Ushering in a New Era of Quantitative Elemental Mapping and Single Cell Analysis

Tom O'Halloran
Director, Elemental Health Institute
Michigan State University
Departments of Microbiology and Molecular Genetics (MMG) and Chemistry

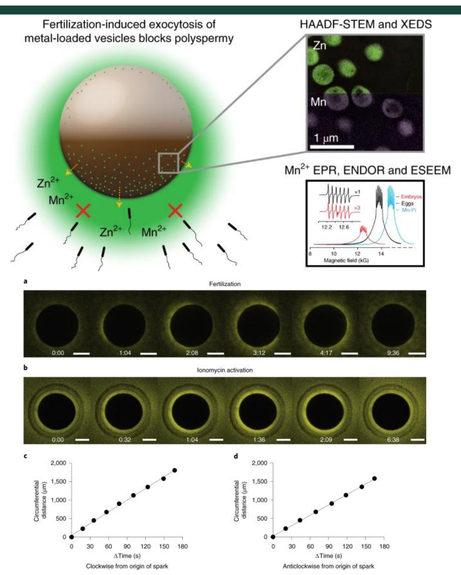
Elemental Health Institute (EHI)

The goal of this P41 National Research Resource is to develop novel analytical and imaging technologies that enable biomedical research teams to image changes in metal localization in a quantitative manner from the cellular level to tissue and whole animal. The Quantitative Elemental Mapping for the Life Sciences (QE-Map) will integrate multiple technologies to create transformative approaches to answer compelling biological questions about the functions of metals and other essential elements in health and disease.

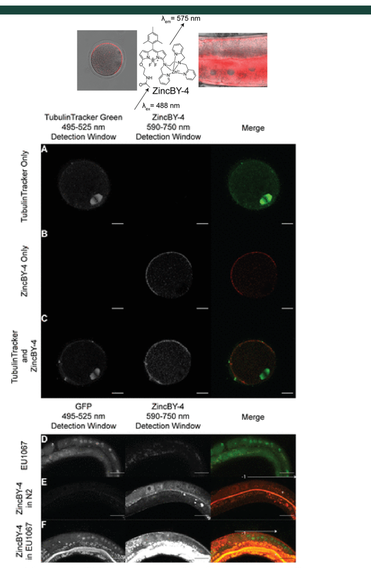
Seth Garwin, PhD
Research Associate
MMG
garwinse@msu.edu

Kiwon Ok, PhD
Research Associate
MMG
okkiwon@msu.edu

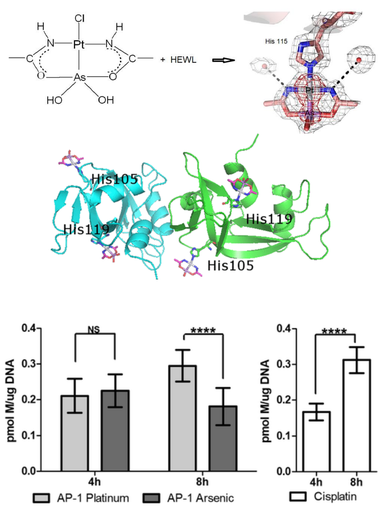
Bong Jin Hong, PhD
Research Assistant Professor
MMG
hongbong@msu.edu



*Zinc is released following both fertilization and chemical activation of a Xenopus egg. **a**, Zinc efflux following fertilization of a Xenopus egg. Images are representative of 14 eggs from four separate frogs over four independent experiments. **b**, Zinc efflux following parthenogenic activation of a Xenopus egg by ionomycin. Images are representative of 12 eggs from three separate frogs over three independent experiments. Scale bars, 500 μm. **c**, Representative plot of the circumferential distance from the origin of the zinc spark at which half-maximal fluorescence is measured over the time since the start of the spark, travelling clockwise from the origin. **d**, Representative plot of the circumferential distance from the origin of the zinc spark at which half-maximal fluorescence is measured over the time since the start of the spark, travelling anticlockwise from the origin.*



Simultaneous excitation of ZincBY-4 and a green-emitting fluorophore in the MII mouse egg and C. elegans worm. (A–C) Detection of zinc and tubulin using a single excitation wavelength in a 2 μm optical section of a MII mouse egg. Both ZincBY-4 (50 nM, red) and TubulinTracker Green (240 nM, green) are excited at 488 nm. Fluorescence images of a live mouse egg that was stained only with TubulinTracker Green (A), only ZincBY-4 (B), or both ZincBY-4 and TubulinTracker Green (C). Scale bar is 20 μm. (D–F) Detection of zinc and tubulin using a single excitation wavelength in C. elegans. EU1067 contains a GFP::histone and GFP::tubulin fusion, and N2 is the wild type. Both ZincBY-4 (50 μM) and GFP are excited at 488 nm. Fluorescence images show nonstained EU1067 worms (D), ZincBY-4 stained N2 worms (E), and ZincBY-4 stained EU1067 worms (F). The −1 is above the −1 oocyte with the arrow indicating the direction of the earlier oocytes. Scale bar is 50 μm. The asterisk (•) indicates the gut and the surrounding gut granules.



MDA-MB-231, triple negative breast cancer cells, were incubated with AP-1 or cisplatin for 4 and 8 h, and the extent of adduct DNA formation was determined by ICP-MS, where the amounts of platinum and arsenic were in pmol M/μg DNA (M = Pt or As). Results shown are an average of at least five independent experiments. The analysis of one-way ANOVA using Bonferroni multiple comparisons has shown that the difference in the amount of platinum and arsenic in DNA adducts in the 8 h experiment is highly significant ($p \leq 0.0001$).

Funding Sources:
P41GM135018
U54CA193419
R01GM115848

Quantitative Elemental Mapping for the Life Sciences (QE-Map)

The goal of this P41 National Research Resource is to develop novel analytical and imaging technologies that enable biomedical research teams to image changes in metal localization in a quantitative manner from the cellular level to tissue and whole animal. The Quantitative Elemental Mapping for the Life Sciences (QE-Map) will integrate multiple technologies to create transformative approaches to answer compelling biological questions about the functions of metals and other essential elements in health and disease.

PI: Prof. Tom O'Halloran
High Throughput ICP-MS Lead
ohallor8@msu.edu

Prof. Hao F. Zhang
Photoacoustic Imaging Co-Lead
hfzhang@northwestern.edu

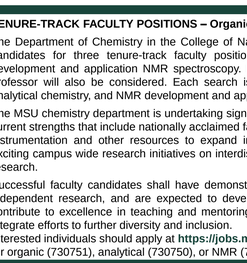
Prof. Chris Jacobsen
SXRF Cryo-Imaging Lead
c-Jacobsen@northwestern.edu

Prof. Cheng Sun
Photoacoustic Imaging Co-Lead
c-sun@northwestern.edu

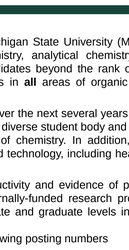
Laser Ablation Inductively Coupled Plasma Mass Spectrometry (LA-ICP-MS)

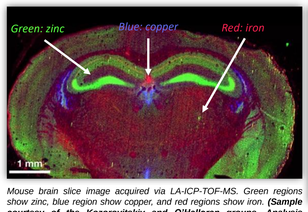
Develop multi-element 2D and 3D imaging of single cells and tissues using LA-ICP-MS

LA-ICP-TOF-MS

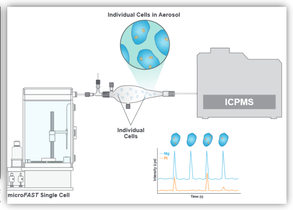


Single Cell ICP-TOF-MS





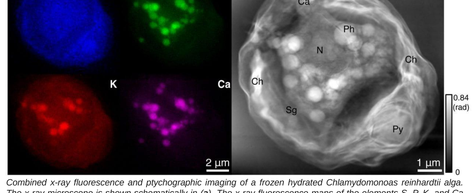
*Mouse brain slice image acquired via LA-ICP-TOF-MS. Green regions show zinc, blue region show copper, and red regions show iron. **(Sample courtesy of the Kozorovitskiy and O'Halloran groups. Analysis software from Tofwerk AG).***

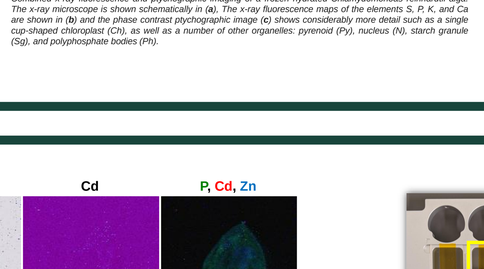


Single Cell ICP-MS schematic

Synchrotron X-Ray Fluorescence Microscopy (SXFM)

Increasing the sensitivity and throughput of SXFM for single cell and tissue analysis

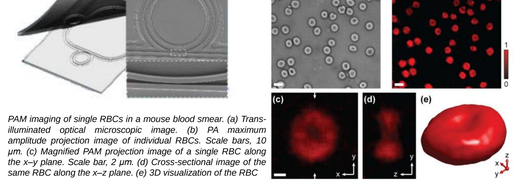


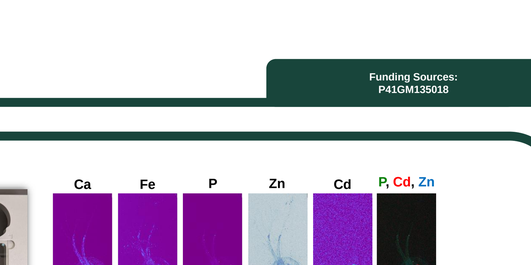


*Combined x-ray fluorescence and ptychographic imaging of a frozen hydrated Chlamydomonoas reinhardtii alga. The x-ray microscope is shown schematically in (**a**), The x-ray fluorescence maps of the elements S, P, K, and Ca are shown in (**b**) and the phase contrast ptychographic image (**c**) shows considerably more detail such as a single cup-shaped chloroplast (Ch), as well as a number of other organelles: pyrenoid (Py), nucleus (N), starch granule (Sg), and polyphosphate bodies (Ph).*

Photoacoustic Microscopy (PAM)

Dynamic imaging of inorganic ion fluxes in vivo



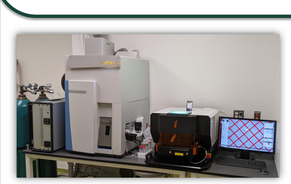


*PAM imaging of single RBCs in a mouse blood smear. (**a**) Trans-illuminated optical microscopic image. (**b**) PA maximum amplitude projection image of individual RBCs. Scale bars, 10 μm. (**c**) Magnified PAM projection image of a single RBC along the x–y plane. Scale bar, 2 μm. (**d**) Cross-sectional image of the same RBC along the x–z plane. (**e**) 3D visualization of the RBC*

Funding Sources:
P41GM135018

Quantitative BioElement Analysis and Mapping (QBEAM) Center

QBEAM was founded by Professor Thomas V. O'Halloran at MSU in January of 2021 as an interdisciplinary center within EHI focused on elemental mapping and analysis. QBEAM's mission is examining elemental quotas in biology from single cells to whole organisms and how the interplay between metals and systems biology can be harnessed to develop therapeutics, elucidate the mechanisms of disease, and further our understanding of the ecological and environmental consequences of metal exposure.

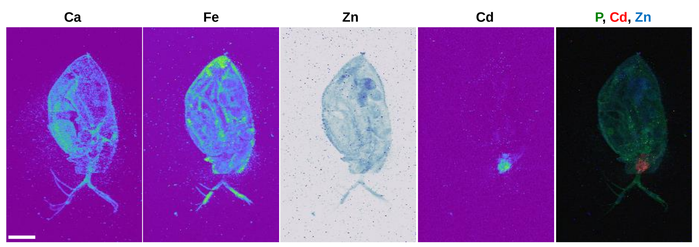


The Tofwerk ICP-TOF-MS and ESL bioimage 266 nm laser ablation system setup in ISTB Room 1307

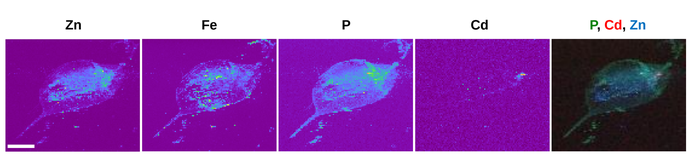
Lab space in ISTB Room 1308 for trace element analysis

PI: Prof. Tom O'Halloran
Founder: QBEAM
Founder, Director: EHI
ohallor8@msu.edu

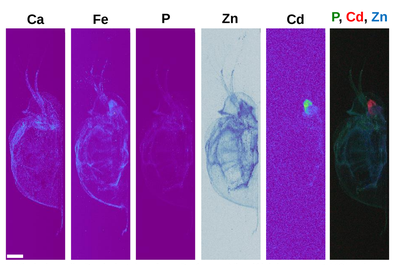
Keith MacRenaris, PhD
Research Associate Professor
MMG
Director: QBEAM
macrenar@msu.edu



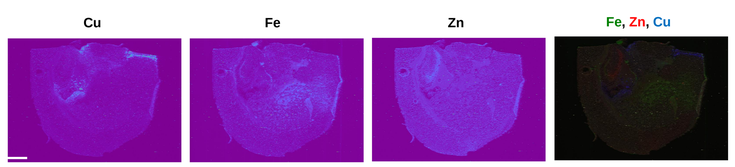
Whole adult Daphnia taken from Professor Nina Wale's group at MSU where sample was attached to Kapton tape. Samples were scanned using a square ablation crater at 10 μm x 10 μm resolution at 20 Hz. Acquisition Time: 75 minutes. Scale Bar = 100 μm.



Whole juvenile Daphnia taken from Professor Nina Wale's group at MSU where sample was attached to Kapton tape. Samples were scanned using a square ablation crater at 10 μm x 10 μm resolution at 20 Hz. Acquisition Time 45 minutes. Scale Bar = 100 μm.



Whole juvenile Daphnia taken from Professor Nina Wale's group at MSU where sample was attached to Kapton tape. Samples were scanned using a round ablation crater at 3 μm diameter at 25 Hz. Sample was scanned in 3 hours. Scale Bar = 100 μm.



Half mouse brain section where sample was frozen in OCT and sectioned at 20 μm thickness and dried. Samples were scanned using a square ablation crater at 10 μm x 10 μm resolution at 100 Hz. Sample was scanned in 3 hours. Scale Bar = 1 mm.

Funding Source(s):
Michigan State University
P41GM135018

Available Positions

Postdoctoral Researcher/Research Associate – Professor Tom O'Halloran/EHI

Professor O'Halloran is seeking a candidate for a postdoctoral researcher/research associate position in the Department of Microbiology and Molecular Genetics (MMG) in the College of Natural Science and the Elemental Health Institute at Michigan State University (MSU). The candidate should have a strong background/interest in bioinorganic chemistry, data visualization and reduction, and cell/animal biology. Successful candidates shall have demonstrated research productivity in the fields of bioinorganic chemistry, elemental mapping, analytical chemistry, or data visualization and can reach out to Professor O'Halloran for more details (**ohallor8@msu.edu**).

Lab Technician/Manager, QBEAM – Professor Tom O'Halloran/EHI

QBEAM at Michigan State University is seeking exceptional candidates for laboratory manager/research technologist position to meet the expanding needs of QBIC. QBEAM is a shared instrumentation research facility that focuses on trace metal analysis and quantitative elemental mapping of a wide variety of sample types ranging from single cells to complex materials. The center is part of the transdisciplinary Elemental Health Institute (EHI) whose mission is to use interdisciplinary approaches to generate transformative scientific advances in ways that traditional, single-discipline methodology cannot. Contact the director, Keith MacRenaris (**macrenar@msu.edu**) for more details.

TENURE-TRACK FACULTY POSITIONS – Organic, Analytical, NMR

The Department of Chemistry in the College of Natural Science at Michigan State University (MSU) seeks candidates for three tenure-track faculty positions in organic chemistry, analytical chemistry and the development and application NMR spectroscopy. Highly qualified candidates beyond the rank of assistant professor will also be considered. Each search is open to candidates in **all** areas of organic chemistry, analytical chemistry, and NMR development and applications.

The MSU chemistry department is undertaking significant faculty hiring over the next several years to build on current strengths that include nationally acclaimed faculty, a talented and diverse student body and impressive instrumentation and other resources to expand into emerging areas of chemistry. In addition, there are exciting campus wide research initiatives on interdisciplinary science and technology, including health related research.

Successful faculty candidates shall have demonstrated research productivity and evidence of potential for independent research, and are expected to develop a vigorous, externally-funded research program and contribute to excellence in teaching and mentoring at the undergraduate and graduate levels in ways that integrate efforts to further diversity and inclusion.
Interested individuals should apply at **https://jobs.msu.edu** with the following posting numbers
for organic (730751), analytical (730750), or NMR (730749).

Industry Partners