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Editorial

Orphan Enzyme Project: A Review Message as an Attempt of Diverting the Trend of Our Clinical Researches

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An orphan enzyme is an enzyme activity that has been experimentally characterized but for which we lack amino acid sequence or nucleotide sequence. Before jumping directly on to the topic, let me start with some of the basics that may easily be linked to the subject we will be discussing. Biochemically, it is an established fact that, finely regulated molecular transformations are required in our body just to show ourselves as living and healthy. It is also a fact that proteins are the main players in making a living body. From among the different classes of proteins, enzymes are the class directly handling molecular transformations by acting as biocatalysts. We can mention some more proteins playing vital roles in a living body like hemoglobin as oxygen transporter, immunoglobulin for developing our immune system, protein hormones as messengers and many more. The Proteins are macromolecules made up of amino acids as their basic units. They are to be synthesized by our cells. Every functional protein contains a fixed number of amino acids arranged in a fixed sequence. A slight mistake if created in the sequencing during synthesis, the synthesized product will be inactive. Central dogma suggests that the information needed to make all our proteins is stored in DNA. The information is for producing proteins with correct amino acid sequence. A nucleotide sequence in the DNA decides the sequence of amino acids to be arranged in the protein. The same sequence from DNA is transferred in the form of a lighter transportable RNA (transcription) to ribosomes for conversion to a polymer of amino acid as per the direction given the DNA (translation). Therefore, we should always keep in our mind that any functionally active protein, if experimentally characterized as having enzyme activity, should always have a segment of DNA with a fixed nucleotide sequence as its parent. While undergoing enzyme characterization study, the search must be extended up to the localization of the concerned gene.

Following the closure of Human Genome Project, the researchers being equipped with all the basic information about the sequencing of three billion chemical base pairs that make up human genomic DNA, they are all living in an exciting era where whole genome can fully be sequenced within 15 min after an organism or pathogen is isolated [1] The rate at which the new genes are sequenced being much higher than their ability to correctly annotate the functional properties of the corresponding proteins, a significant fraction of the gene in many new genome have no function assigned to them [2]. Thus, despite advances in sequencing technology, there are still significant numbers of proteins with well characterized enzymatic activities are lying without any data for their amino acid sequences or the nucleotide sequences of the concerned genes. These proteins are later named as orphan enzymes. Experimentally characterization of an enzyme means the substrate and the product of the reaction catalyzed by the enzyme is only known as its minimum criteria. These orphan enzymes represent glaring holes in our biological understanding and it has come to be a top priority to reunite them with

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their coding sequences. Many of the orphan enzymes have been associated with various disease conditions and therefore, investigating the functions of such enzymes may be of much importance. With the use of computational tools, researchers' can compare the amino acid sequences of the orphan enzymes with enzymes whose functions are known [3]. The orphan enzyme project (OEP) is a project dedicated to connecting modern genome sequence methods with a century of orphaned information about enzymes. When the orphan enzyme project started in 2009, the first thing they looked at was just those 4400 enzymes with assigned enzyme commission (EC) number; out of those, 1122 were orphans. There are many enzymes that have not been classified into EC systems. About a quarter (or more) of those unclassified enzymes are also orphan. It seems that there is an urgent need to explore all the orphan enzymes with or without EC classification just to bridge the wide gap that separates the knowledge of biochemical functions and sequence information. Strikingly, orphan enzymes can even be found among enzymatic activities successfully used as drug targets. Again the knowledge of sequencing could also help in developing molecular targeted therapies suppressing many drug related side effects [4].

A methodology for solving orphan enzymes through a combination of database search and literature review was reported by Alexander G Shearer et al. in May 2014. They could reconnect over 270 orphan enzymes with their corresponding sequences [5]. This success points towards how we may be able systematically eliminate the remaining orphan enzymes and prevent the introduction of future orphan enzymes. Now, my only intention for writing this editorial is to draw the attention of my fellow colleagues towards a higher platform where the nature of the works may be much more original and commendable. This very reconnection of orphan enzymes with their own amino acid sequences itself may be attempted. Sequencing of those protein samples already characterized as having enzyme activity and still lying neglected as orphan may not be too difficult if once we are trained in that. We had been trying to impart the knowledge of enzymes including their genetic aspects to the students but, we never knew that many of the enzymes we have been telling as examples of different activities are not yet fully annotated. Well, it is not very late. We can wait till we get an opportunity to start with a new life as a graded researcher.

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