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MULTIFUNCTIONAL ENZYME IS A SMART SOLUTION FOR EARLY LIFE

Abstract

Multi-functional enzymes (MFEs) are enzymes that perform multiple physiological functions. They are critical for communication and cooperation between different functions and pathways within a complex cellular system or between cells. In this study, we collected literature-reported 6,799 multi-functional enzymes and systematically characterized them in structural, functional and evolutionary aspects. It was observed that multi-functional enzymes are non-evenly distributed in species that Bacteria have relatively more multi-functional enzymes than Archaebacteria and Eukaryota. A comparative analysis indicated that the multi-functional enzymes experienced a fluctuation of gene gain and loss during the evolution from S. cerevisiae to H. sapiens: decreased from S. cerevisiae to D. rerio and then increased from X. laevis to H. sapiens. For early simple life forms with small genome sizes, enzymes were likely driven by the nature selective pressure to broaden their substrate specificity or adopt multiple functions via mechanisms like gene duplication in tandem accompanying with mutational modifications. With the emergence of multi-cell eukaryotic organisms, complex intra-cellular and inter-cellular interactions required more accurate and diverse enzymatic activities. The multi-functional enzymes might be specialized so as to execute a definite catalytic function. On the other hand, novel multi-functional enzymes emerged when broader substrates and reaction specificities are subsequently captured by adaptive evolution. For instance, interacting proteins (direct interaction or upstream-downstream proteins in a pathway) however integrated their functions to achieve more effective cell device. The gain and loss of multiple functionalities of MFEs in some species may suggest a potential mechanism of novel protein generation or functional regulation of biological pathways. Further pathway analyses showed that majority of multi-functional enzymes (about 82% of total MFEs) were well preserved in catalyzing several essential cellular processes, e.g. metabolisms of carbohydrates, nucleotides and amino acids. Considering the very conservation of metabolic enzyme in life domains, the enrichment of MFEs in several metabolism processes may suggest that MFEs could be the early enzymes. Their multi-functionality could be an efficient solution for early life forms to preserve as many basic metabolic activities as possible in small genome size.