Overview: UNM METALS Superfund Research Center

(UNM Metals Exposure and Toxicity Assessment on tribal Lands in the Southwest)

Johnnye Lewis, Ph.D., Director

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Additional leveraged support for METALS:

NIH/OD UG3 OD023344 (NBCS/ECHO) (Lewis/MacKenzie)
CDC U01 TS000135 (NBCS) (Lewis/MacKenzie)
NIEHS & NIMHD P50ES026102 (Native EH Equity) (Lewis/Gonzalez)
USEPA 83615701 (Native EH Equity Center
R01 ES026673 (Campen)
1R01ES021100 (ViCTER supp Hudson)
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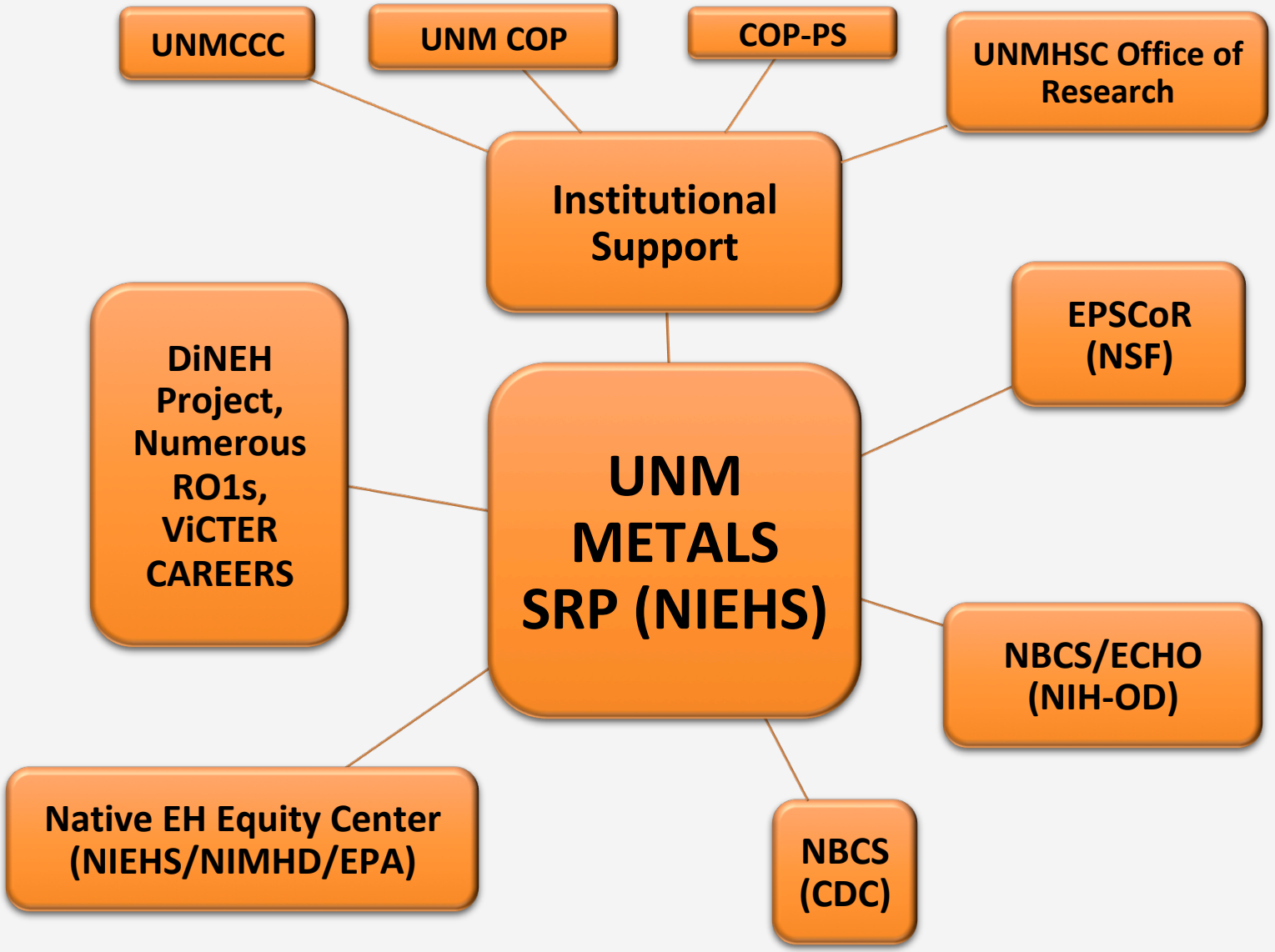
NM EPSCoR #IIA-1301346 &
NSF CAREER 1652619 (Cerrato Corrales

Funding: NIH/NIEHS P42 ES025589 (UNM METALS)

Major linkages & Historic partnerships: METALS



Institutional Support:

- Bridge funding ,
- pilot funds,
- discretionary funds,
- trainee support,
- equipment & lab reno

Other Research Centers/Projects:

- Biospecimens for SRP analyses, Population data on biomonitoring, exposure
- Environmental data,
- Pilot funds

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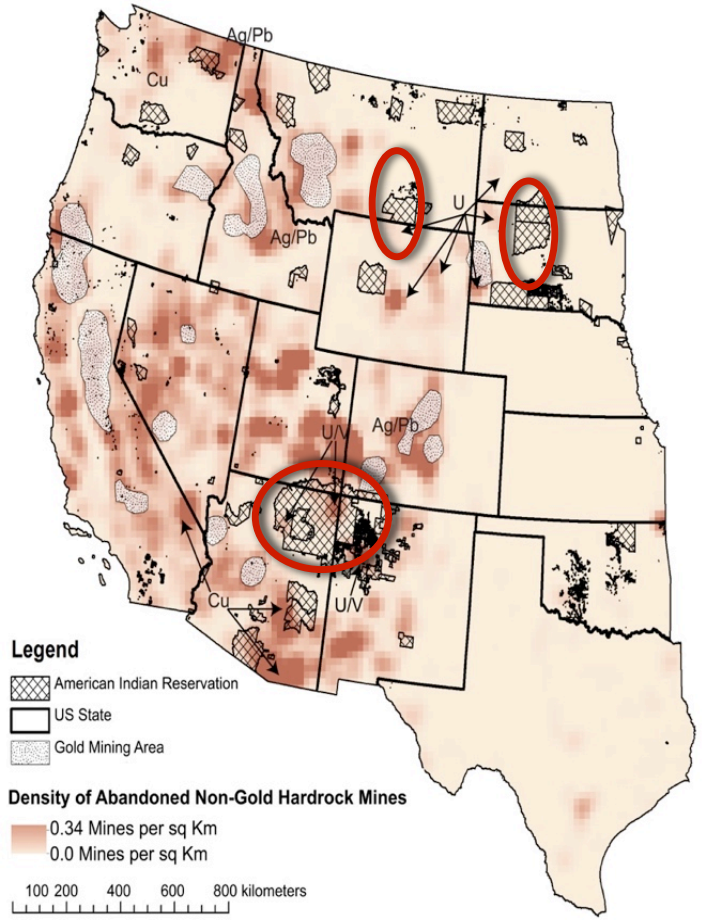
The Need

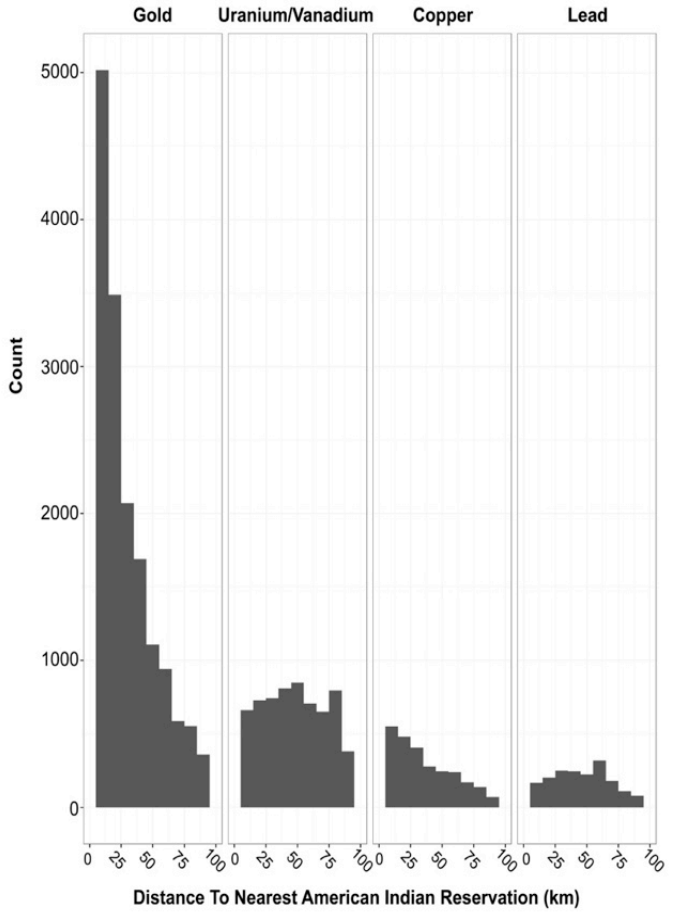
Western States -- US

- >1/2 of US Indigenous population
- 161,000 abandoned hard rock mines
- >500,000 sites – all mixed metals
- >4500 mines -- uranium – mixed waste
- 40% of watershed headwaters in West thought to be contaminated from these mines (USEPA)
- >600,000 Native Americans live within 10 km of abandoned mines

Potential for higher sensitivity to toxicity

- reliance on local resources → increased exposure
- understudied genetic, epigenetic ,metabolic, distribution differences
- limited research limits our understanding





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The Need (cont'd)

Clean-up & Risk Reduction Options Limited

- **Disposal cells still a primary option**
  - Costly and maintenance intensive
  - Hauling creates substantial additional risk
  - Siting not simple – few "want" waste in their homelands
  - Visible reminder remains – transgenerational trauma
- **Health effects of living near waste documented**
- **Clean-up in our lifetime unlikely**
  - $1 B Tronox estimated to address ~ 10% of Navajo waste
- **How to reduce risk?**

Vegetation on Tuba City UMTRA Cell Threatens Radon Barrier

UMTRA Disposal Cell, Mexican Hat, UT

ORIGINAL DINEH PROJECT RESULTS: LIVING IN PROXIMITY TO LEGACY WASTE LINKED TO ADVERSE HEALTH EFFECTS

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

ONGOING EXPOSURE TO LEGACY WASTE→ INCREASED RISK FOR HYPERTENSION, MULTIPLE CHRONIC DISEASES, & IMMUNE DYSREGULATION IN ADULTS

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

Birth cohort studies on two subsequent generations ongoing

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Multigenerational exposures in METALS partner communities

Red Water Pond Road Community Assoc. (RWPRCA)


RWPRCA annual uranium legacy commemoration,July 2018


Boy watches removal of 18" of soil around his home -- 2007

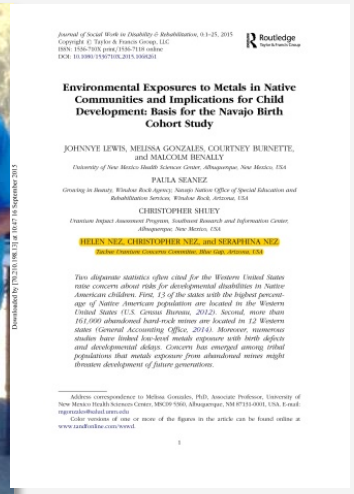
10. 09. 2009

- Between 3 U-waste sites since 1968
- Community occupied since ~1900
- Environmental & occupational exposures
- 1979 – largest US release of radioactive material – 94 million gal
- 3 relocations for temporary actions
  - waste still in place
  - Community goal: restoration

Blue Gap-Tachee Chapter, Tachee Uranium Concerns Committee

- 20 AUMs (1950s-60s -- Navajo Nation, northeastern Arizona)
- Many of today's families descended from former miners
- Pregnant women's reliance on contaminated drinking water → concerns about children's severe & fatal neuropathies
- First requested clean-up in 1988; METALS 2014 Monograph → site prioritization (NNDOJ & USEPA)


Helen Nez, Seraphina Nez


Environmental Exposures to Metals in Native Communities and Implications for Child Development: Basis for the Navajo Birth Cohort Study

JOHNNYE LEWIS, MELISSA GONZALES, COURTNEY BURNETTE, and MALCOLM BENALLY

PAULA SEANEZ

CHRISTOPHER SHUEY

HELEN NEZ, CHRISTOPHER NEZ, and SERAPHINA NEZ

Pueblo of Laguna

- Jackpile Mine – 1952-82 -- once world's largest open-pit U mine partial reclamation '89-95; NPL 2012
- Villages concerned about
  - U mobility in surface water
  - windblown dusts
  - impact of waste on livestock, crops, wildlife
  - cumulative impacts w/ off-site AUMs

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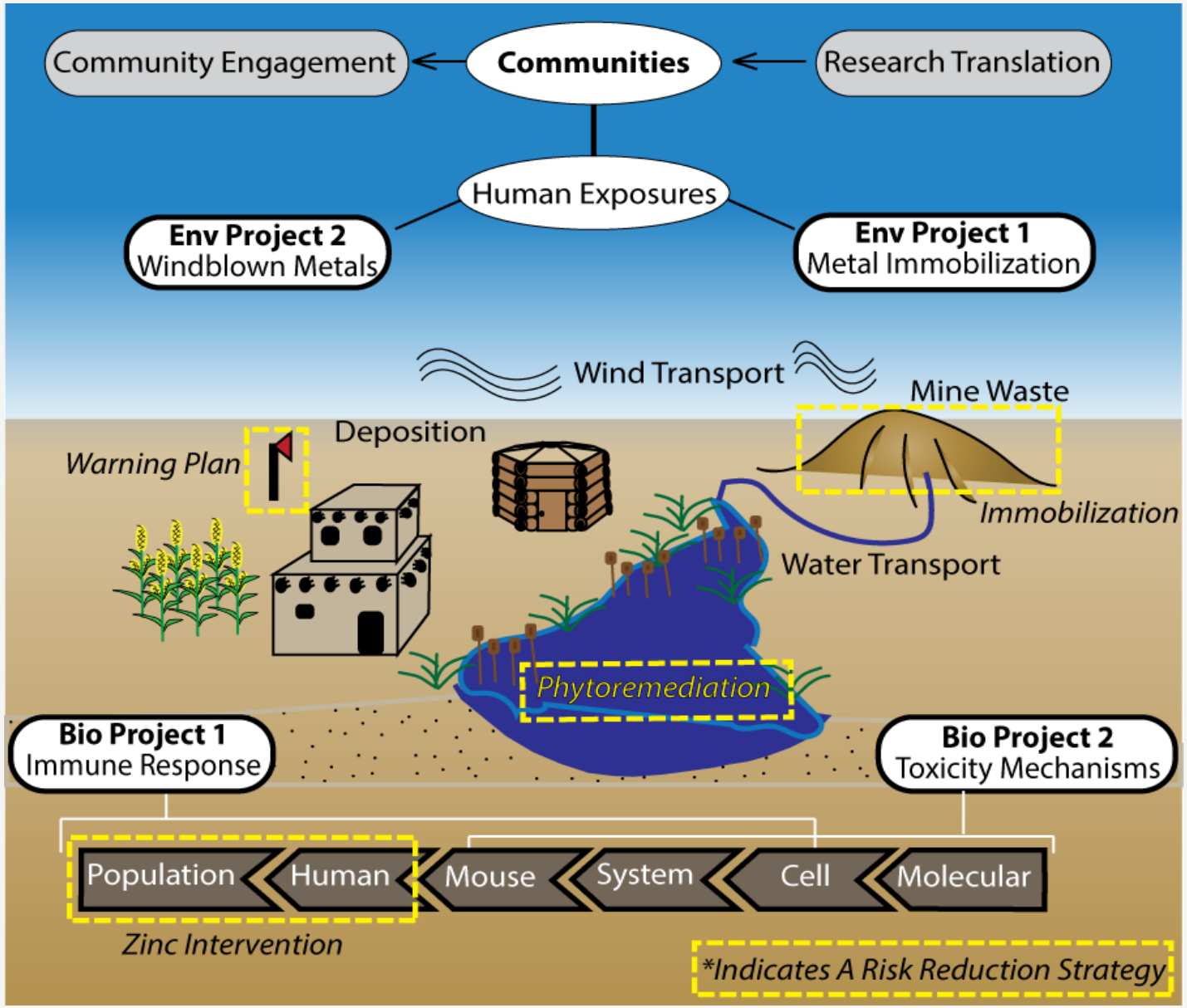
UNM METALS Conceptual Model



Conceptual framework of UNM METALS

- **planned risk-reduction strategies in yellow**
- **components are highly interactive with each other and communities**
- **CEC input and RTC translation of results.**
- **All work in partnership with our indigenous communities**

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Goals of Interventions

Ideal strategies will be

- cost-effective, readily implemented – appropriate to site characteristics
- culturally appropriate -- exploit natural properties
- low water use
- sustainable
- result in removal of waste from communities
- create safe jobs for communities

Maintaining METALS Partnerships: Admin, CEC, RTC, TC

Workshops on cross-cultural research: all Trainees/Researchers

•Indigenous Education Institute (IEI) Partners

Translation through Native art and Symbology

- Mallery Quetawki – artist-in-residence → staff

Community partners critical members of team

- Team science includes their regular input, involvement of trainees

Liaisons: continuous involvement in partner communities

•Participation in monthly METALS mtgs

Facilitate & maintain communication

- EPA Regions 6 and 9, Navajo Nation EPA, communities, Navajo Settlement Trustees
- Quarterly briefings initiated
- All participate in Annual Meeting with EAC

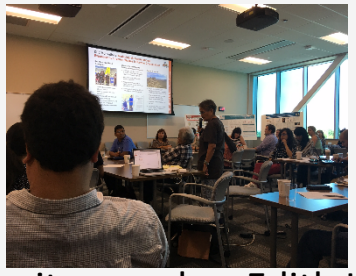
Using Native Art to Communicate our Science

U Damages Immune Cell DNA + **ZN** = **Zinc Leads to Repair of DNA Damage** = **Health Immune Cell Can Function**

July 2018 – 1st Quarterly METALS Progress Briefing

NNEPA Director Dr. Donald Benn

Trainee Gonzalez-Estrella speaks on research results from his studies on sorption using native materials to clean water



Community member Edith Hood

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Examples of recognition of our work….

METALS team gives invited presentations at Restoring K'e Conferences throughout Navajo Nation (2018)

Campen AirCARE1 work at Tachee highlighted in SRP brief

NIH National Institute of Environmental Health Sciences

Superfund Research Program

Research Brief 282 — Release Date: 06/06/18

Dust from Mine Waste in Navajo Nation May Harm Lungs and Heart

Particles in dust from abandoned uranium mines may be damaging to the lungs and heart, according to new research from the University of New Mexico Superfund Research Program (UNM SRP) Center. The researchers showed that exposure to particles less than 10 micrometers in diameter (PM10) from an old uranium mine, compared to PM10 from an area not impacted by a mine, led to increased pulmonary and cardiac toxicity in mice, as well as higher levels of inflammation and oxidative stress in cells.

With funding from SRP and another NIEHS grant, researchers, led by Matthew Campen, Ph.D., focused on PM10 arising from one of more than 500 abandoned uranium mine sites in the Navajo Nation. They took dust samples from the Claim 28 mine site in the Blue Gap Tachee Chapter of the Navajo Nation to study the stucture and toxicity of the particles. They also took dust samples from a nearby area, which is not impacted by historical mining activities, to serve as background PM10 for comparison.

From left, UNM SRP Center trainees Marsha Bitsui and Jessica Begay and UNM SRP Center researcher Chris Shuey, M.P.H., collect dust samples at the Claim 28 mine site. (Photo courtesy of Matthew Campen)

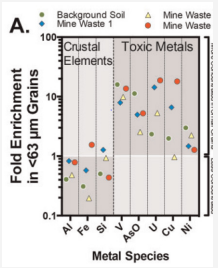
They discovered that the PM10 derived from the mine, called Claim 28 PM10, was highly enriched with uranium and vanadium. These two metals have been previously linked to negative health effects. The Claim 28 PM10 also exhibited a unique structure consisting of aggregated uranium- and vanadium-bearing nanoparticles, which was not seen in the background PM10.

Examining Particulate Toxicity

To determine whether the Claim 28 PM10 was more toxic than background PM10, researchers exposed mice to both types of particles. They found that Claim 28 PM10 led to increased pulmonary inflammation relative to background PM10. They also observed greater vascular toxicity in Claim 28 PM10-exposed mice, as measured by heightened constriction of the aorta, the largest artery in the body.

They also found that human cells exposed to Claim 28 PM10 led to higher rates of cell death and impairment of phagocytosis, an immune system mechanism used to remove pathogens and cell debris. Claim 28 PM10 was also associated with higher oxidative stress responses in cells. Further study of the cell responses revealed that cell death and injury by Claim 28 PM10 exposure was driven primarily by pathways responsible for activating inflammatory responses.

When examining uranium and vanadium from the samples, they found that both metals produced immune responses in the lung, although with different patterns of cytokines. Cytokines are chemical communicators released by cells of the immune system that may indicate different inflammatory responses. Uranium induced a classic inflammatory pattern of cytokines associated with the innate immune system, which included the cytokines interleukin (IL)-1β. On the other hand, vanadium induced a cytokine pattern more consistent with a TH2-like response, which is associated with controlling allergic inflammatory responses.



The researchers characterized elements in the samples and found that particles less than 63 micrometers in size, compared to larger particles in the samples, displayed higher concentrations of toxic metals, including uranium and vanadium. (Image from Zychowski et al., 2018, Respirable uranyl-vanadate containing particulate matter derived from a legacy uranium mine site exhibits potentiated cardiopulmonary toxicity, Toxicol Sci, by permission of Oxford University Press)

Delving into the structural differences of the PM10, they found that Claim 28 mine waste appeared to include carnotite ore, a mineral containing uranium and vanadium. In the samples, these carnotite grains often existed as aggregated nanoparticles. Because nanometer-sized particulates can penetrate deeper into the lung, these structures may be linked to increased toxicity.

Implications for Nearby Residents

According to the authors, a limitation of these studies is their use of high doses of PM10 which are not directly relevant to human exposures, but provide a way to directly compare the potency of dusts from mine waste and background samples.

Moving forward, the researchers are validating the findings on-site in Blue Gap Tachee. They are analyzing how much of the contaminated dust may be traveling to community members in the region. They also are examining potential health effects of inhalation exposures on nearby Navajo communities.

The authors added that although they expect the overall exposure of windblown PM10 to be low in nearby communities, many of the local residents within a few kilometers of mine sites have lived in their homes for several decades. This emphasizes the need to assess exposure over time to gauge the regional health risks imparted by abandoned mine waste sites.

After their discoveries regarding the potential health effects of mine waste dust, the researchers have gone out into the field to validate their findings. Their mobile exposure lab, on loan from Jack Harkema, Ph.D., and Jim Wagner, Ph.D., at Michigan State University, is on site in Blue Gap Tachee to measure the movement of Claim 28 PM10. (Photo courtesy of Matthew Campen)

In addition to SRP funding, this research was funded by NIEHS grant R01ES026673.

Navajo Nation EPA awards METALS Director Lewis 2018 annual Environmental Excellence Award

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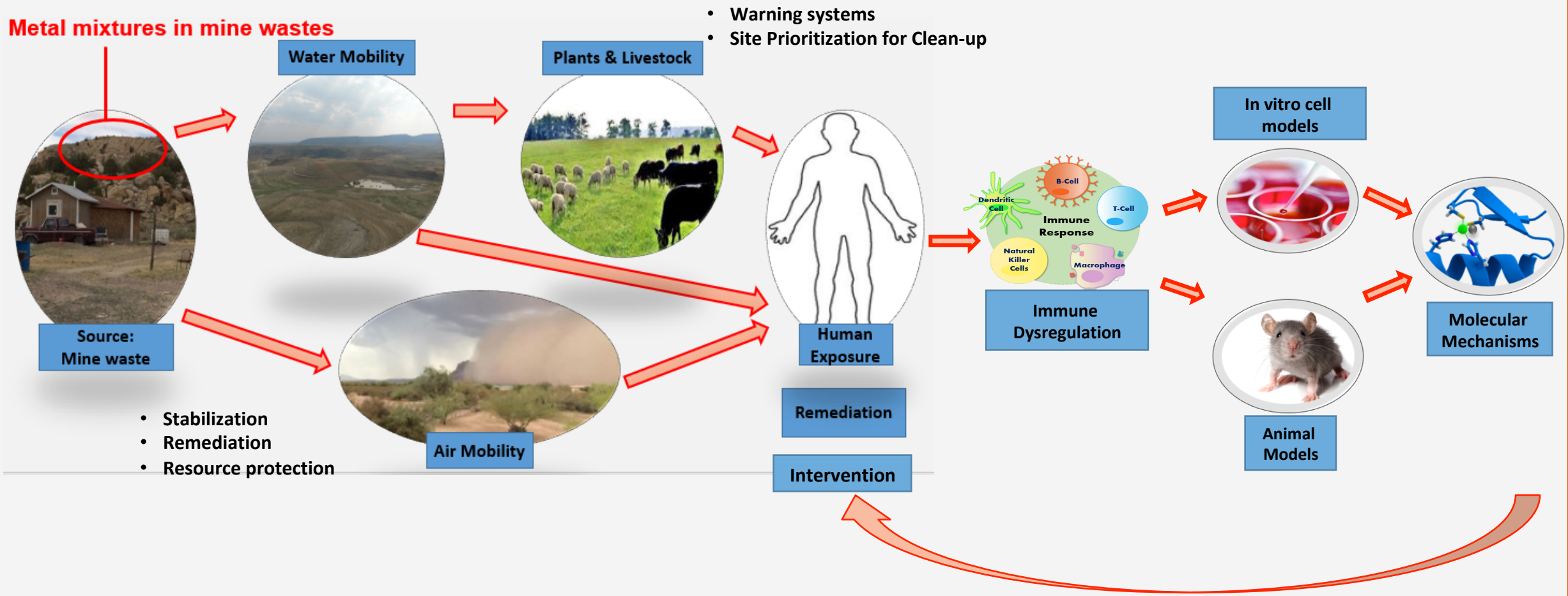
UNM METALS -- Overview

Environmental Projects: Understand mixtures, particle composition, mineralogy to develop risk reduction strategies



Biological Projects: Understand toxicological mechanisms (immune dysregulation) to inform interventions

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UNM METALS – Environmental Projects

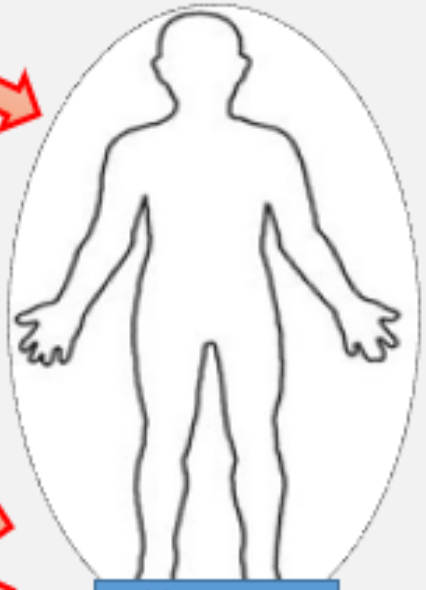
Metal mixtures in mine wastes

Source:
Mine waste

Water Mobility

Plants & Livestock

Risk Reduction
Stabilization
Remediation



Human
Exposure

Air Mobility

Mixture and particle composition
Warning systems
Site prioritization

Remediation

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Aims for Environmental Projects

For Environmental Project 1 (Metal Immobilization for Remediation)

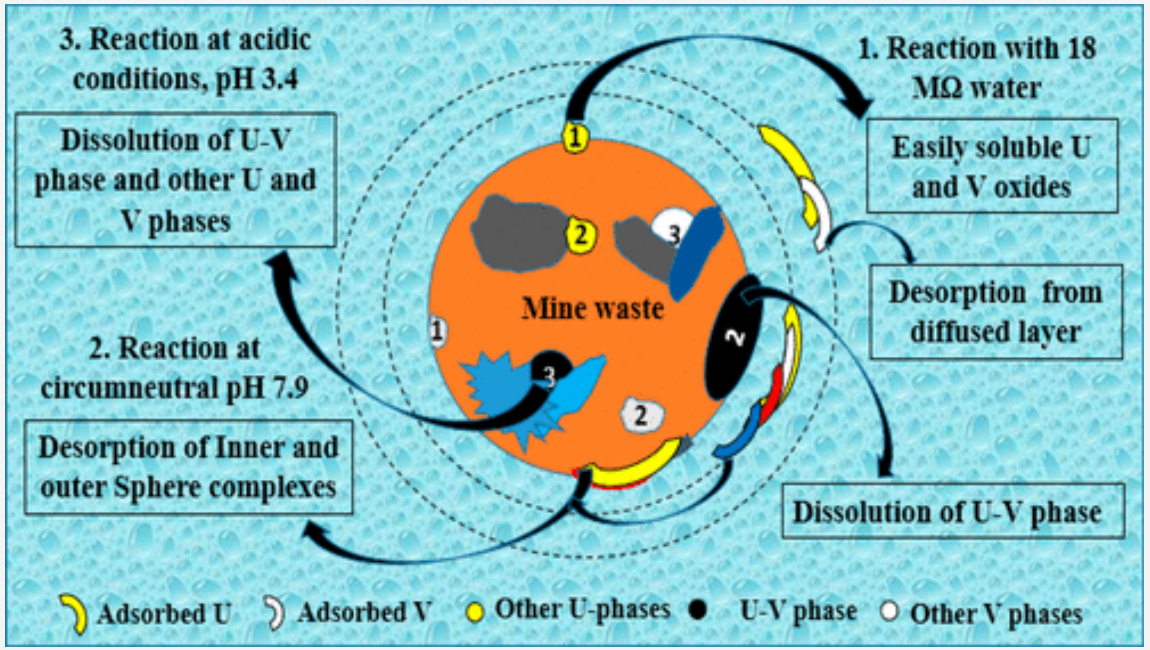
- Primary Aim: *Utilize mineral phases common to mine wastes sites to develop remediation strategies that immobilize metals and thus prevent degradation of community water sources.*

For Environmental Project 2 (Toxic Metals in Airborne Particulate Matter)

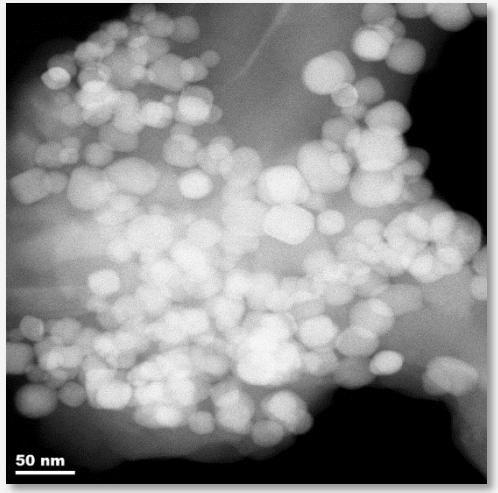
- Primary Aim: *Develop a physically-based process model for the resuspension and transport of metal-bearing particulate matter from mine waste sites to estimate exposure risks for nearby vulnerable communities.*

Highlights: Scientific Findings from SRP Year 1

- Environmental Project 1: Reactive transport modeling coupled with lab experiments showed that the dissolution of U-V minerals is a relevant mechanism for the mobility of U and V in Blue Gap Tachee, AZ (*Main Author* ***Trainee: Sumant Avasarala***, et al. ES&T 2017).



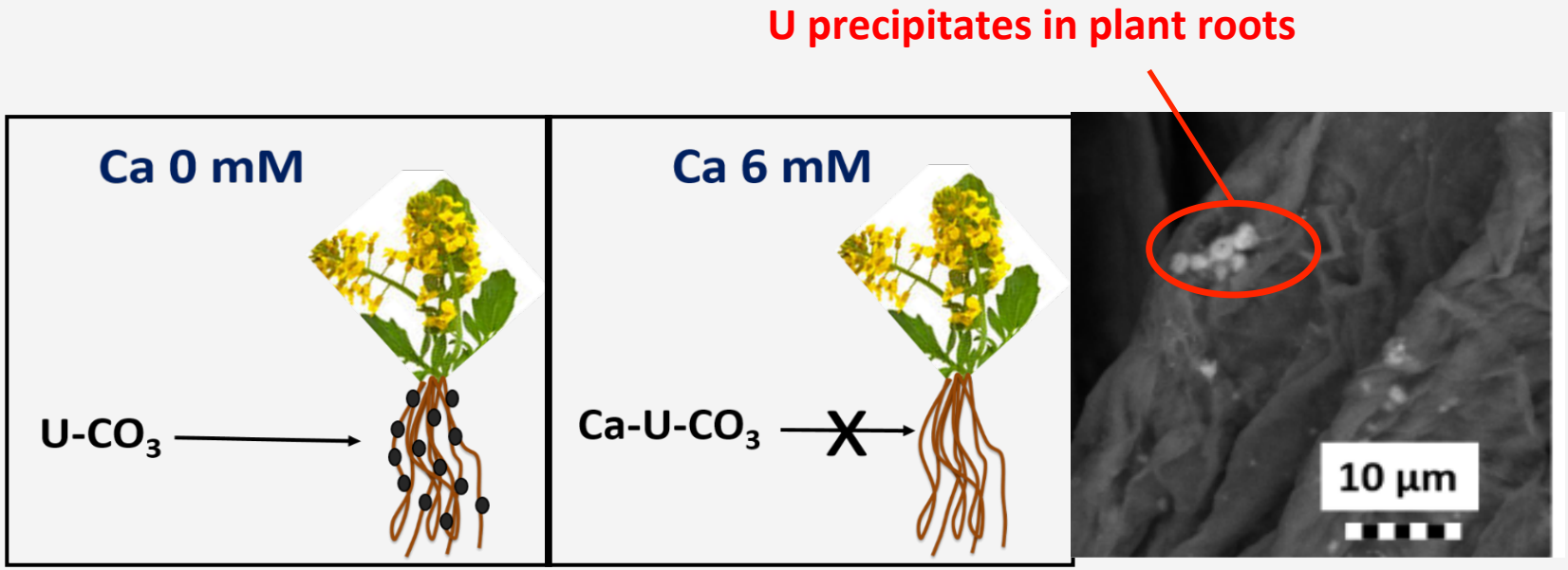
- Environmental Project 2: Respirable particulate matter (e.g., U-V nanoparticles) form mine wastes exhibits cardiopulmonary toxicity (*Main Author* ***Trainee: Katherine Zychowski***, et al. Toxicol. Sci. 2018)



Carnotite clusters of nanoparticles (<100 nm) undergoing fragmentation and dispersion on to surfaces of other micron sized mineral grains. Easily lofted and transported by winds.

Highlights: Scientific Findings from SRP Year 1

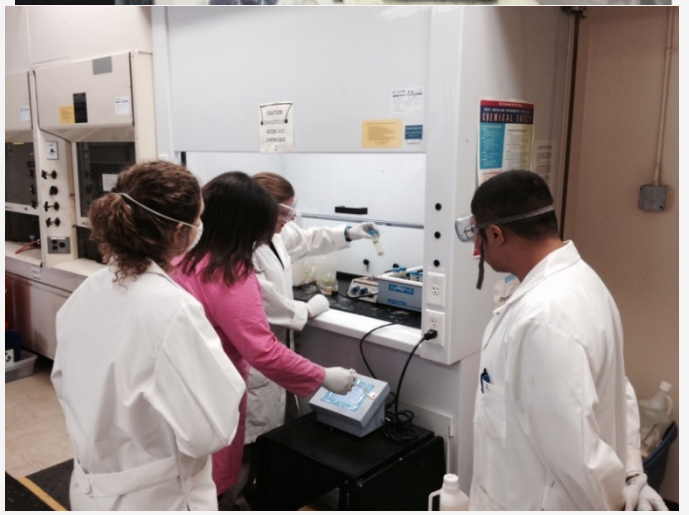
- Uranium uptake in plant roots can be inhibited by Ca and CO_3^{2-} in solution, likely due to interactions with neutrally-charged ternary uranyl-calcium-carbonate complexes (Main Author Trainee: **El Hayek** et al. 2018, submitted to ES&T)./



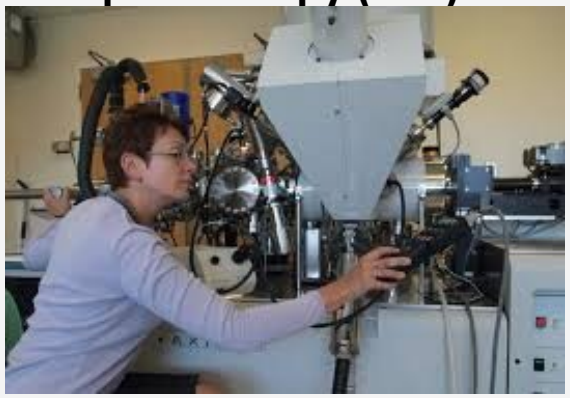
Facilities and Training

- Aqueous Chemistry Analyses:
  Inductively coupled plasma (ICP)
  a) Optical emission spectrometry (ICP-OES)
  b) Mass spectrometry (ICP-MS)
  c) Ion chromatography (IC)
- Solid Analyses (e.g., Electron microscopy, X-ray spectroscopy)

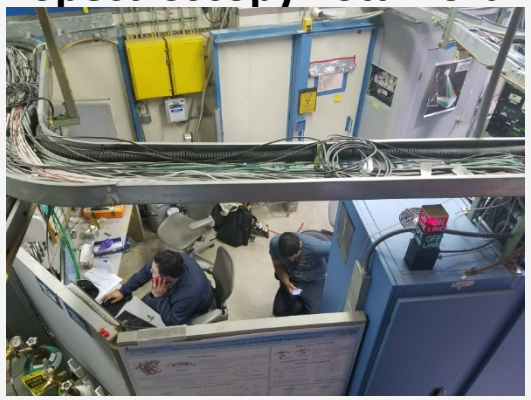
Postdoc, Graduate, Undergraduate, and High School Level Training!



X-ray Photoelectron Spectroscopy (XPS)

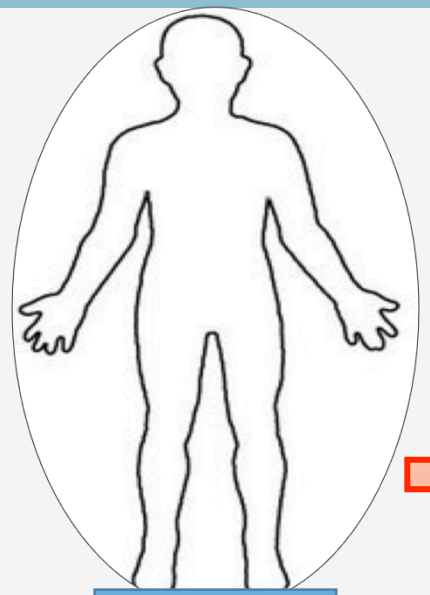


X-ray absorption Spectroscopy - Stanford

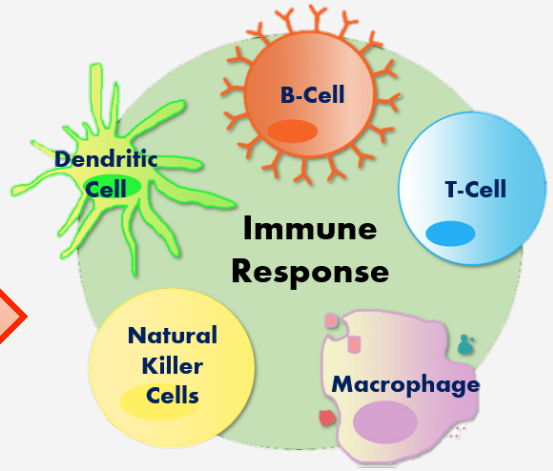


Scanning/Transmission Electron Microscopy

Understanding mechanisms of immune dysregulation to inform intervention



Human Exposure



Immune Dysregulation

In vitro cell models

Animal Models

Molecular Mechanisms

Intervention

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Understanding mechanisms of immune dysregulation

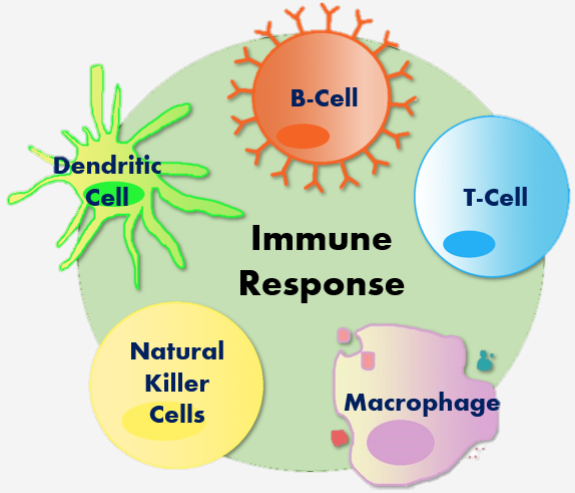
Population studies motivating research:

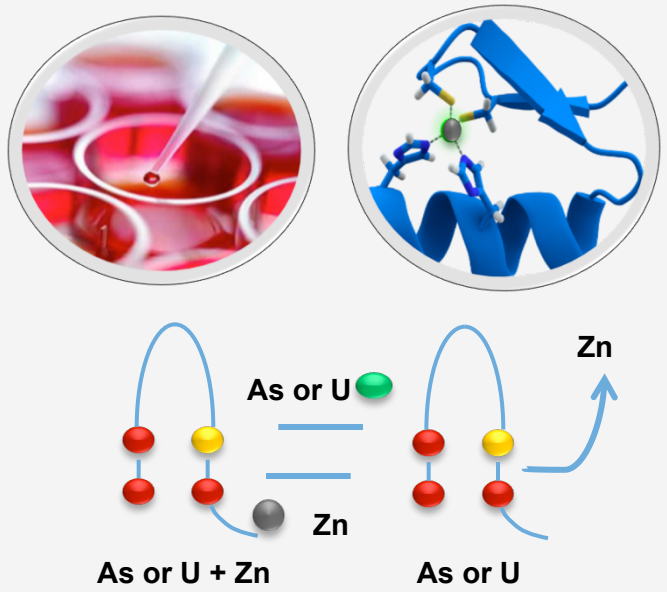
Autoantibody production found in 18% of both female and males (average age 29).

- Associated in males with increased urine uranium levels.
- Increased in relation to living in proximity to abandoned uranium mines.

NK and CD3 cell populations altered with uranium and arsenic, manganese and cadmium.

Inflammatory and autoimmune cytokines increased with increases in uranium and arsenic.





Molecular and structural studies of arsenic and uranium displacement of zinc in the DNA repair enzyme PARP (Hudson, Liu) led to identification of other putative targets using sequence-based pattern-recognition approach

Preliminary data-

- Uranium and arsenic displace zinc from a novel immunoregulatory target known to be expressed in T cells, NK cells, B cells and myeloid cells.
- Immune cell proliferation consistent with disruption of immunoregulatory activity.

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Thinking Zinc-Intervention

Primary Endpoints

- Urinary and serum metal levels as measured by ICP-MS
- Biomarkers of cellular changes of immune function and autoimmunity.

Secondary Endpoints

- DNA damage measurements in white blood cells (lymphocytes).
- PARP enzyme activity in lymphocytes.

Research Volunteers Needed

We are conducting research to understand if taking the daily recommended level of zinc protects our bodies from the effects of heavy metals in the environment.

Community Partners

- Red Water Pond Road Community Association
- Tachee Uranium Concerns Committee
- Blue Gap/Tachee Chapter

Research Partners

- UNM METALS Superfund Center
- UNM College of Pharmacy
- Southwest Research & Information Center
- Indigenous Education Institute

Research Sponsors

- NIEHS Superfund Research Program 1P42ES025589
- UNM Comprehensive Cancer Center P30 CA118100
- UNM Clinical Translational Science Center UL1TR001449

For More Information

email: zinc@sric.org

phone: 877.545.6775

web: www.sric.org/Zinc

Beesh Dootł'izh Bantsáhákees

Thinking Zinc

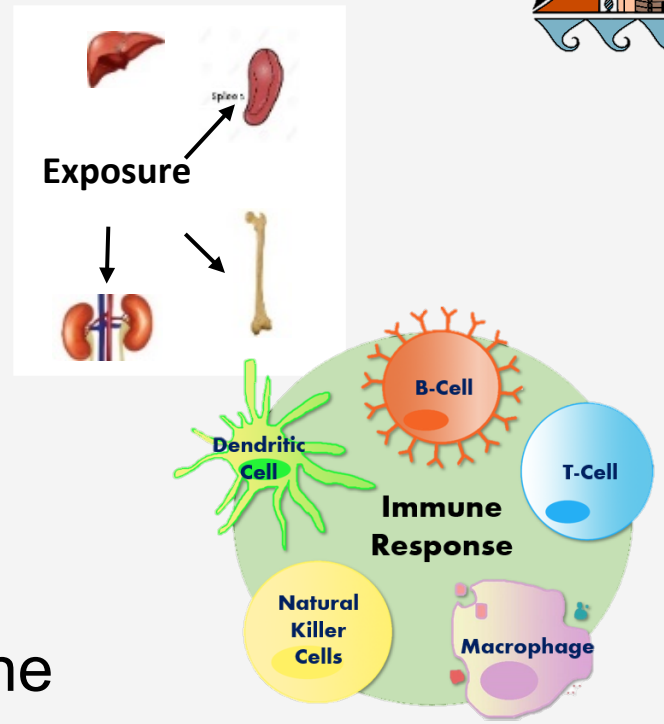
RESEARCH VOLUNTEERS NEEDED

COLLEGE OF PHARMACY

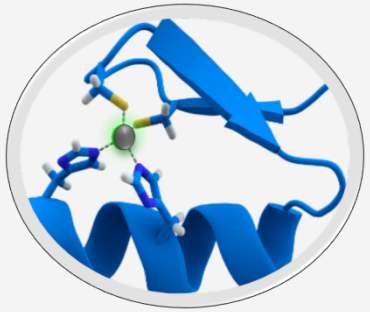
UNM METALS Superfund Center

Project Objectives – Biological Project 2

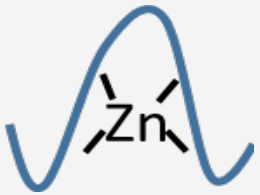
- **Aims 1 and 2**. Investigate drinking water exposures and potential mechanisms for immunotoxicity using animal models
  - Uranium
  - Uranium + Arsenic



- **Aim 3**. Establish the mode of Uranium/Arsenic interaction with PARP-1 (zinc finger domains), and the synergistic production of oxidative stress and DNA damage



PARP-1

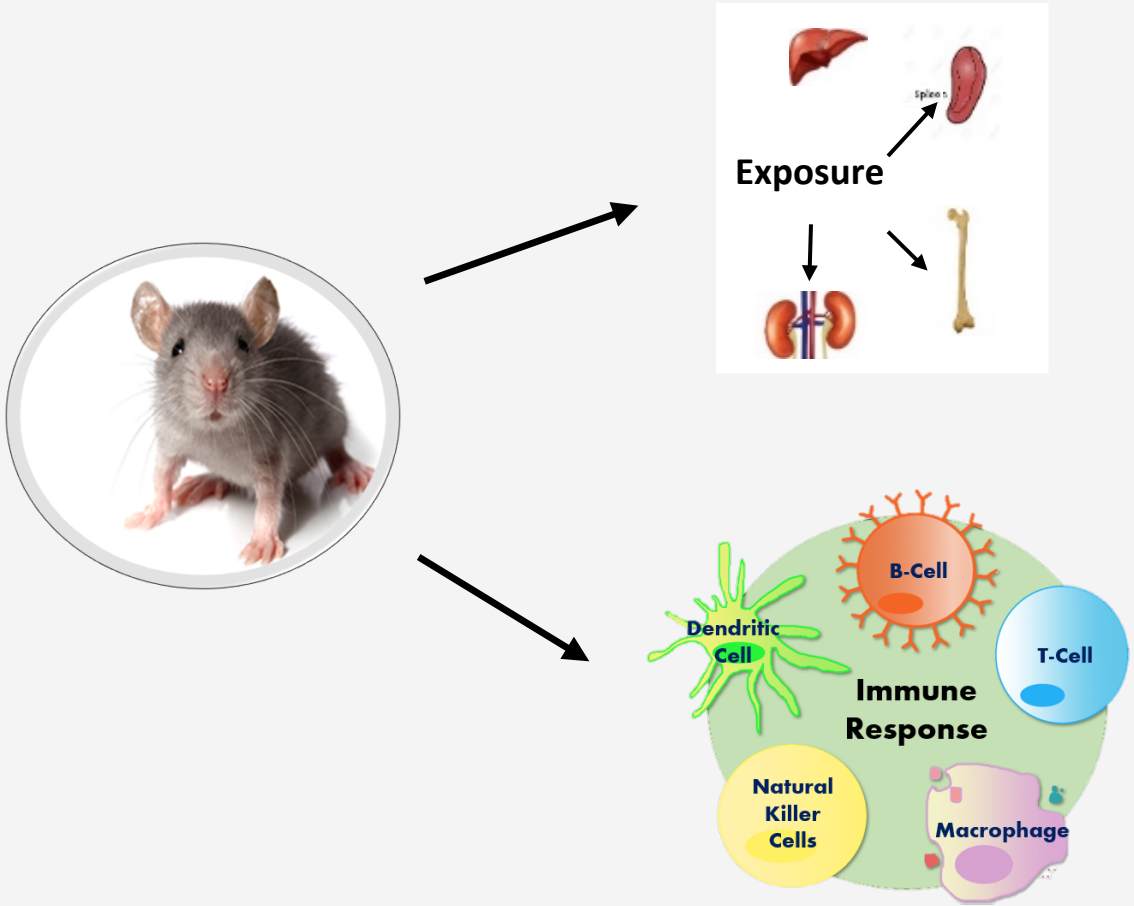


DNA Damage

Completed Our 1st Set of Animal Studies

60 Day – Oral Drinking Water Exposure
5 ppm Uranyl Acetate
50 ppm Uranyl Acetate

Oral exposure to mimic previous arsenic exposures



Key Results to date:

- **Expected distribution to bone & kidney**
- **Limited accumulation of U in immune targets**
  - **(blood, spleen, thymus, bone marrow)**
- **Subtle changes in immune endpoints**
  - **Decrease in macrophages & NK T-Cells (male-specific)**
  - **Consistent with population data: autoantibody production associated with U exposure – Male sensitivity**

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Lindsay Volk
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- **Laguna Pueblo**

And the Navajo communities of

- **Red Water Pond Road**
- **Blue Gap-Tachee**

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- **UNM College of Pharmacy**
- **UNM Comprehensive Cancer Center**

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