Computer Aided Molecular Modeling of Membrane Metalloprotease

MASSOUD MAHMOUDIAN

Razi Institute for Drug Research, Iran University of Medical Sciences, Tehran, Iran

ABSTRACT

Molecular modeling is a set of computational techniques for construction of 3D structure of a protein especially membrane bound proteins whose structures can not be elucidated using experimental techniques. These techniques has been applied in the study of membrane metalloproteases for comparing wild and mutated enzymes, docking inhibitors in the catalytic site and examination of binding pocket and mode of inhibitors binding. The present study was carried out to construct 3D structure of strmelysin-3, an important member of this family, using computer aided techniques to shed light on its biological function and provide a 3 dimensional model which could facilitate the rational design of inhibitors. The results of homology search using FASTA between the sequence of human stromelysine-3 and protein data bank showed that 1fbl has the highest similarity and this protein was used to construct the 3D structure of human stromelysin-3. The results of this modeling study showed that this enzyme has a folding structure similar to haemopexin, i.e. existence of a four-bladed structure like the flights of a dart. Zn binding and catalytic activity were described. Similar to other Zn metalloproteases His-215, His-219 and Glu-216 form the coordinates of Zn atom. It is found that the modeled human stromelysine is thermodynamically stable and agrees with biochemical data.

Address correspondence to: Prof. Massoud Mahmoudian, Razi Institute for Drug Research, Iran University of Medical Sciences, Tehran, Iran. P.O. Box 14155-6183, Tehran, Iran. E-mail: masmah99@iums.ac.ir

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