Letter to the Editor

Embracing the Complexity of Biology with Metallomics and Metalloproteomics

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We agree with Philip Ball [1] and Ajit Varki's [2] recent comments that life is more complex than the central dogma of biology. Nevertheless, a vital role of metals in virtually all aspects of life is largely overlooked in the cherry-picked list of "-omes". According to Alexa McCray's criteria for coining a meaningful Omics term [3], we envisage that METAL-l-OMICS and METAL-l-o-PROTEOMICS are emerging as next-generation "good Omics".

Literally, metallomics is a large-scale study of all metals (or metalloids) in a biological entity. Besides the quantity, speciation and biodistribution of metals, metallomics aims at dissecting the interaction of metals with DNA, RNA, proteins, and other biomolecules. As an integral part of metallomics, metalloproteomics focuses more specifically on the exploration of metal-protein association, including metal-induced perturbations of protein expression, protein folding, protein activity and protein-protein interaction. In a proteome, about one quarter to one third of proteins are estimated to be functionally associated with various metals. Instead of analyzing metal-protein interaction individually, metalloproteomics is devoted to the identification and characterization of metal-protein association on a proteome-wide scale.

By and large, metals can modulate a number of proteins in cells. Proteomics approaches that are capable of identifying metal-related proteins in a high throughput manner would be useful for dissecting the biology of metals. For instance, quantitative proteomics has been widely applied to identifying the proteins with altered expression levels in cells upon metal exposure [4]. However, conventional proteomics approaches may largely overlook the metalloproteins that only undergo metal association/dissociation but have little change in expression, as well as the metalloproteins with relatively low abundance in a proteome. To tackle these problems, we and others have developed nuclear analytical techniques-based metalloproteomics approaches for the identification of a broad spectrum of metal-binding proteins with high sensitivity and specificity [5,6]. As a non-destructive and sensitive tool for mapping element distribution in biological samples, synchrotron radiation X-ray fluorescence spectroscopy (SRXRF), when coupled with two-dimensional gel electrophoresis (2-DE), can be used to readily detect the metal-binding protein spots without staining 2-DE gels [6]. Subsequently, these protein spots of interest can be identified by matrix-assisted laser desorption/ionization time of flight mass spectrometry (MALDI-TOF-MS) or electrospray ionization mass spectrometry (ESI-MS). By taking advantages of SRXRF/2-DE, metalloproteins (Hg-binding proteins) in *E. coli* have recently been successfully identified [6].

As other Omics, the advance of metallomics and metalloproteomics entails multidisciplinary endeavors. State-of-the-art techniques integrating (bio) chemical and nuclear analytical methods are being developed to offer a sensitive and high throughput analysis of metalloproteins. In view of increasing evidence of metals/metalloproteins implicated in biology and medicine, more input from biologists and physicians is solicited to address key questions in public health and devastating diseases with metallomics and metalloproteomics.

References

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