

Structural and Bioinformatic Analysis of an Ancient Enzyme Family

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Ribonucleotide reductases (RNRs) convert the precursor building blocks of RNA to the precursor building blocks of DNA and are found in every organism that synthesizes its DNA de novo. Because of its potential role in the transition from the hypothesized RNA world to the modern DNA world, understanding the diversity and evolution of this enzyme family has been of great interest. In our study, we have reconstructed the largest RNR phylogeny to-date that unifies all known classes of the enzyme. Surprisingly, our dataset has revealed a small, phylogenetically distinct clade, which we denote as class \emptyset , placed as a clade diverging near the root of the tree. Using small-angle X-ray scattering (SAXS), cryo-electron microscopy (cryo-EM), and AlphaFold2, we show that the class \emptyset enzyme is the most minimal RNR structurally characterized to-date. Combined with our phylogenetic analysis, our structural data give insight into how a minimal RNR scaffold resembles the ancestor to the modern RNRs of the aerobic world.