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Design of novel semisynethetic metalloenzyme from thermolysin

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Background

Initial applications of biocatalysis involved the used of naturally occurring enzyme. With new challenges in green chemical reaction, biocatalyst that shed the light is metalloenzyme, which function as enzyme and contain metal that are tightly attached and always isolated with the protein [1]. In recent years, enzyme engineering has proven to be an invaluable tool for elucidating biocatalytic mechanisms as well as producing enzymes for industrial purposes. Approaches developed for *in vivo* chemical modification and *in silico* computational methods promise to increase the scope and have already been used successfully to alter existing protein so that they have better stability and functionality [2]. This task might be good to address in designing a new biocatalyst with improved properties.

Methods

The AutoDock programme 3.05 was employed in order to identify the binding conformations of the ligands and the metal ions and to perform docking using Lamarckian Genetic Algorithm (LGA) [3]. The coordinate of thermolysin-substrate free structure coded as 1KEI was taken from Brookhaven Protein Data Bank (PDB).

Results

The predicted KEI-ligand complexes with the lowest final docked energy for PSE and PHN were -6.71 kcal/mol at pocket 45 and -6.60 kcal/mol at pocket 47, respectively. Non-covalent interactions of hydrogen bond and hydrophobic interaction between protein and ligands established the final conformation. Analysis on finding the most favorable metal ions to dock onto each complex found that Mg^{2+} was docked onto KEI-PSE45 complex with final docked energy of -1.09 kcal/mol and performed four interactions with the PSE ligand. Meanwhile, Ca^{2+} represented the best metal ions to dock to the KEI-PHN47 complex with final docked energy of -4.12 kcal/mol and performed three interactions with the nearby residues.

Conclusion

An important branch of novel protein design is through engineering and design of new metal-binding sites into native proteins. By employing *in silico* approach of molecular docking, screening of putative ligand for possible interactions may enhance the discovery of novel semisynthetic enzyme and lead to a new protein function. Finally, the framework which was introduced for the experiment may be a competent method for screening potential metal ions in this *in vivo* route.

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