From Genes to Enzymes to Compounds. A Chemical Basis for Evolution of Function

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Virtually all of the organic molecules required to support life are the products of biosynthesis. The enzymes that catalyze the individual reactions in biosynthetic pathways are typically highly evolved to efficiently synthesize a single stereochemically defined product. Recent advances in genomics and X-ray crystallography have revealed similarities among the structures of biosynthetic enzymes that allow many of them to be grouped into families whose individual members apparently evolved from a common ancestor. Over time, similarities at the amino acid level have become indistinct and only elements of the three-dimensional structure of the proteins remain to identify members of an extended “superfamily”. These changes permit enzymes to acquire and optimize the ability to synthesize different molecules.

Highly evolved enzymes, which synthesize a single compound with high efficiency, can hide important clues about their ability to catalyze other reactions. Perturbing the conditions for an enzyme-catalyzed reaction or altering the structures of the substrates or the enzyme can lead to the appearance of a range of products often found for the uncatalyzed reaction. These new products can provide important clues about potential functions of other enzymes within a superfamily. Examples of how nature has exploited the inherent chemical behavior of isoprenoid substrates to synthesize different molecules will be discussed.