Prion as Conformational Isomerase: A Proposal for Novel EC Classification

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Abstract: Based on the molecular mechanism of PrP^{Sc} prion-PrP^{C} catalyzed $PrP^{Sc} + PrP^{C} \rightarrow 2PrP^{Sc}$ conformational conversion, this paper demonstrates that it conforms to the core definition of the Enzymology Commission (EC) of the International Union of Biochemistry and Molecular Biology (IUBMB), and proposes to classify it as EC 5.99.1.5 (new category: prion-type isomerase)

Keywords: prion, conformational isomerase, autocatalysis, β-sheet template, enzyme classification, IUBMB classification

1、 Introduction

While browsing through books related to biochemistry, the author observed that PrP^{Sc} prions exhibit characteristics of catalysts (i.e., enzymes), but found that the academic community has not recognized these prions as enzymes, nor have they been assigned a number in the IUBMB database. This led to the idea of proposing that PrP^{Sc} prions be classified as a type of conformational isomerase.

The core of the definition of enzymes encompasses several elements: primarily, catalytic activity, high efficiency, specificity, and structure-dependent properties. This article aims to demonstrate PrP^{Sc} that these characteristics align, and further, that they meet PrP^{Sc} the EC classification criteria.

2、 Argument

(1) The core mechanism conforms to the essential characteristics of enzymes

PrP^{Sc} The mechanism of action can be described as follows:

$$PrP^{Sc} + PrP^{C} \rightarrow 2PrP^{Sc}$$

This process meets the core definition of an enzyme:

1 Catalytic and efficient: PrP^{Sc} significantly reducing $PrP^{C} \rightarrow PrP^{Sc}$ the activation energy of conformational transitions (experimental fact: PrP^{C} the

spontaneous transition rate is extremely low, requiring PrP^{Sc} template-initiated chain reactions [1]), but the specific data have not been measured by the author due to unavailability of conditions.

2 Specificity: It strictly recognizes homologyPrP^{C} (historical and experimental facts: cattlePrP^{Sc} can catalyze human-induced diseases, but not necessarily catalyze distant speciesPrP^{C} [2][5])

3 Structural dependency: Although its pathogenic mechanism has not been fully elucidated, there is evidence indicating that its activity indeed relies on a specific conformation [3]

(II) Comparability with existing enzymes

Comparison items	**Prion (PrP^{Sc})**	**case**
Non-covalent bond catalysis	Hydrogen bonding/hydrophobic interaction-mediated conformational rearrangement	EC 5.6.2.3: DNA helicase
Autocatalytic characteristics	Self-activating catalyst	L-19 IVS RNA (Cech, 1986) (although not as rigorous)
Conformational change catalysis	$PrP^{C}PrP^{Sc}$isomerization	EC 5: Common characteristics of isomerases

III. Response to Potential Questions

In response to potential disputes, the following arguments are provided:

1 **"Non-covalent bond changes" questioned:** EC 5.6.2.3 (DNA helicase) also catalyzes non-covalent bond changes mediated by hydrogen bonding/hydrophobic interactions, and $PrP^{C}PrP^{Sc}$ the physicochemical property differences between its conformational isomers have reached the criteria for "different substance entities" (such as protease resistance, aggregation, etc.) [4].

2 **"Self-replicating specificity" questioned:** Autocatalysis is a verified enzymatic mechanism (such as the role of Mn^{2+} in the oxalic acid-potassium

permanganate reaction), and the identity overlap between the product and the catalyst does not affect the catalytic essence (refer to the retention of active fragments in the self-cleavage product of ribozyme).

3 **"Lack of classical active sites" challenge:** The definition of enzymes only requires a specific spatial structure - PrP^{Sc} a characteristic β-sheet core interface formed by a complementary template through hydrophobic structures and hydrogen bonding networks (confirmed by cryo-electron microscopy [6]). The mechanism of specific recognition on the molecular surface PrP^{C} is similar to antibody-antigen binding [1][7]. The mechanistic analysis of the yeast Sup35 prion protein is also relatively clear in [8], which can further confirm the universality of β-sheet template-mediated conformational catalysis.

IV. Specific Suggestions

The author wishes to consider the following classification scheme:

EC 5.99.1 [Proposed]: Protein Conformation Isomerase

└— EC 5.99.1.5: *Prion-type conformational isomerase*

Definition: A specialized isomerase that catalyzes the $PrP^{C} \rightarrow PrP^{Sc}$ irreversible conformational transformation of homologous proteins through the β-sheet template interface, with the catalytic unit integrated into the product

Classification basis:

1 The main class is EC 5 (isomerase), showing conformational changes, which is consistent with the characteristics of isomerase;

2 ".99" codes for special, unclassified enzymes;

3 The self-replicating characteristic can be clearly described as "prion-like".

5、 Conclusion

PrP^{Sc} They basically meet the core elements defined by the IUBMB for enzymes, and their systematic classification by the IUBMB can facilitate the enzymatic understanding of protein misfolding diseases.

6、 Conclusion

This proposal aims to elucidate PrP^{Sc} the core characteristics of enzymes:

achieving efficient and specific catalysis by reducing the activation energy. Due to the limited independent research conditions for high school graduates, this proposal is solely based on theoretical deduction from literature evidence and does not yet cover the determination of enzyme kinetic parameters or high-resolution structural analysis. The author anticipates conducting in-depth research with collaborative support once sufficient preliminary evidence is available.

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