

Colorado Industrial City Inspires Research Into Heavy Metals' Impact

Exploring an “important but poorly understood” topic, Tin Tin Su, PhD, is investigating how a combination of toxins found in Pueblo County’s soils interact to affect DNA—and cancer risk.

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In June 2022, [University of Colorado Cancer Center](#) member [Tin Tin Su](#), PhD, joined other CU faculty members on a “listen and learn” visit to Pueblo and other communities in southeast Colorado, where they heard from local residents as part of a university [Community Perspectives](#) outreach program.

“We just wanted to listen to people,” Su says. “And it struck me that I kept hearing from people about environmental toxins in the area and their concern about cancer.”

For more than a century and a half, the history of Pueblo has been intertwined with heavy industry. A railroad link to Denver opened in 1872. A steel mill – the first west of the Mississippi River – launched in 1881 and still operates today. In the early 20th century, several smelters processed ore mined nearby to produce lead, gold, and other metals. A coal-fueled power complex that opened in 1973 grew to be the largest energy producer in Colorado.

No wonder Pueblo has acquired the nicknames “Steel City” and “Pittsburgh of the West.” But with the city’s industrial heritage has come a legacy of environmental contamination and health impacts.

“This has been a long-running topic of conversation and concern in Pueblo, going back decades,” says Su, a co-leader of the CU Cancer Center’s [Molecular and Cellular Oncology Program](#) and a professor in the [Department of Molecular, Cellular, and Developmental Biology](#) at CU Boulder.

[A 2006 study](#) by James Carsella, PhD, and others at Colorado State University Pueblo reported higher-than-average levels of various heavy metals in Pueblo’s topsoils, including in low-income and minority residential communities, with much of it coming from industrial activity.

An area of about 2,000 homes around a long-closed smelter is a [Superfund cleanup site](#).

Pueblo County now has [one of the highest cancer incidence rates](#) in Colorado as well as higher-than-average rates of heart disease and respiratory ailments. In 2018, Carsella co-authored [a](#)

[study](#) based on tests of 240 children in Pueblo showing they were three times more likely to have elevated levels of lead in their blood than children nationwide, especially those who lived near smelter sites, even though the smelters closed more than a century ago.

Seeking an NIH grant

Inspired by her 2022 visit, and after learning more about Carsella's groundbreaking work, Su and [her lab](#) are investigating the health implications of heavy metals in Pueblo.

Following preliminary work funded by a \$50,000 CU Cancer Center pilot grant, Su is now seeking major funding from the National Institutes of Health in collaboration with Carsella to further explore how the combination of three heavy metals – lead, arsenic, and cadmium – found in high concentrations in Pueblo's soils can impact genomes, the genetic coding of people. She hopes her grant will be reviewed in March.

Su says that, individually, lead, arsenic, and cadmium are known to have harmful health effects, including increased risk of cancer, particularly [lung](#) and [brain](#) cancers. For example, “there has been a lot of studies of lead, especially on the development of the nervous system in children, and we all know about the risk of lead poisoning from house paints. There's less known about how lead affects our genomes, which is my field.”

Lead can inhibit enzymes that reduce reactive oxygen species (ROS) – molecules that can cause cellular damage and are involved in the development of cancer. Arsenic can impede enzymes that help repair DNA. And cadmium can catalyze ROS production.

“But when I started reading about it, I found that while there have been many studies on individual metals, there haven't been many on the metals in combination as they are typically found in the environment,” Su says.

Su says that researchers who study environmental toxins often “focus on their favorite toxin and study it in depth. Looking at combinations is rare. It's challenging; it's daunting. You may spend your lifetime studying lead, and that's complicated enough. Now you're throwing in one or two more metals, and you say, ‘Oh, no, too complicated!’ But hopefully, combination studies will not only tell you how things work but may help us set more realistic safety levels for metals. Studying toxins in combination has a lot of public health policy implications.”

She adds: “I know from my work trying to develop cancer drugs that there are lots of drug-drug interactions. When you have two or more materials in combination, the synergy can have more of an effect than you expect, or one can reduce the effect of another. We're applying that idea to studying heavy metals.”

Lining cells and insect larvae

Su aims to assess the heavy metals' combined effects on genomes using two experimental models.

One model involves human epithelial cells, which form a protective lining on skin, organs, and other body surfaces. The other model involves larvae of [Drosophila fruit flies](#), a widely used method of assessing the effects of toxins because of genetic similarities to humans. Much of Su's previous research work over a quarter-century involves Drosophila, and she co-founded Boulder-based [SuviCa Inc.](#) to work on translating basic research findings on Drosophila into small molecule cancer therapeutics.

In the Pueblo study, Su and her colleagues will expose the human epithelial cells and Drosophila to various combinations of lead, arsenic, and cadmium, and then analyze for cell viability, DNA damage, increased ROS production, and other impacts.

"These experiments will be designed to determine whether metal mixtures produce different damage profiles or phenotypic effects" – changes to an organism's characteristics produced by environmental interaction – "than what is expected from a simple sum of single exposures to each of these metals," Su writes in her grant application.

A complicating factor, Su notes, is the presence of "good" metals such as zinc and calcium in Pueblo soils alongside "bad" heavy metals. "We don't know if they can reduce the effect of bad metals or even make them worse. And there are also plastics, 'forever' chemicals and so on. All of that needs to be studied."

In her grant application, Su says that "what we learn will serve as the starting point for future studies on the genotoxic effect of heavy metal combinations, an important but poorly understood area of study with high biomedical significance."

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