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Metalloproteomics: linking metals in cells to the proteins that bind them

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Abstract

Metals like copper, zinc and iron are important nutrients to all life. Their special properties which make them so useful to us in things like batteries and catalysts also make them useful to living organisms. Using hard x-ray fluorescence microprobes at the Advanced Photon Source, we have been able to see, often for the first time, where the metals themselves are inside cells and tissues. Yet, many of the images we acquire lead us to new questions. Are these metals required for the activity of proteins? Which proteins are binding which metals inside the cell? With over a third of all proteins thought to bind metals, knowing which metals are bound and how that binding changes in response to the environment could have big implications. For instance, the mismanagement of metals is involved in many diseases, including Lou Gehrig's disease, Wilson and Menkes disease, and possibly even Alzheimer's disease. Metals are also an environmental toxin and they are used in drugs, like the platinum in cisplatin that treats prostate cancer. Knowing which metal is in which protein at a given point in time could lead to new insights into how they do their work. We have developed a new tool to investigate this, combining native two-dimensional gel electrophoresis and x-ray fluorescence imaging, to quantitatively measure the amount of sulfur, iron, zinc, and other metals at every point of the 2-D separation of proteins. By coupling this with mass-spectrometry, we have identified a novel protein (PA5217) as a zinc-binding protein in *P. aeruginosa*. Our finding highlights how this method not only determines changes in metal occupancy, but also identifies the associated protein.

Biography

Lydia Finney leads research in the roles of metals in cell physiology, particularly utilizing x-ray fluorescence microscopy, as a Physicist at the Advanced Photon Source (APS). Prior to joining APS, Dr. Finney was a postdoctoral fellow in the Biosciences Division at Argonne National Laboratory from 2005-2007. She obtained her Ph.D with Dr. Thomas O'Halloran at Northwestern University in Inorganic Chemistry. She was awarded a Fannie and John Hertz Fellowship for her graduate studies, and more recently her work been featured in a C&EN News article on metalloproteomics. She has published over 30 peer-reviewed publications.