THE UNIVERSITY OF ARIZONA

Southwest Environmental Health Sciences Center

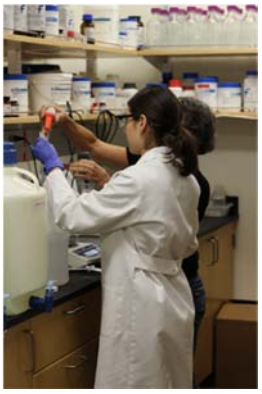
SWEHSC

September 2018

SWEHSC Engagement Core Summer Programs Reach 1000 Youth

Community Engagement Core

This summer the Southwest Environmental Health Sciences Center Community Engagement Core ran two summer programs and provided activities at three tribal and two university programs. During the programs described below, students were given the opportunity to visit different areas of campus, learn about environmental health, and some even got to work in labs on campus and get hands-on STEM experience!



Steps 2 STEM

A total of 14 students were selected into the Steps 2 STEM High School Research Internship Program. The Steps 2 STEM interns spent four weeks working in labs across campus. This opportunity gave the interns a chance to experience what a STEM career could look like.

Environmental Scholars

This summer, 20 high school students participated in Environmental Scholars. The program's goal is to expose students who are passionate about the environment to a hands-on learning experience with environmental science lab and field experiments.

STEM RiSE

SWEHSC was also able to participate in the STEM RiSE program. Alex Benevidas, an undergraduate intern at SWEHSC, led middle school students in activities focused on environmental health and toxicology.

Special thanks to all of our partners and supporters for making this summer a success!

Southwest Environmental Health Sciences Center

As the only NIEHS supported center located in the desert Southwest, SWEHSC strives to become a leader in environmental health issues associated with at-risk populations residing in arid environments. Our mission is to facilitate and implement innovative research aimed at understanding the mechanisms underlying the modulation of human disease risks due to environmental exposures among populations living in arid environments. The themes of the SWEHSC are based on the unique environment and distinctive populations in the desert Southwest, which are unlike any other in the US yet similar to many other global environments. The desert Southwest is the only US region that adequately represents much of the world's arid habitats.

Upcoming Events

Learn more about advanced EM techniques October 23, 2018, Skaggs 325 (see page 3 for more information).

Save the Date!

The annual SWEHSC Showcase will be held on Monday, January 14 from 2:00 – 4:00 pm.

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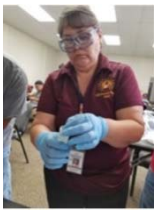
SWEHSC Investigators Share Water Sampling with Diné College

Diné College and NN CHR Water Sampling



Approximately three years after three million gallons of acid mine drainage were accidently released from the Gold King Mine affecting the San Juan River of the Navajo Nation, the Gold King Mine Spill Diné Exposure Project (originally funded by a NIEHS Time Sensitive R21) consisting of UA researchers, Navajo Nation Community Health Representatives (CHRs) and Diné College interns continue to collaborate. From June 12th – 14th, 2018 the University of Arizona team, 14 Diné College TCUP interns, and 7 CHRs met at the Diné College Campus North to receive training in environmental health, learn to collect water samples along the river and irrigation canals, and engage in discussion on improving emergency response and results communication following a spill. Teams consisting of 3-5 interns, 1 CHR, and 1 UA team member set off to collected water samples, GPS location, and water parameters using scientific equipment while the CHRs did the same protocol using


locally available materials (e.g. mason jars, fish tank pH strips, pool thermometers). “Community partners are usually involved in the recruitment and sampling efforts to achieve study goals, with our multi-directional partnership we wanted to involve the CHRs and the interns in not only the sample collection but also in the steps that come after such as sample processing and data analysis” - Dr. Paloma Beamer (RFG1). With this in mind the UA team led a training to teach the students and CHRs how to process the water samples for analysis at Northern Arizona University. The students and CHRs learned how to filter and how to preserve the samples for transportation. Additionally, the students and CHRs also learned how to prepare and format the data they collected. Reflecting on the experience one student noted, “Everyone in this room is inspiring, they give time and dedication to the community which is something we can all take back home” - Diné College TCUP intern. To date the Gold King Mine Spill Diné Exposure project has trained over 80 students and 35 community members, highlighting the importance of diversifying the academy and training the next generation of environmental health scientists.

The goal of Research Focus Group 1, Environmental Exposures in Underserved Southwest Populations, is to partner with Indigenous, Hispanic, and rural communities in the Southwest to determine the contribution of chemical and other environmental exposures to health inequities and to support efforts to eliminate these disparities.

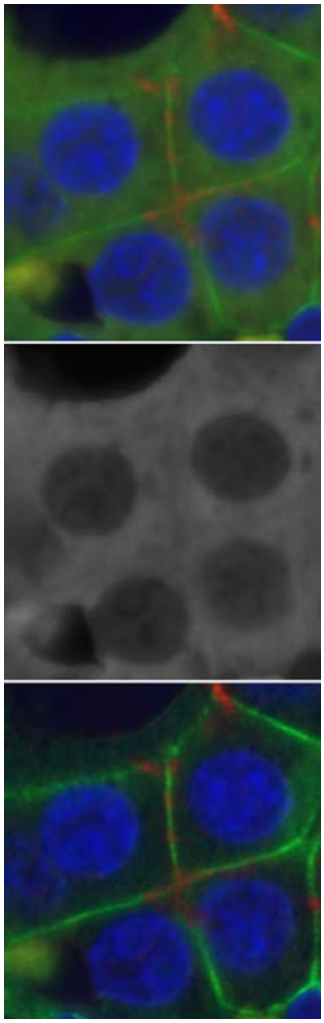
Imaging Facility Facilitates Novel Research Using Transmission Electron Microscope Upgrades

Overcoming autofluorescence

Tissues that contain high levels of lipid (brain, liver, etc.) have a tendency to be highly autofluorescent. This background fluorescence can be very bright and make it difficult to see specific fluorescence staining, particularly in the "green" channel (FITC, Alexa 488, GFP, etc.). Working with Dr. Nathan Cherrington's lab (RFG3) over a number of years the Cellular Imaging Facility Core had referred students and staff to several techniques that were supposed to reduce this background fluorescence, however, none the techniques seemed to work for them. Because the emission spectra of autofluorescence tends to be very broad, even using red-shifted fluorochromes the lab had problems with background fluorescence. Sitting at the fluorescence microscope with them one day we noticed that the pattern of the fluorescence in the green channel (which had been abandoned for use with specific labeling) was identical to the background in the red channels (e.g., rhodamine and CY5). Using image processing we were able to subtract the background (using the image from the otherwise unused green channel) from the red and far-red channel images and create cleaner, more convincing images of the staining in each of those channels. The image processing protocol was included in the methods section of the paper.

Dzierlenga, A. L., Clarke, J. D., and Cherrington, N. J., (2016) Nonalcoholic Steatohepatitis Modulates Membrane Protein Retrieval and Insertion Processes, Drug Metab Dispos 44 (11) 1799-1807, DOI: https://doi.org/10.1124/dmd.116.071415

The Cellular Imaging Facility Core is now working with Dr. Cherrington's lab to add another biomarker to the images by dropping the DNA stain (nuclei) and replacing it with a biomarker specific blue secondary. The one advantage to the autofluorescent channel image (middle image) is that it clearly shows where the nuclei are located.



TOP: Original microscope image, Hoechst 33342 (Blue, nuclei), Alexa 568 (Green, pan-cadherin), Alexa 647 (Red, Mrp2)*
MIDDLE: Autofluorescence
BOTTOM: Processed image with greatly reduced background

Note: because fluorescence images are typically captured with a greyscale camera, in these images the displayed green color would normally appear red to the human eye, and the bright red channel would appear to be a dark red. The colors were reassigned for visualization purposes.

Upgrades for the Biological TEM

The biological transmission electron microscope (FEI Tecnai Spirit, Imaging Core – LSN) has recently received an upgrade as part of an internal RDI Core Enhancement grant (Dr. Nancy Horton, PI). The microscope adds a more sensitive, bottom mounted 8Mpix camera in addition to the existing side mounted camera used for routine TEM image capture. The new camera, in combination with newly installed software, allows the microscope to better correct for aberrations and to perform autofocus, allowing the user to do single molecule TEM and tomography much more easily and accurately. This new capability allows UA users to screen samples, partially in preparation for using the CryoTEM at ASU (https://le-csss.asu.edu/equipment/titan-krios-fei). CryoTEM has become the go-to method for determining chemical structure such as the three dimensional structure of protein complexes, membrane proteins, and viruses. In many cases CryoTEM has proved to be more useful than x-ray crystallography. Sample preparation for CryoTEM is challenging, so having a screening option at the UA ensures more productive use of the instrument at ASU.

Learn more about advanced EM techniques

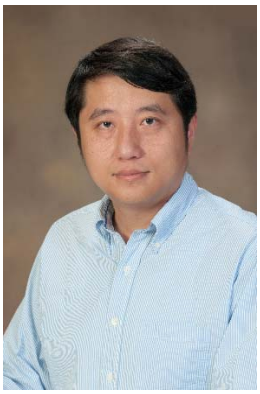
The Cellular Imaging Facility Core, in collaboration with the RDI Imaging cores, will be hosting a symposium (October 23, 2018, Skaggs 325) by electron microscope vendor FEI that will include presentations titled:

- Recent Advances in Cryo-EM; An Essential Technology for Structural Biology
- New Perspective on Cellular Organization with Serial Block Face Imaging and 3D Analysis
- Air Particulates for SEM/EDS Analysis

For more information, see: http://microscopy.arizona.edu/event/new-research-approaches-em

SWEHSC Investigators Collaborate on new NIEHS Grant

Effects of Retinoids on Augmentation of Club Cell Secretory Protein



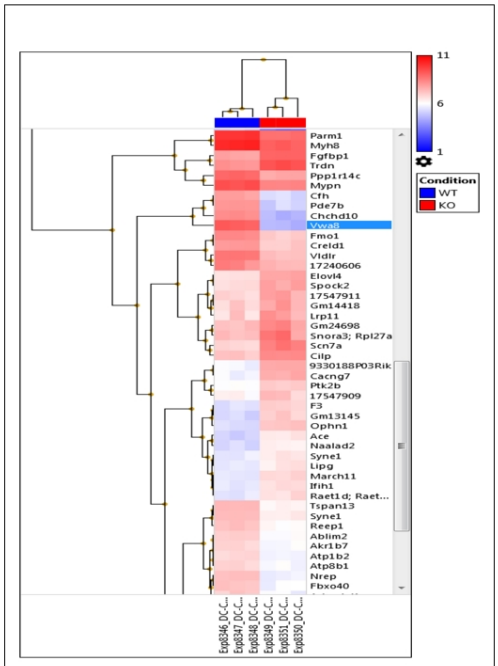
Club cell secretory protein (also called CC16 and CC10) is a protein mainly produced in the airways that has been shown to have anti-inflammatory and protective properties in the lung. Therefore, molecules that augment CC16 production may be of potential interest for prevention or therapeutic use in lung diseases, including asthma and chronic obstructive pulmonary disease (COPD). In a study published in the American Journal of Respiratory and Critical Care Medicine, Drs. Yin Chen (RFG2) and Stefano Guerra (RFG2) found that retinoic acid – an active metabolite of vitamin A – increased CC16 production in cultured human bronchial epithelial cells from both normal individuals and COPD patients. Further, they found that, in 71 subjects who participated in a randomized placebo-controlled clinical trial, treatment with vitamin A over 12 months resulted in a significant increase of their circulating CC16 levels. In a recently funded NIEHS project, they also found that retinoic acid, presumably through CC16 elevation, was able to mitigate lung inflammation induced by arsenic exposure. These findings warrant further studies to evaluate the value of vitamin A dietary intake and its potential pharmacological supplementation to prevent and/or treat early stages of COPD and other lung diseases caused by exposures to environmental toxicants.

The goal of Research Focus Group 2, Environmental Lung Diseases, is to promote interdisciplinary research into the mechanisms by which environmental agents affect lung structure and function and lead to or exacerbate disease.

Genomics Facility performs transcriptome gene expression analysis

Genomics Facility Core

Drs. Lawrence Mandarino (RFG1) and Dawn Coletta in the Division of Endocrinology, Diabetes and Metabolism, Department of Medicine are characterizing the role of a protein VWA8 (von Willebrand factor A domain containing 8) in liver cells. Based on data from Dr. Mandarino's lab, they hypothesized that VWA8 would be involved in fuel oxidation and affect pathways related to mitochondrial biogenesis. The researchers set out to determine which cellular pathways would be altered following CRISPR knockout of VWA8 in AML 12 mouse liver cells utilizing proteomic and genomic approaches. The Genomics Facility Core performed whole transcriptome gene expression analysis utilizing Affymetrix GeneChips and RNA provided by the investigators. The results corroborated those found by proteomic methods, which indicate that loss of VWA8 does indeed affect metabolic pathways related to mitochondrial biogenesis.



Hierarchical clustering of gene expression changes between 3 replicate analyses of wild-type and knockout AML12 cells following CRISPR knockout of the VWA8 genes (highlighted in blue). Relative expression is shown with blue indicating low expression and red indicating high expression. Wild-type, left three replicates; VWA8 knock-out, right three replicates.