposures reflect patterns of mixtures

- More than 20% of moms have low exposures
- Overall rate of preterm birth in cohort 7%
- ~45% have mixture exposures that create a 3-fold greater risk of preterm birth (clusters 5 & 6)
- Mercury modulates the risk downward-indicates complexity of metals toxicity and mixed metals effects



* Indicates equivalence of 3rd and 4th quartiles in cluster

Summary of mean posterior probability from the fully adjusted model and relative risk of preterm birth by exposure cluster					
Exposure Cluster	**Group Size (N)**	**Empirical Probability**	**Mean Posterior Probability (95% CI)**	**Relative Risk (95% CI)**	**Probability EC_i>EC1**
1	88	0.034	0.045 (0.018-0.081)	*Reference Group*	*Reference Group*
2	31	0.032	0.049 (0.012-0.109)	1.362 (0.25-3.638)	50.46
3	48	0.042	0.059 (0.023-0.108)	1.647 (0.44-3.936)	65.97
4	67	0.090	0.093 (0.049-0.148)	2.587 (0.9-5.678)	92.57
5	141	0.092	0.097 (0.065-0.134)	2.706 (1.059-5.768)	96.26
6	42	0.119	0.117 (0.058-0.19)	3.295 (1.046-7.437)	95.74
*Posterior probability >0.95 that EC is above 1 compared to reference cluster (EC2).					

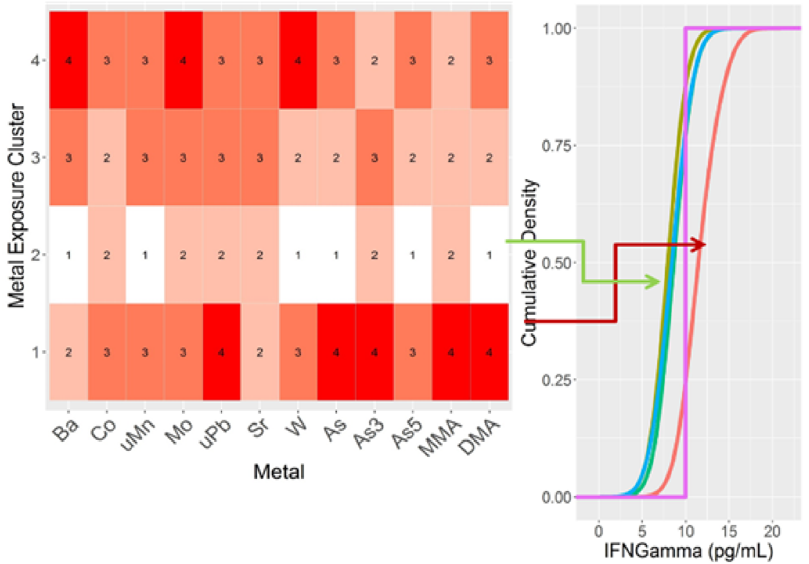
Potential immune dysregulation associated with metals

Table 4. Significant Associations of Cytokines with Metals in the NBCS

Cytokine	Univariable model	Multivariable model
IFNα	tAs↑, DMA↑, MMA↑	DMA↑
IFNγ	Hg↑	Hg↑
IL-4	AsIII↓	AsIII↓
IL-7	Mn↓	Mn↑, MMA↓
IL-17A	U↑, Mn↑, AsIII↓	U↑, Mn↑, AsIII↓
IL-29	Mn↑, AsIII↓, DMA↓, MMA↓	Mn↑, AsIII↓, MMA↓

[1] Significant (p<0.10) association with metal. [2] Significant metal predictors after variable selection. All metals were measured in urine. tAs=total arsenic; MMA and DMA are mono and dimethylated metabolites of As, respectively; Hg=mercury; AsIII=arsenite; Mn=manganese, U=uranium. Directionality: positive ↑; negative↓ N=200

Inflammatory marker levels vary by metal exposure clusters



Jennifer Ong PhD (dissertation)
Debra MacKenzie
Li Luo

Detailed Neurodevelopmental Assessments (between ages of 3-5 and again at 7-8)

Domain	Measure
Cognitive	DAS-II
Language	OWLS-2
Adaptive skills	Vineland
Social-Emotional	CBCL, SRS-2 (questionnaires)
Behavioral Observation	TOF, CARS-2
Medical	Medical and Developmental History, Physical Exam
Social cognitive functioning	Eye tracking measure

ND Assessment Summary

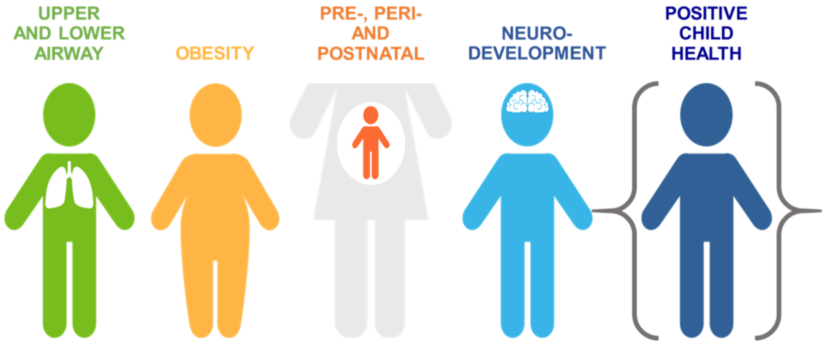
- Navajo preschoolers performed within the average ranges across multiple direct assessments and parent-report measures, except on the verbal domains across both modalities.

- High prevalence of language disorder independent of intellectual disability, general developmental delay, and autism spectrum disorder (validity of test instrument?, other reasons?)

- **See Posters Nozadi, Lecke, Wegele, Rennie for NBCS related work**

Outcomes of NBCS/ECHO Study

- Assess the relationship between exposures to environmental contaminants (metals, others) with ND trajectories and other health outcomes.
- Compare NBCS to national sample of over 50,000 children to increase our power to identify impacts of environmental exposures on child health as well as increasing our understanding of the influence of early life environmental exposures on health trajectory of Navajo children.



The Navajo Birth Cohort Study - **NIH OD UH3OD023344 and CDC U01 TS 000135.**

The presented data are solely the responsibility of the authors and do not necessarily represent the official views of the NIH, Centers for Disease Control and Prevention, or the Department of Health and Human Services.

NBCS Navajo Birth Cohort Study

ECHO Environmental influences on Child Health Outcomes
A program supported by the NIH

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Myra Francisco
Lisa Kear
Della Reese
Johnna Rogers, RN
Diedra Sam
Charlotte Swindal, CNM, RN
Marcia Tapaha

Navajo Team Members
Other Native Team Members
Bold indicates Current Team
Non-bold are former team members

The people of the Navajo Nation:

- > 1000 participating Navajo families
- Many supporting chapters
- HEHSC, Tribal and Agency Councils, Executive Branch, NNEPA, GIB
- NAIHS & PL-638 hospital laboratory staff, leadership, and health boards

And many others who have contributed to and supported this work!

Our funders:

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Original Navajo Birth Cohort Study (2010-2018) was funded by the Centers for Disease Control and Prevention (U01 TS 000135).

Thinking Zinc: A nutritional intervention for metal toxicity

COLLEGE OF PHARMACY
METAL EXPOSURE AND TOXICITY ASSESSMENT ON TRIBAL LANDS IN THE SOUTHWEST

Debra MacKenzie, PhD and Erica Dashner-Titus, PhD

Laurie Hudson, PhD; Esther Erdei, PhD, MPH; Chris Shuey, MPH; David Begay, PhD; Sarah Henio-Adeky; Li Luo, PhD, Tamara Anderson-Daniels







Stanford University

SOUTHWEST RESEARCH AND INFORMATION CENTER

National Institute of Environmental Health Sciences
Your Environment. Your Health.



Paintings by Mallery Quetawki, Zuni Pueblo

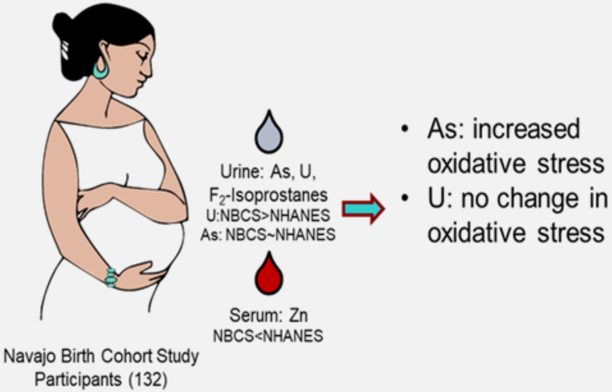
Funding: NIH/NIEHS P42 ES025589 (UNM METALS)

This material was developed in part under cited research awards to the University of New Mexico. It has not been formally reviewed by the funding agencies. The views expressed are solely those of the speakers and do not necessarily reflect those of the agencies. The funders do not endorse any products or commercial services mentioned in this presentation.

Experimental and Population Studies

As and U share mechanism of action

U less potent in tested activities



	ARSENIC	URANIUM
CYTOTOXICITY	≥ 1 µM	>>10 µM
ROS GENERATION	Sustained	Transient, < As
HO-1 induction	High	Low
PARP-1 ZF PEPTIDE	Interaction	Interaction
PARP-1 ZINC LOSS	Yes	Yes, U < As
PARP-1 INHIBITION	Yes	Yes, U < As
DNA REPAIR INHIBITION	Yes	Yes, U < As
PROTECTION BY ZINC	Yes	Yes
ZF TARGET SELECTIVITY	Yes	No

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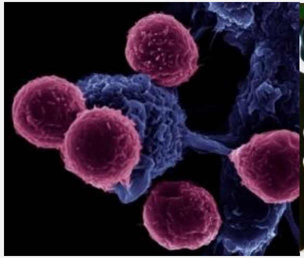
Why Zinc?

Zinc-binding proteins are regulators of cell function.

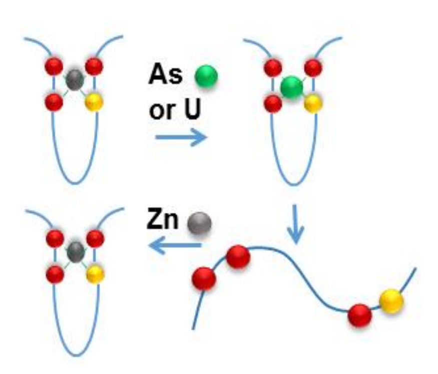


Painting by Mallery Quetawki

Low zinc status (<70 ug/dL) in many members of the Navajo Nation.

As target selectivity: C3H1 and C4 zinc fingers

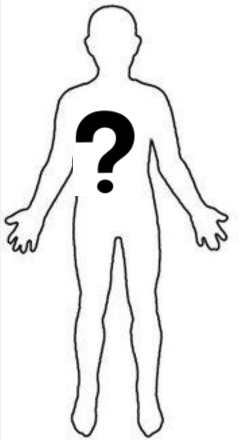
Supplemental zinc is protective against As/U.



>40 bench research publications by UNM METALS researchers

*other metals, including Cd

Zinc supplements have a good safety profile.



Zinc supplementation in elderly or zinc deficient subjects improves immune and DNA damage endpoints.

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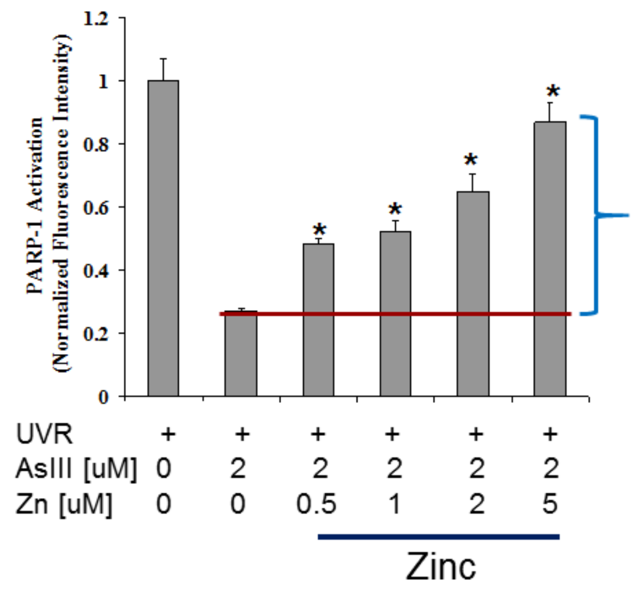
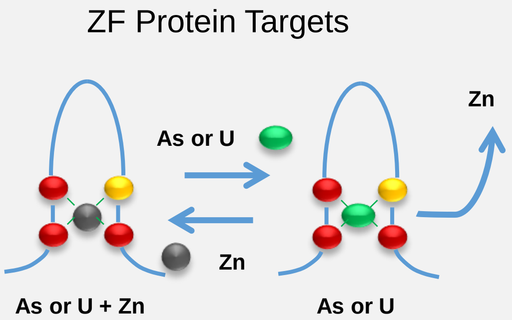
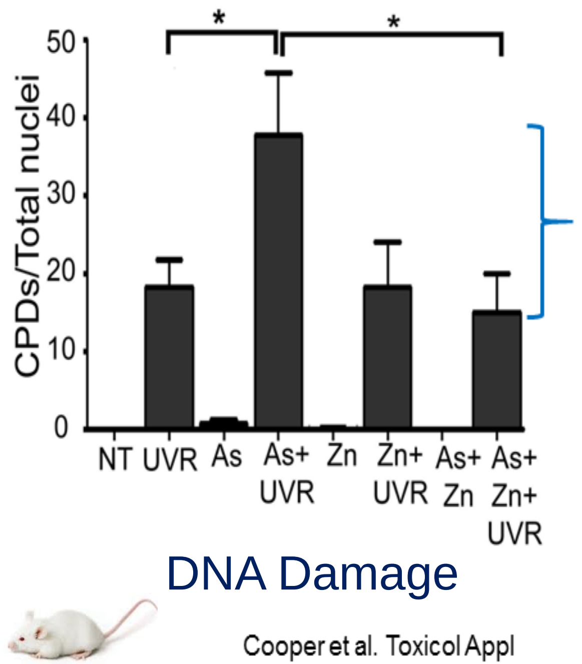
Zinc is protective



PARP-1 Activity

Ding et al. J. Biol Chem. 2009;





DNA Damage

Cooper et al. Toxicol Appl Pharmacol. 2013 269(2):81-8.

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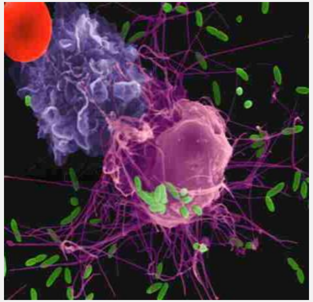
Thinking Zinc

Long Term Goal: Determine whether dietary zinc supplementation reduces metal-induced human disease

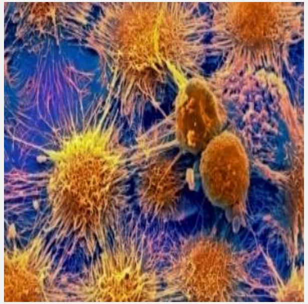
Project Goal: Conduct clinical trial of dietary zinc supplementation to assess effects on biomarkers of metal-induced toxicity

Immune Disorders



ANA-markers of autoimmunity
Immune cell numbers and types
Immune cell communication (cytokines)

Cancers



DNA damage
DNA repair protein activity

Thinking Zinc Study Design

0 Start of study	3 months later (3rd to 4th month)	3 months later (6th to 7th month)	3 months later (9th to 10th month)
Baseline	**Baseline**	**Zinc**	**Last visit**
▪ Enrollment and Consent ▪ Blood and Urine ▪ Gift card	▪ Nutrition Survey ▪ Blood and Urine ▪ **Receive Zinc (RDA)** ▪ Gift card	▪ Blood and Urine ▪ **Receive Zinc (RDA)** ▪ Gift card	▪ Nutrition Survey ▪ Blood and Urine ▪ Gift card

Urine: As, U, other metals

Cells from blood: ANA, immune cells
Serum: Zn, cytokines

We measure:

- Metal levels in urine and blood
- Markers of immune function
- DNA damage and DNA repair protein activity
- Zinc in diet (nutrition survey)

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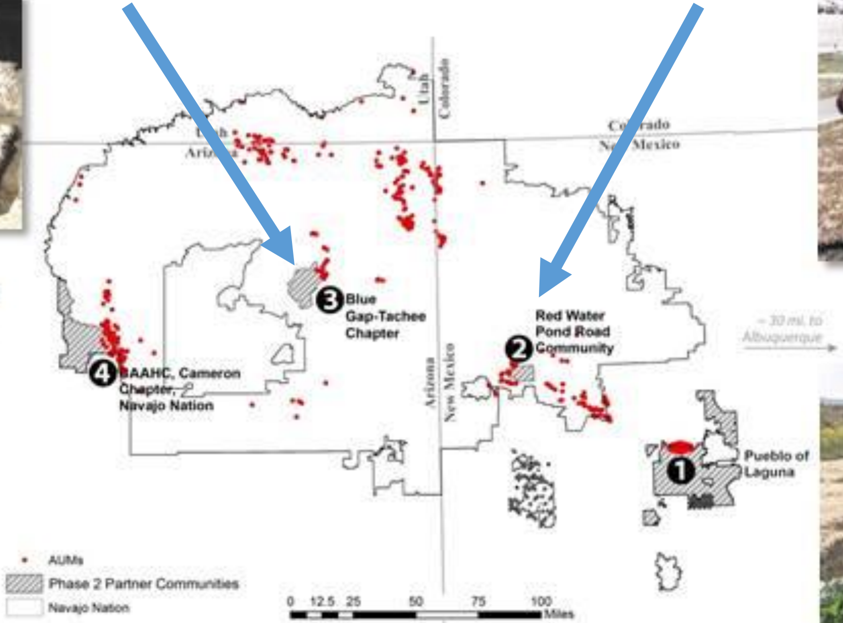
Blue Gap-Tachee Chapter, Navajo Nation

Red Water Pond Road Community



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Status/Progress

Approvals

- Navajo HRRB January 2019
- Registration Clinicaltrials.gov NCT03908736

Continued Community Engagement (CEC/SRIC)

- >50 community activities (i.e. chapter meetings and booths at events)

Enrollment (52 of 80 goal as of March 2022)

34 women, 18 men ages 21-64, median ~59

- RWPR Community Completed in April 2022
- Blue Gap Community – ongoing

Retention—71+%

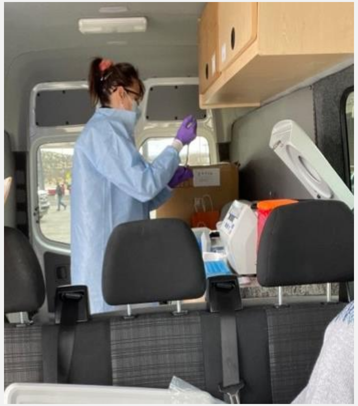
Sample and Data Analysis—in progress

Pinedale Chapter House

Conducting TZ during COVID





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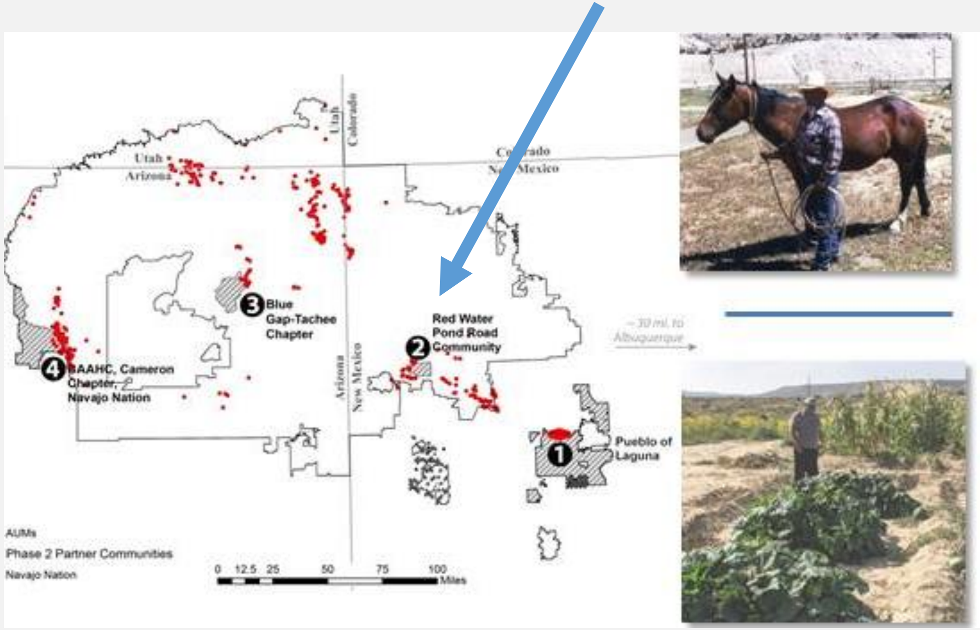
Initial findings from RWPRC Participants



Red Water Pond Road Community

Uranium levels greater than Navajo Nation median

Thinking Zinc Participant Pre-Zinc Urinary Metal Levels							
Metal	**Median**	**Range**	**%>95th percentile NHANES/NBCS**	**NHANES 50th**	**NHANES 95th**	**NBCS 50th**	**NBCS 95th**
Antimony	0.077	0.020 - 1.540	15%/1.7%	0.046	0.151	0.077	0.964
Arsenic	4.392	1.495 - 135.014	3.3%/4.9%	5.62	56.2	5.392	16.81
Barium	1.201	0.058 - 437.227	5%/1.7%	1.24	4.83	3.903	27.9
Beryllium	0.002	0.000 - 0.047	NA/6.7%	<LOD	<LOD	0.011	0.014
Cadmium	0.163	0.031 - 1.207	5%/16.7%	0.188	0.882	0.096	0.44
Cesium	3.199	0.921 - 25.151	6.7%/1.7%	4.22	10.4	4.675	16.771
Cobalt	0.416	0.106 - 4.794	6.7%/3.3%	0.404	1.2	1.012	2.522
Lead	0.129	0.016 - 2.706	1.7%/1.7%	0.315	1.14	0.306	1.884
Manganese	0.092	0.002 - 1.963	8.3%/0%	0.209	0.487	0.244	6.89
Molybdenum	24.148	1.728 - 130.684	1.7%/0%	36.3	94.7	55.193	245
Platinum	0.013	0.000 - 0.398	28.3%/30%	<LOD	0.035	0.007	0.03
Strontium	101.669	10.867 - 3100.765	11.7%/3.3%	101	266	185	696.056
Tin	0.954	0.116 - 14.605	11.7%/0%	0.431	3.06	2.07	20.975
Tungsten	0.030	0.002 - 0.193	0%/0%	0.061	0.279	0.137	1.276
Uranium	0.019	0.002 - 19.162	31.7%/6.7%	0.005	0.026	0.016	0.109
Vanadium*	0.156	0.019 - 28.837					

Median metal levels are shown for Visit 1 and Visit 2 samples collected before zinc supplementation. Values are corrected for urinary creatinine and reported as micrograms per gram creatinine (µg/g creatinine). For reference, the 50th and 95th percentile levels are provided for the 2019 (January) National Health and Nutrition Examination Survey (NHANES) values and participants in the Navajo Birth Cohort Study including women, men and babies (N=1661-1782 for each metal). Metals results highlighted in blue represent those where more than 10% of samples had levels in excess of the NHANES 95th percentile values. *Urine levels for vanadium are not included in NHANES reporting. NA - Not available due to measurements below the level of detection of the instrument

- Certain metals had 10% of samples exceeding the NHANES 95th percentile (blue). Antimony, Platinum, Strontium, Tin, and Uranium
- For Uranium 31.7% and 6.7% of samples exceeded the NHANES and Navajo Birth Cohort Study (NBCS) 95th percentile, respectively.

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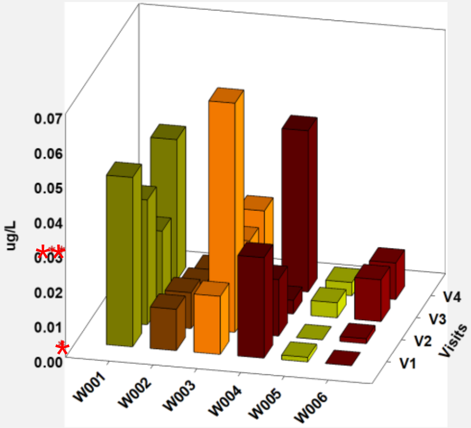
Longitudinal biomonitoring reveals fluctuations

Uranium

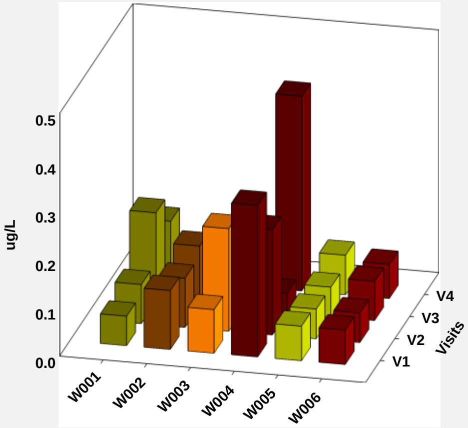


NHANES Values

* 50th percentile 0.005

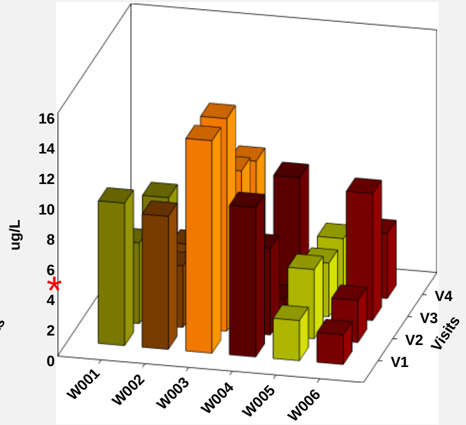
** 95th percentile 0.031

Vanadium



Synchronized participant group for collections

Total Arsenic

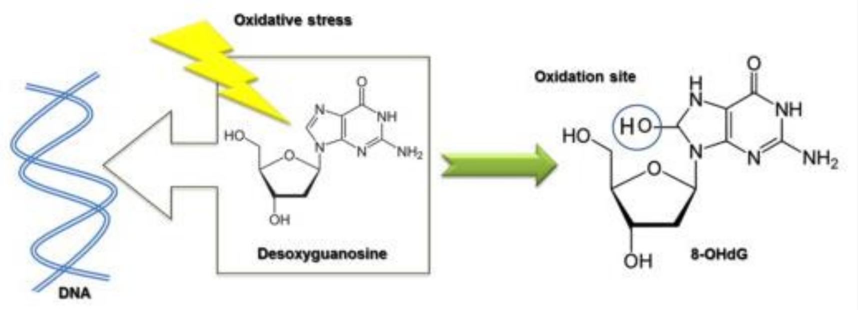


NHANES Values

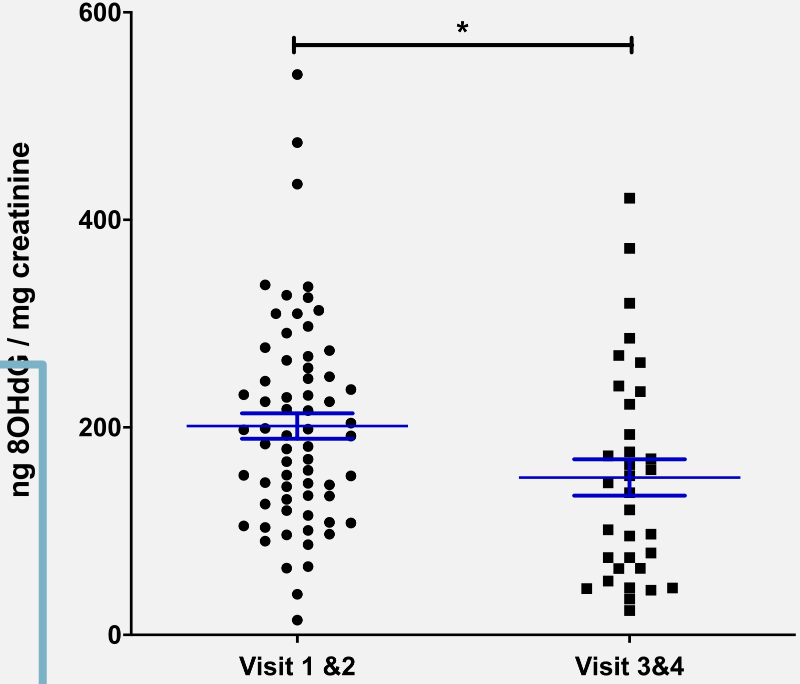
* 50th percentile 5.74

** 95th percentile 49.9

Post-zinc reduction in DNA damage marker 8-OHdG



Emam et al. 2014



- ***Preliminary population results from TZ demonstrate a reduction in oxidative DNA damage with zinc***
- ***(See Dasher-Titus, Poster on Thinking Zinc)***
- ***Also see reductions in cytokines associated with inflammation and autoimmunity (GM-CSF, IFNγ, IL12-P70, IFNβ, IL29 and IFNα)***

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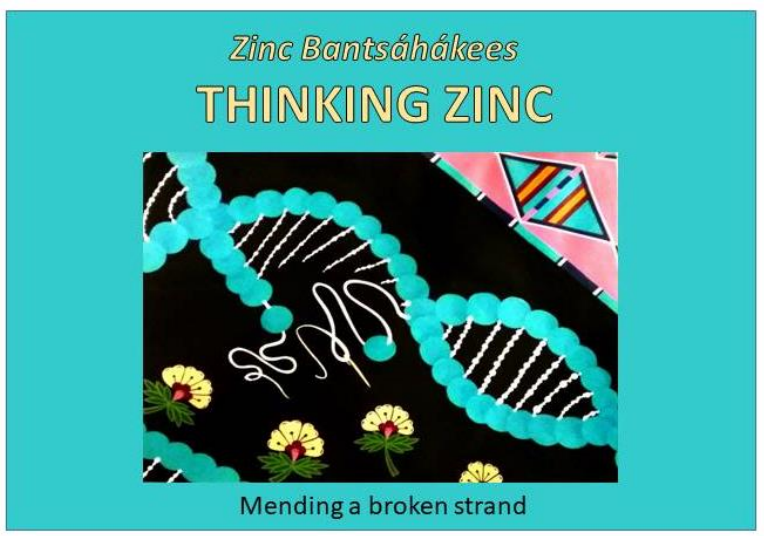
Paintings by
Mallery
Quetawki
Zuni Pueblo

Thinking Zinc built on Community Input

Sarah Henio-Adeky, Chris Shuey, MPH; David Begay, PhD

- Study Design: Single-arm cohort design, not placebo-controlled
- Study name from community input: Thinking Zinc — *Beesh Dootł'izh Bantsáháhákees*
  [metal + blue (the one that is) + thinking about it]
- Expanded age inclusion criteria
- Community vetting of recruitment and outreach materials
- Translation of scientific language to Navajo for presentations and consenting



Painting by M. Quetawki

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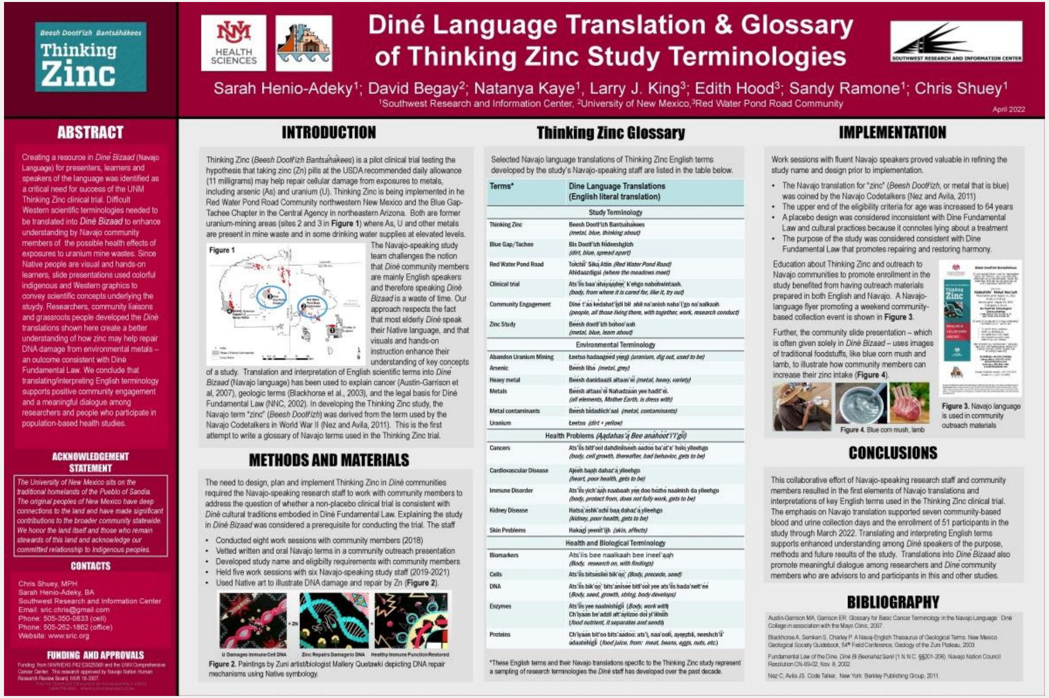
Diné Language Translation & Glossary of Thinking Zinc Study Terminologies



Beesh Dootł'izh Bantsáhákees

Thinking Zinc

HEALTH SCIENCES

Diné Language Translation & Glossary of Thinking Zinc Study Terminologies

Sarah Henio-Adeky[1]; David Begay[2]; Natanya Kaye[1], Larry J. King[3]; Edith Hood[3]; Sandy Ramone[1]; Chris Shuey[1]

[1]Southwest Research and Information Center, [2]University of New Mexico, [3]Red Water Pond Road Community

SOUTHWEST RESEARCH AND INFORMATION CENTER

April 2022

ABSTRACT

Creating a resource in Diné Bizaad (Navajo Language) for presenters, learners and speakers of the language was identified as a critical need for success of the UNM Thinking Zinc clinical trial. Difficult Western scientific terminologies needed to be translated into *Diné Bizaad* to enhance understanding by Navajo community members of the possible health effects of exposures to uranium mine wastes. Since Native people are visual and hands-on learners, slide presentations used colorful indigenous and Western graphics to convey scientific concepts underlying the stuydy. Researchers, community liaisons and grassroots people developed the *Diné* translations shown here create a better understanding of how zinc may help repair DNA damage from environmental metals – an outcome consistent with Diné Fundamental Law. We conclude that translating/interpreting English terminology supports positive community engagement and a meaningful dialogue among researchers and people who participate in population-based health studies.

ACKNOWLEDGEMENT STATEMENT

The University of New Mexico sits on the traditional homelands of the Pueblo of Sandia. The original peoples of New Mexico have deep connections to the land and have made significant contributions to the broader community statewide. We honor the land itself and those who remain stewards of this land and acknowledge our committed relationship to Indigenous peoples.

CONTACTS

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INTRODUCTION

Thinking Zinc (*Beesh Dootł'izh Bantsáhákees*) is a pilot clinical trial testing the hypothesis that taking zinc (Zn) pills at the USDA recommended daily allowance (11 milligrams) may help repair cellular damage from exposures to metals, including arsenic (As) and uranium (U). Thinking Zinc is being implemented in he Red Water Pond Road Community northwestern New Mexico and the Blue Gap-Tachee Chapter in the Central Agency in northeastern Arizona. Both are former uranium-mining areas (sites 2 and 3 in **Figure 1**) where As, U and other metals are present in mine waste and in some drinking water supplies at elevated levels.

Figure 1

The Navajo-speaking study team challenges the notion that *Diné* community members are mainly English speakers and therefore speaking *Diné Bizaad* is a waste of time. Our approach respects the fact that most elderly *Diné* speak their Native language, and that visuals and hands-on instruction enhance their understanding of key concepts of a study. Translation and interpretation of English scientific terms into *Diné Bizaad* (Navajo language) has been used to explain cancer (Austin-Garrison et al, 2007), geologic terms (Blackhorse et al., 2003), and the legal basis for Diné Fundamental Law (NNC, 2002). In developing the Thinking Zinc study, the Navajo term "zinc" (*Beesh Dootł'izh*) was derived from the term used by the Navajo Codetalkers in World War II (Nez and Avila, 2011). This is the first attempt to write a glossary of Navajo terms used in the Thinking Zinc trial.

METHODS AND MATERIALS

The need to design, plan and implement Thinking Zinc in *Diné* communities required the Navajo-speaking research staff to work with community members to address the question of whether a non-placebo clinical trial is consistent with *Diné* cultural traditions embodied in Diné Fundamental Law. Explaining the study in *Diné Bizaad* was considered a prerequisite for conducting the trial. The staff

- Conducted eight work sessions with community members (2018)
- Vetted written and oral Navajo terms in a community outreach presentation
- Developed study name and eligibilty requirements with community members
- Held five work sessions with six Navajo-speaking study staff (2019-2021)
- Used Native art to illustrate DNA damage and repair by Zn (**Figure 2**).

U Damages Immune Cell DNA + ZN Zinc Repairs Damage to DNA = Healthy Immune Function Restored

Figure 2. Paintings by Zuni artist/biologist Mallery Quetawki depicting DNA repair mechanisms using Native symbology.

Thinking Zinc Glossary

Selected Navajo language translations of Thinking Zinc English terms developed by the study's Navajo-speaking staff are listed in the table below.

Terms*	Dine Language Translations (English literal translation)
Study Terminology	
Thinking Zinc	Beesh Dootł'izh Bantsáhákees *(metal, blue, thinking about)*
Blue Gap/Tachee	Bis Dootł'izh Ńdeeshgiizh *(dirt, blue, spread apart)*
Red Water Pond Road	Tółchíí' Sikáá Átiin *(Red Water Pond Road)* Ahidaazdigai *(where the meadows meet)*
Clinical trial	Ats'íís baa'áháyáádee' K'ehgo nabóhwiintaah. *(body, from where it is cared for, like it, try out)*
Community Engagement	Diné t'áá kédahat'įįdi bił ahił na'anish naha'įįgo na'aalkaah *(people, all those living there, with together, work, research conduct)*
Zinc Study	Beesh dootł'izh bóhoo'aah *(metal, blue, learn about)*
Environmental Terminology	
Abandon Uranium Mining	Łeetso hadaageed yęęgi *(uranium, dig out, used to be)*
Arsenic	Beesh łibá *(metal, grey)*
Heavy metal	Beesh danidaazii áłtaas'éí *(metal, heavy, variety)*
Metals	Beesh áłtaas'éí Nahadzáán yee hadit'éí. *(all elements, Mother Earth, is dress with)*
Metal contaminants	Beesh bidadiich'aal *(metal, contaminants)*
Uranium	Łeetso *(dirt + yellow)*
Health Problems *(Ąądahas'ą Bee anáhóót'i'í'gíí)*	
Cancers	Ats'íís bitł'ool dahdiniiseeh áádoo ba'át'e' hóló yileehgo *(body, cell growth, thereafter, bad behavior, gets to be)*
Cardiovascular Disease	Ajéíh baah dahaz'ą yileehgo *(heart, poor health, gets to be)*
Immune Disorder	Ats'íís yich'ááh naabaah yee doo hózhó naalnish da yileehgo *(body, protect from, does not fully work, gets to be)*
Kidney Disease	Hatsá'áshk'ézhí baah dahaz'ą yileehgo *(kidney, poor health, gets to be)*
Skin Problems	Hakágí yeenit'įįh *(skin, affects)*
Health and Biological Terminology	
Biomarkers	Ats'íís bee naalkaah bee íneel'ąąh *(Body, research on, with findings)*
Cells	Ats'íís bitsésiłei bik'oo' *(Body, precede, seed)*
DNA	Ats'íís bik'oo' bits'áníseé bitł'óól yee ats'íís hada'nelt'ee *(Body, seed, growth, string, body develops)*
Enzymes	Ats'íís yee naalnishígíí *(Body, work with)* Ch'iyáán be'adzil ałt'áyiizoo doo yí'ííníih *(food nutrient, it separates and sends)*
Proteins	Ch'iyáán bitł'oo bits'áádoo: ats'į, naa'ołí, ayęęzhii, neeshch'íí' ádaatehígíí *(food juice, from: meat, beans, eggs, nuts, etc.)*

*These English terms and their Navajo translations specific to the Thinking Zinc study represent a sampling of research terminologies the *Diné* staff has developed over the past decade.

IMPLEMENTATION

Work sessions with fluent Navajo speakers proved valuable in refining the study name and design prior to implementation.

- The Navajo translation for "zinc" (*Beesh Dootł'izh*, or metal that is blue) was coined by the Navajo Codetalkers (Nez and Avila, 2011)
- The upper end of the eligibility criteria for age was increased to 64 years
- A placebo design was considered inconsistent with Dine Fundamental Law and cultural practices because it connotes lying about a treatment
- The purpose of the study was considered consistent with Dine Fundamental Law that promotes repairing and restoring harmony.

Education about Thinking Zinc and outreach to Navajo communities to promote enrollment in the study benefited from having outreach materials prepared in both English and Navajo. A Navajo-language flyer promoting a weekend community-based collection event is shown in **Figure 3**.

Further, the community slide presentation – which is often given solely in *Diné Bizaad* – uses images of traditional foodstuffs, like blue corn mush and lamb, to illustrate how community members can increase their zinc intake (**Figure 4**).

Figure 4. Blue corn mush, lamb

Figure 3. Navajo language is used in community outreach materials

CONCLUSIONS

This collaborative effort of Navajo-speaking research staff and community members resulted in the first elements of Navajo translations and interpretations of key English terms used in the Thinking Zinc clinical trial. The emphasis on Navajo translation supported seven community-based blood and urine collection days and the enrollment of 51 participants in the study through March 2022. Translating and interpreting English terms supports enhanced understanding among *Diné* speakers of the purpose, methods and future results of the study. Translations into *Diné Bizaad* also promote meaningful dialogue among researchers and *Diné* community members who are advisors to and participants in this and other studies.

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Nez C, Avila JS. Code Talker. New York: Berkley Publishing Group, 2011.

- Creating a resource in *Diné Bizaad* (Navajo Language) for learners and speakers identified as a critical need for success of the UNM Thinking Zinc clinical trial.
- Western scientific terminologies needed to be translated into *Diné Bizaad* to enhance understanding by Navajo community members
- Respects the fact that most elderly *Diné* speak their Native language, and that visuals and hands-on instruction improve their understanding of key concepts

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Navajo Translations of Key Terms in the Thinking Zinc Study

Terms*	**Dine Language Translations (English literal translation)**
	Study Terminology
Thinking Zinc	Beesh Dootł'izh Bantsáhákees *(metal, blue, thinking about)*
Blue Gap/Tachee	Bis Dootł'izh Nídeeshgiizh *(dirt, blue, spread apart)*
Red Water Pond Road	Tółchíí' Siką́ Atiin *(Red Water Pond Road)* Ahidaazdigai *(where the meadows meet)*
Clinical trial	Ats'íís baa'áháyą́ą́dę́ę́' k'ehgo nabóhwintaah. *(body, from where it is cared for, like it, try out)*
Community Engagement	Diné t'áá kédahat'íįdi bił ahił na'anish naha'į'go na'aalkaah *(people, all those living there, with together, work, research conduct)*
Zinc Study	Béésh dootł'izh bóhoo'aah *(metal, blue, learn about)*

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Navajo Translation of Scientific Terms

Health Problems *(Ąądahas'ą Bee anáhóót'i'l'gíí)*	
Cancers	Ats'íís bitł'óól dahdiníiséeh áádóó ba'át'e' hóló̜ yileehgo *(body, cell growth, thereafter, bad behavior, gets to be)*
Cardiovascular Disease	Ajéeh baąh dahaz'ą yileehgo *(heart, poor health, gets to be)*
Immune Disorder	Ats'íís yich'ąąh naabaah yę́ę doo hózhó naalnish da yileehgo *(body, protect from, does not fully work, gets to be)*
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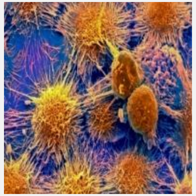
Skin Problems	Hakágí yeenít'įįh *(skin, affects)*
Health and Biological Terminology	
Biomarkers	Ats'íís bee naalkaah bee íneel'ąąh *(Body, research on, with findings)*
Cells	Ats'íís bitsésiléi bik'ǫǫ' *(Body, precede, seed)*
DNA	Ats'íís bik'ǫǫ' bits'ánísée bitł'óol yee ats'íís hada'nełt'ée *(Body, seed, growth, string, body develops)*



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Methods in Community Engagement

- Conducted eight work sessions with community members (2018)
- Vetted written and oral Navajo terms in a community outreach presentation
- Developed study name and eligibility requirements with community members
- Held five work sessions with six Navajo-speaking study staff (2019-2021)
- Used paintings (below) by Zuni artist Mallery Quetawki to illustrate DNA damage and repair by Zn

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Traditional Foods Used in Outreach

- Outreach and educational materials prepared in both English and Navajo.
- Community slide presentation given solely in *Diné Bizaad*
- Uses images of traditional foodstuffs, like blue corn mush and lamb, to illustrate how community members can increase their zinc intake

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Conclusions

- Translating and interpreting English terms supports enhanced understanding among Diné speakers of the purpose, methods and future results of the study.
- Translations into Diné Bizaad also promote meaningful dialogue among researchers and Diné community members who are advisors to and participants in this and other studies.

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