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Enzyme Engineering

ISSN: 2329-6674

Short Communication

Impact of Protein Sequences Analysis on Enzyme Activity

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DESCRIPTION

The use of engineering enzyme function continues to expand as biotechnology advances. As they require high-throughput screening or three-dimensional structures to direct target residues of activity control, conventional techniques are only partially applicable. Sequence evolution through natural selection is a different approach. During the evolution, a variety of mutations were chosen to fine-tune the activities of the enzymes in order to adjust to various environments. The method called sequence co-evolutionary analysis to control the efficiency of enzyme reactions (SCANEER), which examines the evolution of protein sequences and employs a direct mutation approach to enhance enzyme activity. In contrast to loss-of-function mutations, which are avoided because they are depleted during evolution, postulated that amino acid pairs for different enzyme activities were encoded in the evolutionary history of protein sequences. The enzyme activities of beta-lactamase and aminoglycoside 3-phosphotransferase were appropriately anticipated by SCANEER. cis-aconitate decarboxylase, α-ketoglutaric semialdehyde dehydrogenase, and inositol oxygenase were three different enzymes of significant importance in chemical production that SCANEER was further experimentally validated to control. At locations distant from known active sites or ligand-binding pockets, mutations that enhance substrate-binding affinity or turnover rate were discovered [1,2].

Basic science, food science, biomedicine, and biotechnology are just a few of the varied bio-industrial disciplines that have benefited from the development of enzymes to enhance catalytic activity. In earlier studies, auxotrophic systems or screening methods for basic enzyme activities were used to engineer enzymes. Recent biotechnological developments have made it possible to create directed evolution, which adds random mutations for enzyme engineering. However, directed evolution is frequently time-consuming, has applicability restrictions due to technical issues, and is dependent on pricey high-throughput screening methods. Using random mutagenesis, it is virtually impossible to explore large sequence spaces [3].

It was possible to predict changes that improved enzyme activity using a variety of structure-guided techniques. *Via* structural analysis, these techniques frequently sought to identify ligand-binding regions, and they frequently altered active site residues to enhance enzyme activity utilizing Rosetta design or phylogenetic analysis. However, the increase in enzyme activity typically does not correlate with how far a modification is from the active site. According to several studies on direct evolution, mutations that increase enzyme activity are typically found outside of the active region. These alterations, known as allosteric mutations, alter the distribution of ensemble populations, impact protein shape and stability, and either completely or partially abolish or increase enzyme activity despite being far from the active site. These studies of allosteric mutations imply that mutation targets for modifying enzyme activity could be located far from the active site. Unfortunately, due to the enormous amount of search space that needs to be combed through, it is very difficult to forecast mutations that increase activity when they are distal from the active site [4].

The molecular evolution analysis of protein sequences could identify residues that can regulate the activity of an enzyme when they are close to or far from the active site. Natural selection adjusted enzyme functions by mutations distal to or nearby the active region, allowing for adaptation of the enzyme to the many environmental conditions that each species encounters. Investigating homologous sequences from other species can help to find areas for controlling enzyme function. Functionally significant residues, such as essential residues for protein conformational changes and allosteric modulation, were successfully found using evolutionary analysis of co-variations in Amino Acid (AA) patterns in two places of homologous protein sequences. Co-variation is the development of compensatory substitutions at cooperating residues in response to a mutation at a functionally significant location in order to prevent loss-of-function. As a result, evolutionary hotspots that alter enzyme activity through the introduction of mutations typically exhibit significant levels of coevolution [5].

CONCLUSION

The SCANEER approach, which, based on sequence co-evolution analysis, identifies AA residues for substitution to enhance enzyme activity. Finding mutation candidates that might increase enzyme activity can assist cut the expense of the

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Received: 28-Feb-2023, Manuscript No. EEG-23-22150; **Editor assigned:** 02-Mar-2023, Pre QC No. EEG-23-22150 (PQ); **Reviewed:** 16-Mar-2023, QC No. EEG-23-22150; **Revised:** 23-Mar-2023, Manuscript No. EEG-23-22150 (R); **Published:** 30-Mar-2023, DOI: 10.35248/2329-6674.23.12.205

Citation: Banerjee M (2023) Impact of Protein Sequences Analysis on Enzyme Activity. Enz Eng. 12:205

experiment because the modified sequence space to be investigated is too large and mutations on functional residues typically result in loss-of-function. SCANEER analyzes the distribution of amino acid pairs at the co-evolved locations of homologous sequences to identify candidates for amino acid replacement. Various amino acid pairs make up each co-evolutionary relationship inside the Multiple Sequence Alignment (MSA). AA pairings that are missing or infrequently present in Multiple Sequence Alignment (MSA) are likely to result in enzyme loss-of-function.

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