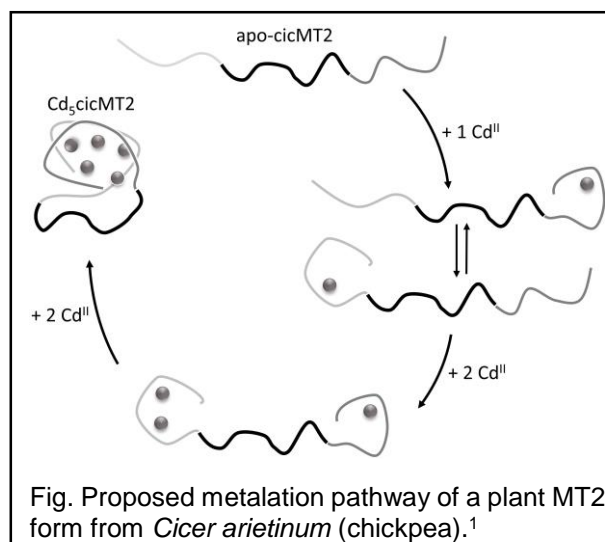


Metallothioneins – looking beyond the fully metalated state

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Metallothioneins (MTs) form a superfamily of small, cysteine-rich proteins found in the most diverse organisms. *In vitro*, MTs can coordinate all different kinds of soft metal ions; however, *in vivo* the range of target ions is narrowed down to Zn^{II} and Cu^I, for which they have a homeostatic role. Another physiological function associated with metal ions is the detoxification of, mainly, Cd^{II} and Hg^{II} resulting in thermodynamically highly stable complexes. The protein ligands, i.e. the thioneins, are mostly devoid of secondary structural elements, giving their backbones sufficient flexibility to enable efficient metal-thiolate cluster formation and thus to maximise the metal ion binding capacity of the corresponding MT. As a scientific drawback, this high flexibility interferes with structure determination attempts and consequently, the number of 3D structures is limited and largely constrained to the fully-metalated species. Mechanistically, however, and probably also functionally, investigation of sub-metalated species is of increasing and high interest. In this contribution, selected results of our



attempts to characterize such species and to decipher metalation pathways of MTs from different families (i.e. from plants, fungi, and bacteria) will be presented.¹⁻³

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³ J. Habjanič, O. Zerbe, E. Freisinger *Metallomics*, **2018**, *10*, 1415-1429.