Evolutionary Conservation of Interfaces of Secondary Structural Elements in proteins shown for the Proteasomal Subunits

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Abstract

Homologous proteins tend to retain a similar fold even when the sequence similarity drops to a low level during evolution. This generally accepted rule is basing on protein backbone comparisons. Here we want to check, whether it also applies to interfaces of secondary structural elements (SSE).

We investigate the homology between 17 proteasomal subunits for which the crystal structure is already solved i.e. 14 different types of subunits of the yeast proteasome, 2 types of subunits from Thermoplasma acidophilum and one subunit from the homododecameric proteasome like protease hslv from E. coli. The proteasomal subunits represent a family of proteins with a poor pairwise sequence identity (11 - 43%) but with a well conserved three-dimensional fold.

The analysis includes the relationship between the proteasomal structures on three different levels: First we performed pairwise rigid superpositions of the C-alpha atoms for the 17 known proteasomal crystal structures and determined the root mean square value (RMSD) for each pair. Second we generated a multiple sequence alignment which was refined on the bases of the three-dimensional protein structure. From this alignment the pairwise sequence identities between all pairs of proteasomal subunits were calculated. The sequence identity is the most often used measure of distance between two proteins. In the third approach we compared equivalent interfaces. Interfaces are formed by two structurally adjacent SSEs. The SSEs were aligned by fold comparison and equivalent interfaces were superimposed automatically.

Our results show that pairs of equivalent interfaces have a lower RMSD than randomly chosen interfaces from uncorrelated proteins even when the local sequence similarity is nearly zero. However, the correlation of individual interface RMSDs and local sequence similarity was low and had a wide range from -0.008 to -0.4. The correlation coefficient was not related to the size or type of interface. By averaging the 61 interface RMSDs we found out, that the resulting mean interface RMSD correlates surprisingly well to the global sequence similarity with a correlation coefficient of -0.63. Thus the correlation is slightly stronger than between the C-alpha backbone RMSD and global sequence similarity. Therefore the mean interface similarity may serve as a structurally based measure of evolutionary distance.

References

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