金属プロテアーゼにおける亜鉛結合モチーフの金属選択性

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Metal preferences of zinc-binding motif on metalloproteases

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ABSTRACT: Almost all naturally occurring metalloproteases are mono-zinc enzymes, The zinc inany number of zinc metalloproteases has been substituted by some other divalent cation. Almost all Co(II)- or Mn(II)-substituted enzymes maintain the catalytic activity of their zinc counterparts. However in the case of Cu(II) substitution of zinc proteases, a great number of enzymes are not active, e.g. thermolysin, carboxypeptidase A, endopeptidase from *Lactococcus lactis* or aminopeptidase B, while same do have catalytic activity, e.g. astacin (of 37%) and DPP III (of 100%). Here, from structural studies of various metal-substituted enzymes, e.g. thermolysin, astacin, aminopeptidase B, dipeptidyl peptidase (DPP) III and del-DPP III, the metal-coordination geometries of both an active and an inactive Cu(II)-substituted enzyme are proved to be the same as those of the wild-type Zn(II) enzymes. Therefore the enzyme activity of a copper-ion-substituted zinc metalloprotease may depend on the flexibility of the metal-coordination geometry.

抄録　金属ペプチダーゼのほとんどは亜鉛酵素である。酵素中の亜鉛イオンは多くの二価金属イオンで置換する事が出来る。Co(II) 及び Mn(II) で亜鉛イオンを置換酵素は一般に酵素活性を持つが、多くの Cu(II) 置換酵素は Thermolysin、Carboxypeptidas A、Aminopeptidase B などで活性を消失する。しかし、Dipeptidyl peptidase III の銅置換体は高い酵素活性を発現する。我々は、Thermolysin, Aminopeptidase B, Dipeptidyl peptidase III などの金属置換酵素の配位構造を比較検討する事により、銅置換 Dipeptidyl peptidase III の銅イオンの配位構造が、柔軟性を持つことで、その酵素活性を発現する事を明らかにした。

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