Integrative Metallomic Approach to Identify Metalloproteins in Microbes

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ABSTRACT: Metal ions operate as cofactors for around 40% enzymes, however, they also exhibit toxic effects. It is crucial to identify metal-protein interactions at a proteome-wide scale (1) which are difficult due to some *weak* and *transient* interactions. We developed an integrated approach consisting of gel electrophoresis and inductively coupled plasma mass spectrometry, LA-ICP-MS, IMAC, fluorescence and bioinformatic approach to identify metal-associated proteins using bismuth antiulcer drug as an example (2, 3). Using such an approach, we have identified metal-associated proteins as well as to quantify the metals for fast metallome/proteome-wide profiling of metal-binding proteins. Metal-tunable fluorescence probe can track both His-tagged proteins and metal-binding proteins in live cells (4). We recently investigated how bismuth (III) drugs are metabolized by mammalian cells and why the heavy metal is toxic to certain pathogens but not humans. We demonstrated that >90% of bismuth was passively absorbed, conjugated to glutathione and transported into vesicles by MRP transporter (2).
We further established a bioinformatic method which allows potential metal-binding proteins both sequentially and spaciously to be searched (5). We show that histidine-rich proteins (HRPs) are extensively distributed in prokaryotic proteomes, with the majority of HRPs being involved in metal homeostasis. Importantly, the occurrence of histidine-rich proteins in the proteomes of prokaryotes is related to their habitats.

This work was supported by the RGC of Hong Kong (7039/13P, 173046/14P), and HKU (for an e-SRT on Integrative Biology).
KEY WORDS: Metallomics, protein, bismuth, fluorescence

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