

ABSTRACT

Metallothioneins (MT) are low molecular weight cysteine rich proteins present in all taxa except eubacteria. MTs are multi-purpose proteins. A single MT protein performs more than one function i.e. anti-inflammatory, proliferative, anti-oxidant, anti-apoptotic, angiogenic activities, chemotherapy resistance etc. In the present study, MTs are explored to study their structural diversity in different groups of animals and to analyze metal binding domains of these proteins and their mechanism of metal ion sequestration. We have analyzed MT sequences of protozoans, invertebrates and vertebrates. Their sequences were retrieved from NCBI and homology search was carried out using BLAST program. The multiple sequence alignment and Weblogos were formed by using Clustal Ω and Weblogo.berkeley, respectively. The phylogenetic relationship was analyzed by using Jalview software. The three dimensional protein structures were modeled using Swissmodel.expasy and homology modeling was carried out by using Swiss PDB Viewer. Our results showed high level of sequence conservation in the order vertebrates > protozoans > invertebrates. And later graphical representation of the MT protein sequences also confirmed high level of cysteine conservation in all animal groups. The cysteine specific motifs are unique to each animal taxa and difference lies mainly in their cysteine residue clustering. The phylogenetic relationships of each phylum are described separately in our results. The three dimensional structural analysis revealed the structural diversity in different groups of animals as these proteins are formed of two domains i.e. α domain and β domain. We observed variations in the number of α -helices, β -sheets and number of metal atoms in different organisms. The homology modeling of vertebrates showed one domain of protozoans is nearly conserved however the other domain showed variation in the sequence. In invertebrates, structural variation in both domains is observed as models were not superimposed very well. However, vertebrates showed highest level of conservation as all the models are highly superimposed. When homology was observed of all the three groups, very little structural homology was observed. It showed that metallothionein families may have evolved independently during evolution. The similarity in structural traits is due to various convergent evolutionary processes. Hence, MT from different organisms shows homogenous functional properties but heterogeneous amino acid, nucleotide sequences and gene organization.