Phase II: Metal Exposure and Toxicity Assessment on Tribal Lands in the Southwest (UNM METALS)

Overall

José Cerrato PhD, Deputy Director (presenting)

Johnnye Lewis PhD, Director

Funding: NIH/NIEHS P42 ES025589 (UNM METALS)

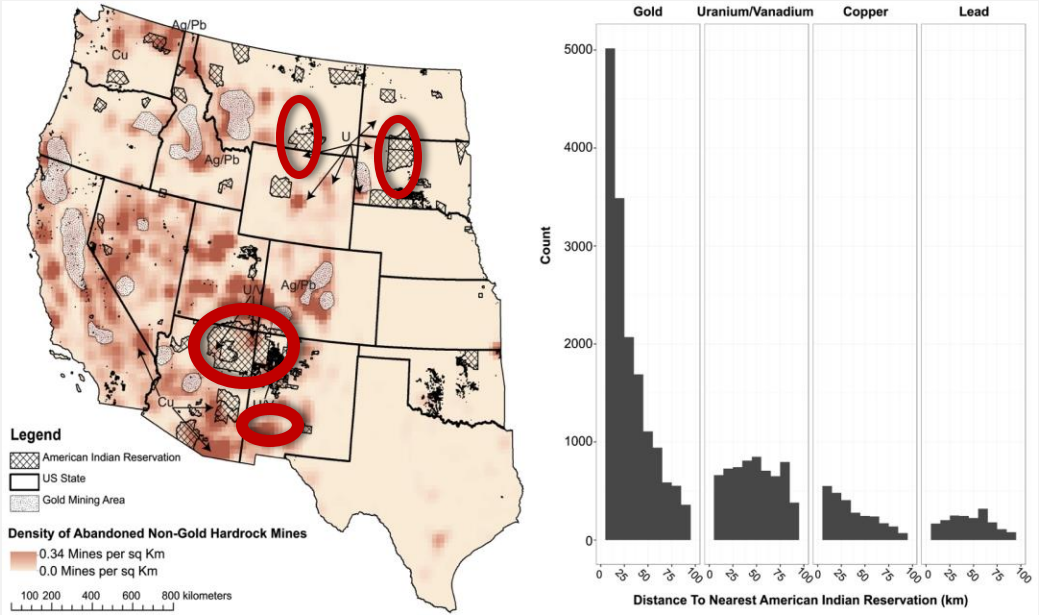
Why METALS?

Responding to decades of concerns about exposures to mine wastes

- >1/2 of Indigenous population is in 13 western US states where 161,000 abandoned hard rock mines also located.
- Traditional reliance on local resources increases risk for exposure.

Goals:

- Advance the basic science needed to understand the complex relationships between metal mixtures and toxicity.
- Understand, through multidirectional communication and translation, how culture and practice of all stakeholders affects exposures, toxicity, policy, and interventions.



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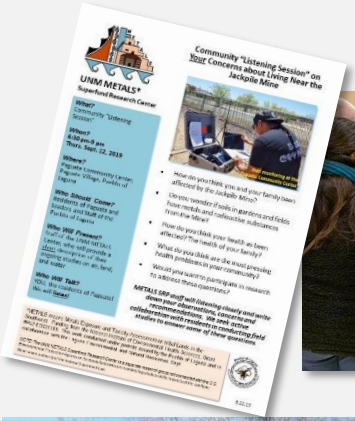
Science & Community Engagement



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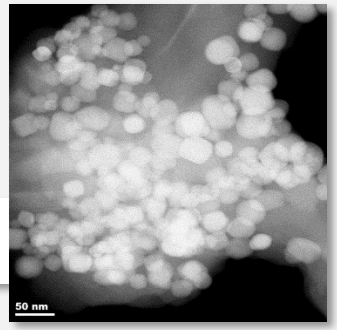
Progress from Phase I: Environmental Projects

- Discovered previously unrecognized nanoparticles of uranium-bearing minerals in mine waste samples, airborne dust, and weathering products.
- Definitive evidence of airborne transport of toxic metals mixtures in dust.
- Uranium and vanadium bearing minerals are found in particulate matter smaller than 2.5um → highly respirable.
- Plants with root-associated fungi can uptake uranium and arsenic → possible avenue for bioremediation.



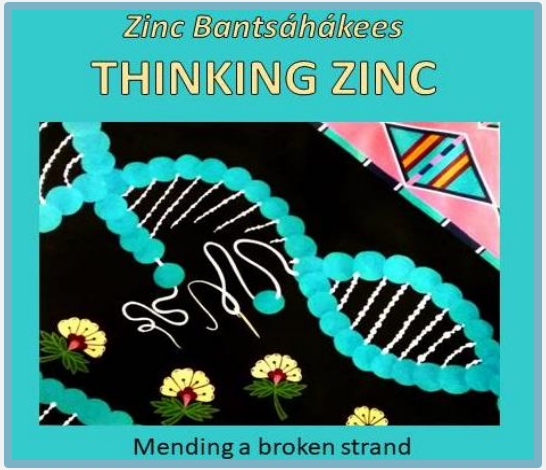
Transmission electron microscopy (TEM) image of uranyl vanadate nanoparticles (<100 nm) in mine wastes from Navajo Nation.

Progress from Phase I: Biological Projects

- Minimal uptake in gut of ingested U → high exposure of intestinal immune cells → Identified a new organ to target.

- Identified a gap in our understanding of how inhalation exposure to metal mixtures contributes to toxicity and health concerns.

- Appropriate cultural and community planning → strong participation in ongoing Thinking Zinc clinical intervention trial.



- Repeated biomonitoring indicates multiple exposure patterns, including episodic and to varying mixtures.

- Concerns remain about role of immune dysregulation: COVID-19 susceptibility & severity.

Specific Aims

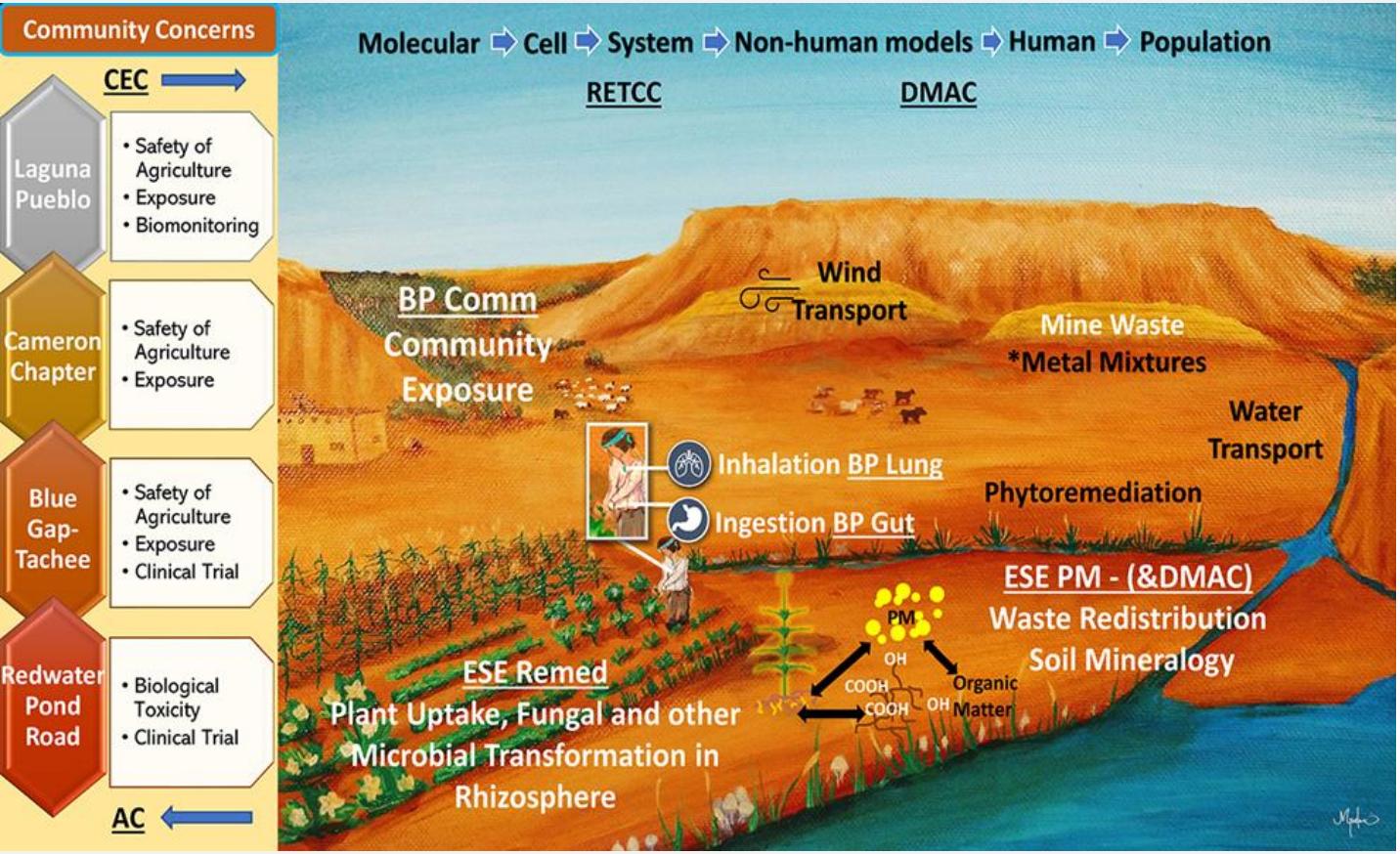
- **Specific Aim 1:** Understand mechanisms whereby exposures to U and metal-mixtures can reprogram systemic immune responses, and their direct and indirect modulation by environmentally relevant geochemical/mineralogic properties, mixtures, routes of exposure, and microbiological transformation.

- **Specific Aim 2:** Develop interventions built on Aim 1 and cultural beliefs to reduce risks, and use responses to interventions to iteratively inform biological and environmental studies.

- **Specific Aim 3:** Continue to ensure strong translation through ensuring research relevance through a) multi-directional communication with community partners, decision-makers and clinicians, and b) design and communication of stakeholder-informed multi-modal translation strategies.

- **Specific Aim 4:** Expand the role of METALS Center in bringing together a diverse institutional network to address a broader range of indigenous community issues, team science, and training.

Integration in Overall Center: Conceptual Model



Conceptual Model for METALS Phase 2

- integration of all Center components
- responsive to community concerns (CEC) while advancing the science of metal mixture toxicity, mobility, and remediation.
- RETCC trainees participate in all projects and cores;
- DMAC provides data management, analysis, and integrated modeling;
- AC supports translation for all to communities, regulators, clinicians.

Artwork: Mallery Quetawki, (Zuni) (AC)

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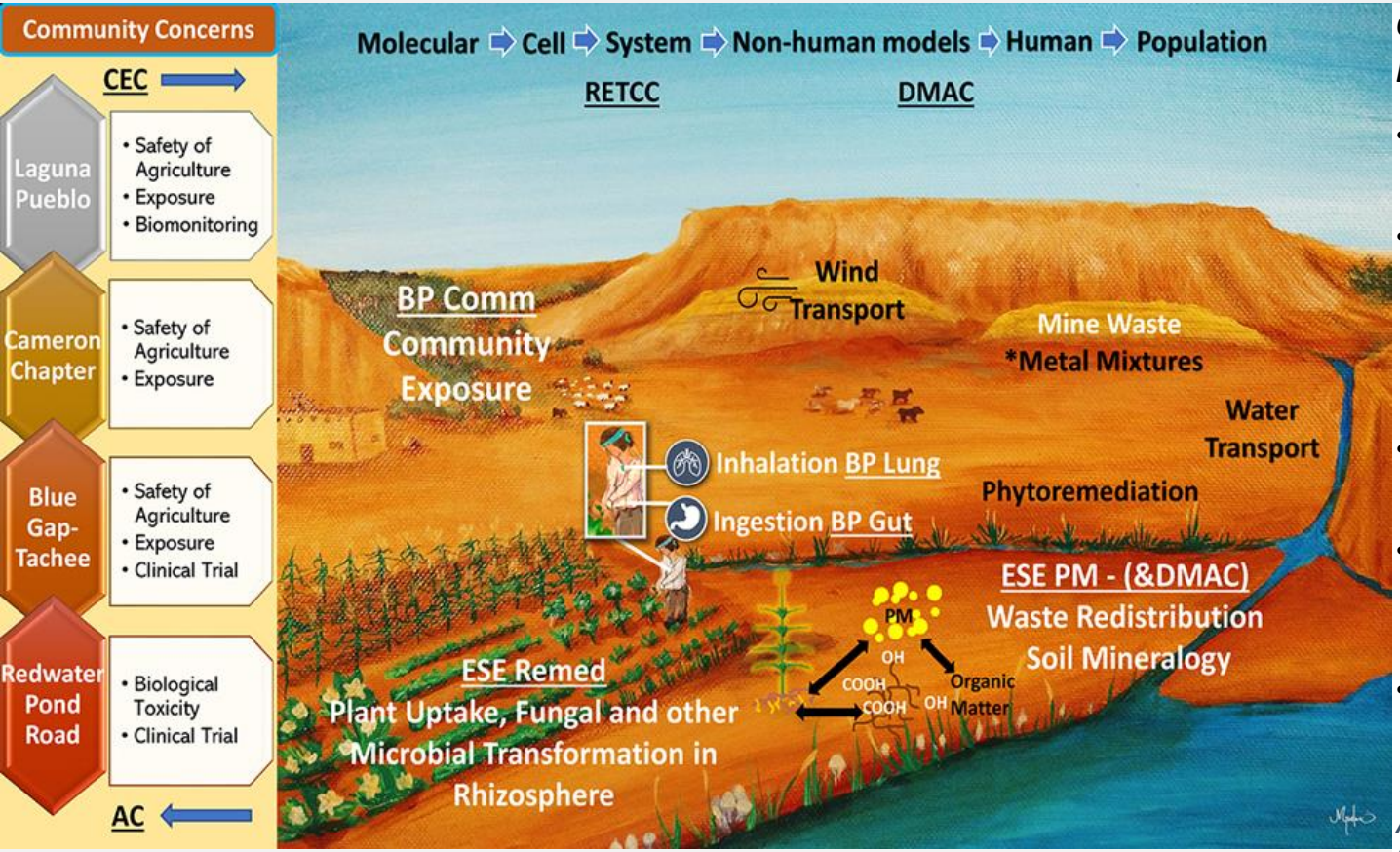
UNM Metals Environmental Projects

Anjali Mulchandani PhD

Project Co-Lead – Environmental Science and Engineering - Remediation (ESE-Remed)

Funding: NIH/NIEHS P42 ES025589 (UNM METALS)

Integration in Overall Center: Conceptual Model



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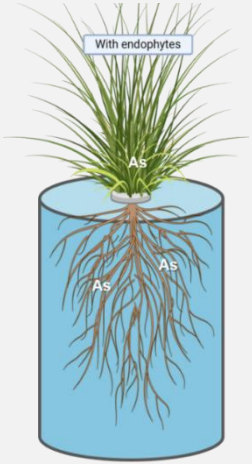
UNM METALS Environmental Projects

- **Goal – Assess amount and characteristics of metals in mine wastes, soils, and airborne particles associated with abandoned uranium mines.**
- **Goal – Assess concentrations of metals in agricultural products grown near abandoned uranium mines.**
- **Goal – Use naturally available materials and processes (e.g., limestone, bioremediation) to immobilize metal mixtures in waters, soils and wastes associated with uranium mines.**



A) Endophytic fungi

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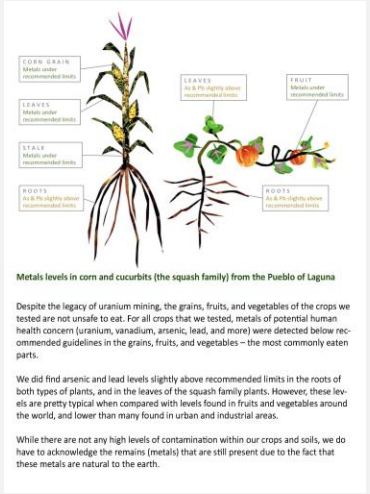
Science, Art, and Community Engagement



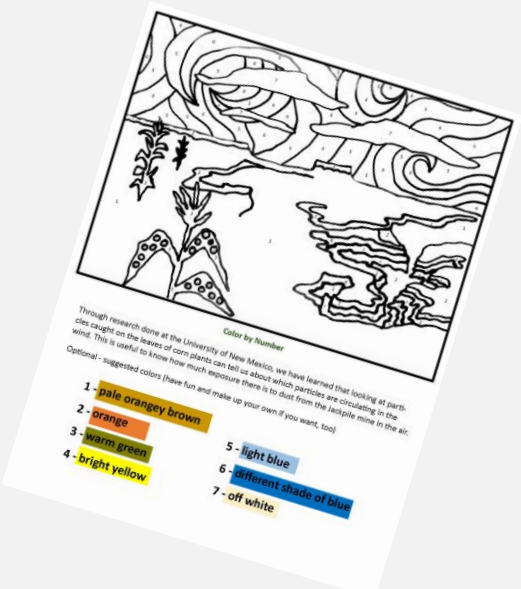
Metals levels in corn and cucurbits (the squash family) from the Pueblo of Laguna

Despite the legacy of uranium mining, the grains, fruits, and vegetables of the crops we tested are not unsafe to eat. For all crops that we tested, metals of potential human health concern (uranium, vanadium, arsenic, lead, and more) were detected below recommended guidelines in the grains, fruits, and vegetables – the most commonly eaten parts.

We did find arsenic and lead levels slightly above recommended limits in the roots of both types of plants, and in the leaves of the squash family plants. However, these levels are pretty typical when compared with levels found in fruits and vegetables around the world, and lower than many found in urban and industrial areas.

While there are not any high levels of contamination within our crops and soils, we do have to acknowledge the remains (metals) that are still present due to the fact that these metals are natural to the earth.

Artwork by Mallery Quetawki – Artist in Residence UNM METALS SRP



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Environmental Science and Engineering – Particulate Matter

"Role of Nanoparticles in Bioavailability and Transport of U and Co-occurring Metals in Particulate Matter from Agricultural Tribal Lands Affected by Mining Legacy".

UNM: Adrian Brearley PhD, Eliane El Hayek PhD, Joseph Galewsky PhD

Funding: NIH/NIEHS P42 ES025589 (UNM METALS)

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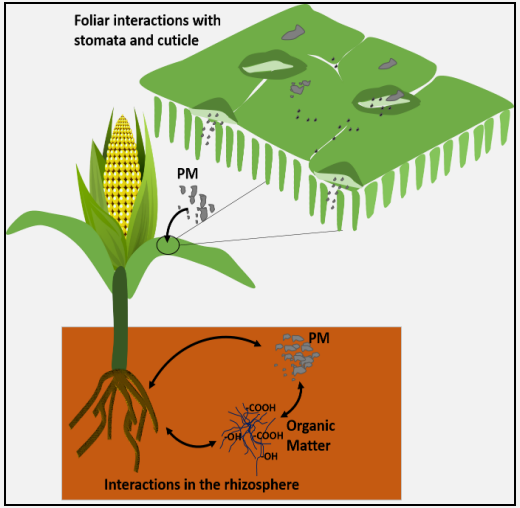
Research Aims

Project: Evaluate transport and bioavailability of uranium-bearing minerals in wastes, soils, and airborne particles associated with mines.

Aim 1: Understand the distribution, abundance, and physical characteristics of nanoparticles of U-bearing minerals in mine waste, soils, and airborne particulates associated with abandoned U mines.

Aim 2: Identify the mechanisms that control the bioavailability of U and co-occurring metals in agricultural soils and the physicochemical interaction of U and other metals with the rhizosphere and with the foliar part of plants.

Aim 3: Identify historical dust transport and depositional processes and pathways during active and post-mining phases and their potential impact on agricultural lands near abandoned mines.



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Environmental Science and Engineering – Remediation

"Bioremediation of metal mixtures by fungi communities associated with plants mediating adsorption and chemical precipitation".

UNM: Jose Cerrato PhD, Anjali Mulchandani PhD, Jennifer Rudgers PhD

Funding: NIH/NIEHS P42 ES025589 (UNM METALS)

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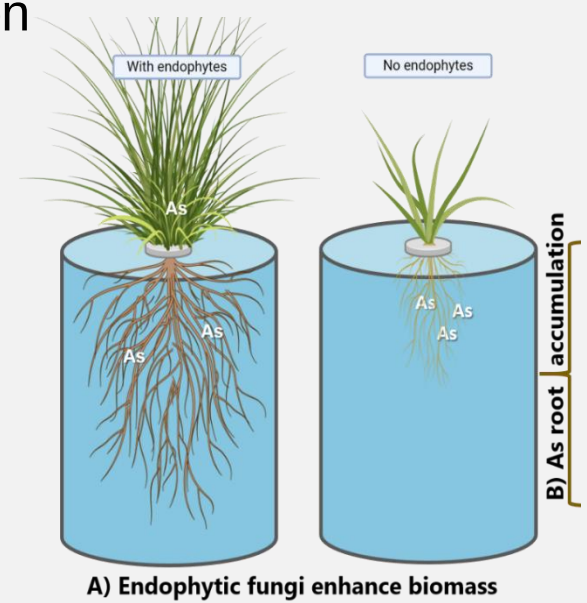
Research Aims

Project: Evaluate bioremediation using plants with root-associated fungi that can immobilize and precipitate metals in plant roots.

Aim 1: Identify mechanisms underlying the interaction between fungi and plants that mediate the adsorption and precipitation of metal mixtures (e.g., U, As, V).

Aim 2: Manipulate bioreactors containing fungi and plants under environmentally relevant water chemistries for remediation of metal mixtures.



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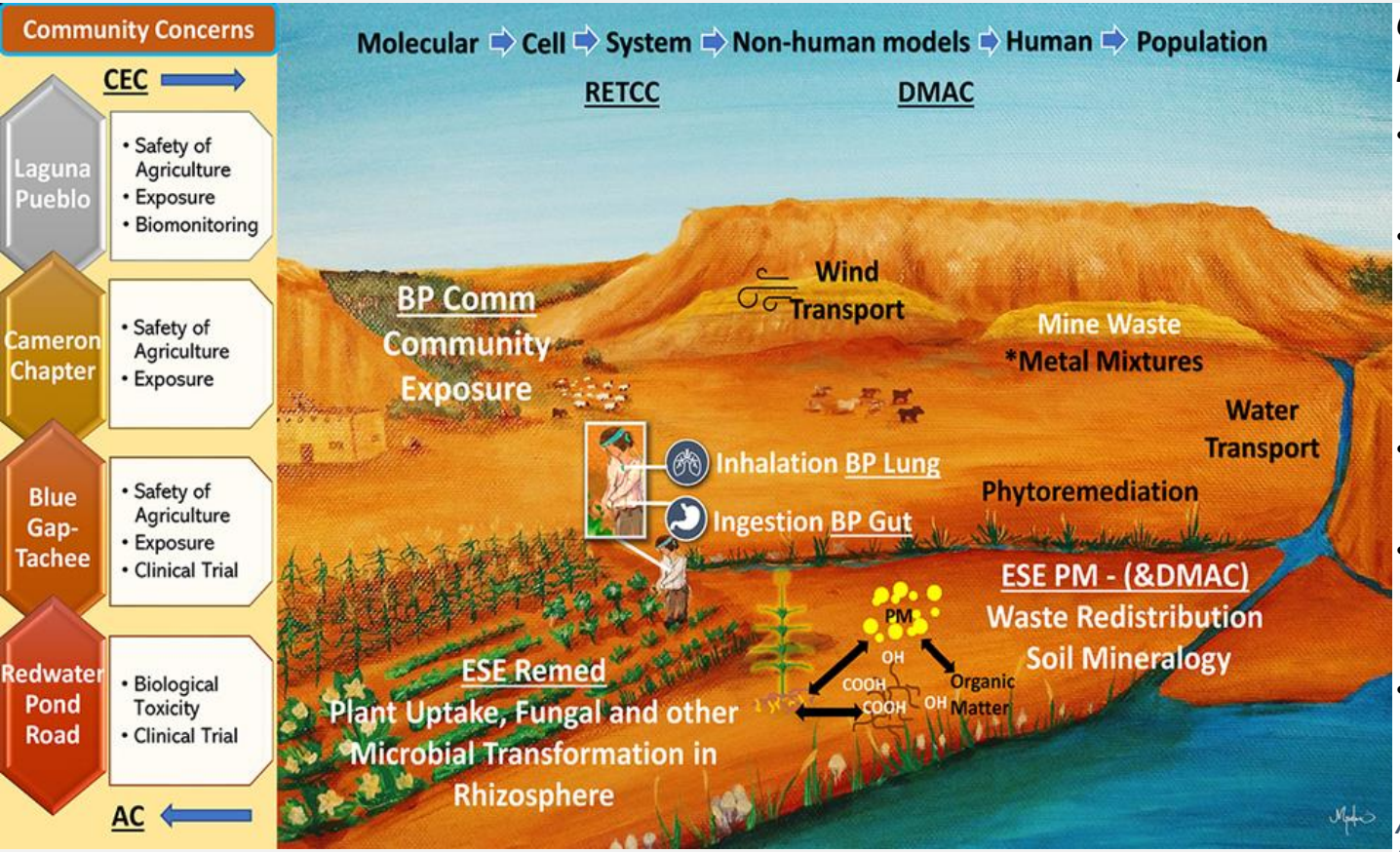
UNM Metals Biomedical Projects

Alicia Bolt PhD, Project Lead – Bioproject Lung (BP Lung)

Funding: NIH/NIEHS P42 ES025589 (UNM METALS)

Integration in Overall Center: Conceptual Model



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Artwork: Mallery Quetawki, (Zuni) (AC)

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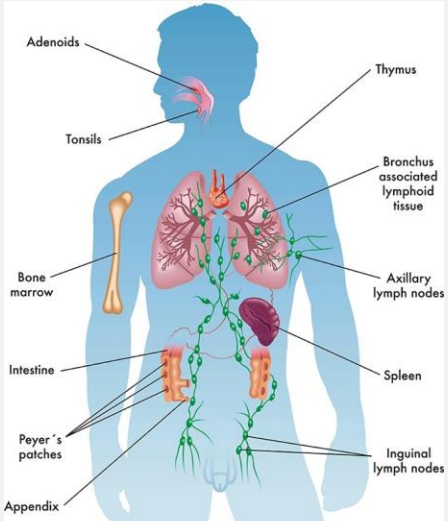
UNM METALS Biomedical Projects

- **Goal – Evaluate human exposure levels of metals due to living near abandoned uranium mine waste.**
- **Goal - Assess how exposure to abandoned uranium mine waste affects human health – Immune dysfunction.**
- **Goal - Understand mechanisms whereby exposures to metal mixtures can reprogram systemic immune responses contributing to disease.**



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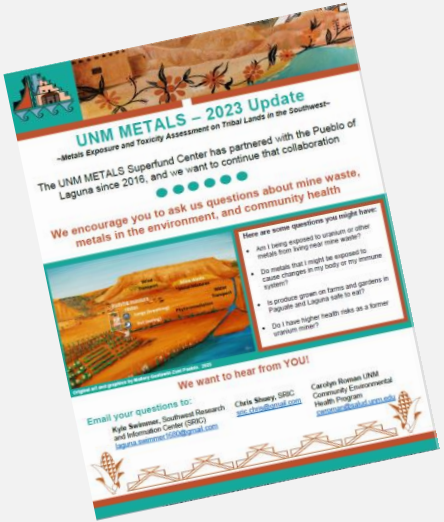
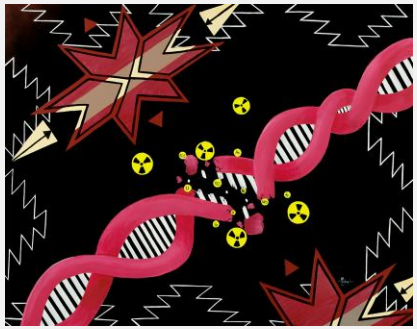
Science, Art, and Community Engagement



Artwork by Derek Capitan, UNM Student from Laguna Pueblo



Artwork by Mallery Quetawki – Artist in Residence UNM METALS SRP

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BP Lung – "Inhaled mine-site derived metal particulate matter drives pulmonary and systemic immune dysregulation".

UNM: Alicia Bolt PhD, Katherine Zychowski PhD, Sarah Blossom PhD, and Matthew Campen PhD

Funding: NIH/NIEHS P42 ES025589 (UNM METALS)

Research Aims

Project: Evaluate how exposure to metal mixture (particulates) contributes to immune dysfunction and the development of autoimmunity.

Aim 1: Ascertain drivers of immunological dysregulation in complex metal-bearing particulates using a high-throughput high-content imaging platform.

Aim 2: Mechanistically evaluate the role of circulating neutrophils as drivers of lung and systemic autoimmunity following mine-site metal PM exposure.

Aim 3: Assess airway inflammatory mediators in relation to residential abandoned mine-site proximity.

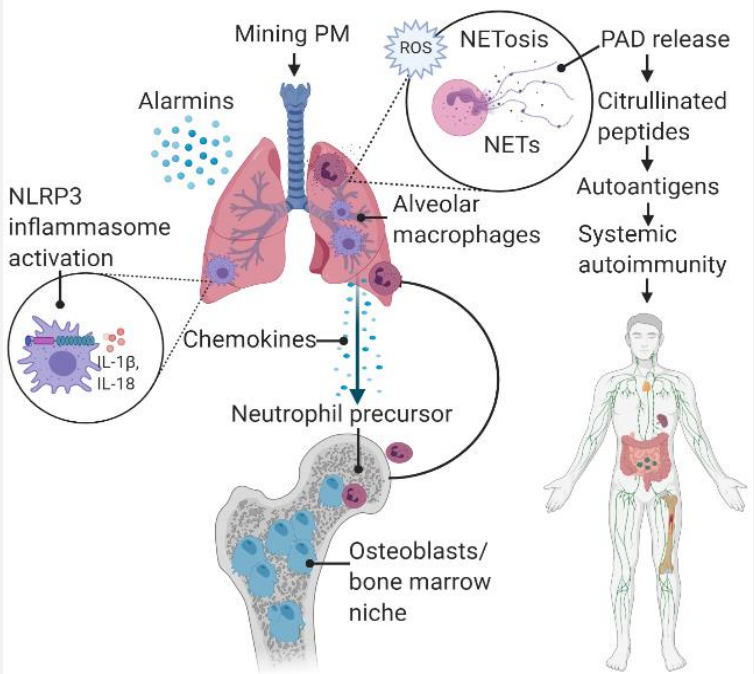

Figure 1. Summary of BP Lung Aims

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BP Gut – “Mechanisms of modulation of gut immunity by ingested uranium and mixed metal exposures”.

UNM: Eliseo Castillo PhD, Julie In PhD, and Fredine Koenig MPH

Funding: NIH/NIEHS P42 ES025589 (UNM METALS)

Research Aims

Project: Examining the impact of ingestible metals on the gastrointestinal tract.

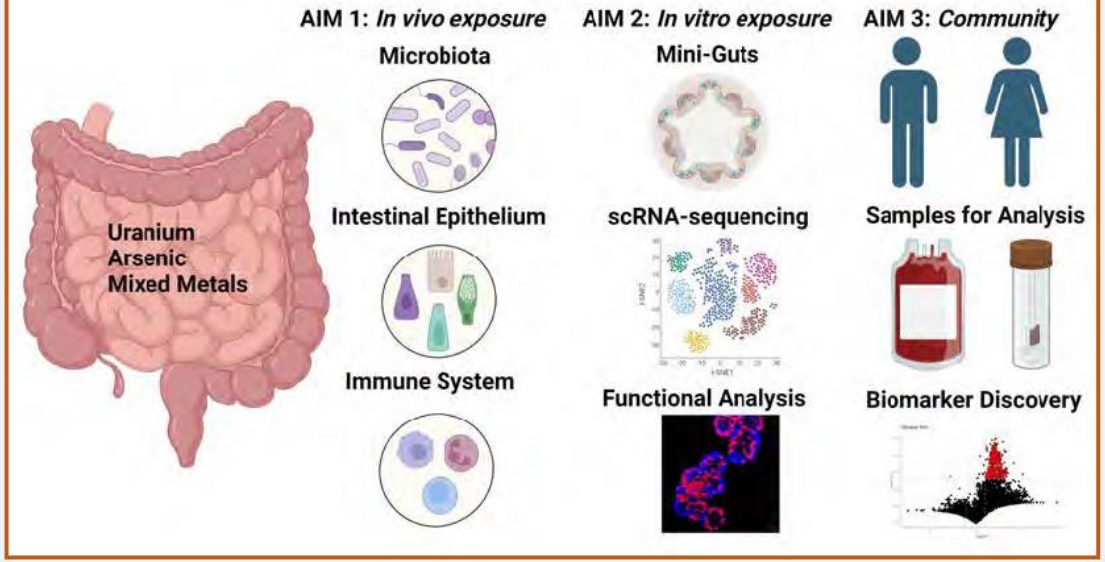
Questions

What are the health consequences of ingesting heavy metals?

- Inflammation?
- Metabolism?
- Changes in the gut microbiota?

Can we identify biomarkers in our laboratory models that can be assessed in the community?

Three aims to address our questions.



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BP Comm- “Biomarkers and mechanisms of metal and mixed metal exposures”.

UNM: Laurie G. Hudson PhD, Debra MacKenzie PhD, Jim Liu PhD, Esther Erdei PhD, Erica Dashner-Titus PhD

SRIC: Chris Shuey MPH, Paul Robinson MCRP, Sarah Henio-Adeky, Rose Dan

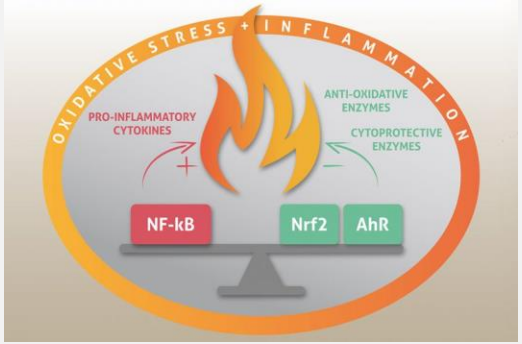
Funding: NIH/NIEHS P42 ES025589 (UNM METALS)

Research Aims

Project : Initiate health-related research activities (biomonitoring, biomarker analyses) in highly impacted communities. Facilitate populations studies in BP Lung and BP Gut. Conduct mechanistic studies to complements populations studies.

Aim 1: Delineate associations between metals detected by biomonitoring and biomarkers of oxidative stress, inflammation & immune modulation in partner communities.

Aim 2: Identify cellular mechanisms of community-relevant metals and metal mixtures on induction of oxidative stress, inflammation, immune cell responses, cytotoxicity, DNA damage and repair and potential mechanism-based mitigation by dietary antioxidants and/or metal micronutrients.



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SRIC
Chris Shuey, MPH
Paul Robinson, MCRP
Sarah Henio-Adeky
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Floyd Baldwin
Kyle Swimmer
Wilfred Herrera

IEI
Nancy Maryboy, Ph.D

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Scott Fendorf, Ph.D.
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Environmental Researchers
Abdul-Medhi Ali, Ph.D.
Jacquelyn Delp
Joseph Galewsky, Ph.D.
Ricardo Gonzalez-Pinon, Ph.D.
Eric Peterson, Ph.D.
Andrew Schuler, Ph.D.

Biostats and Data Management
Miranda Cajero
Ruofei Du, Ph.D.
Li Li, Ph.D.
Curtis Miller, Ph.D.
Elena O'Donald, Ph.D.

Research Translation/Admin
Carolyn Roman, Ph.D.
Mallery Quetawki
Carol Laselute

Biomedical Researchers
Tamara Anderson
Jessica Begay
Karen Cooper, Ph.D.
Erica Dashner-Titus, Ph.D.
Rama Gullapalli, Ph.D.
LaTasha James
Fredine T. Lauer, MPH
Jim Liu, Ph.D.
Nina Marley
Bernadette Pacheco
Robert L. Rubin, Ph.D.
Jodi Schilz, Ph.D.
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Katherine Zychowski, Ph.D

Internal Advisors
Christine Kasper, Ph.D., RN
Donald Godwin, Ph.D.
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Sara S. Nozadi, Ph.D.
Jennifer Ong, Ph.D.
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- ***Cameron***

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- **UNM Comprehensive Cancer Center**

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