Short Communication

Similarities between Soluble Inorganic Pyrophosphatase from Yeast and some Nucleotide-Binding Polypeptides*

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Inorganic pyrophosphate (PPi) is an alternative to ATP in the energy conversion reactions of chromatophore membranes from the purple non-sulfur photosynthetic bacterium *Rhodospirillum rubrum*. The chromatophores contain an uncoupler-stimulated inorganic pyrophosphatase (PPase).[1,2] They show light-induced formation of PPi[3,4] and PPi-driven energy-requiring reactions.[5–7] A proton-pumping PPi synthase from chromatophores has been solubilized and partially purified and characterized,[8–9] and a PPi synthase appears also to occur in chloroplasts[10] and yeast mitochondria.[2,11] This PPi synthase appears to be less complex than the corresponding ATP synthase, just as PPi is a simpler compound than ATP. Early electron-transport-coupled formation of energy-rich phosphate compounds may well have evolved from systems involving inorganic phosphate (Pi) and PPi to systems involving Pi, ADP and ATP,[12,13] i.e. a PPi synthase may be the original membrane-bound unit for coupling between biological electron transport and phosphorylation.[13]

Kuranova *et al.*[14] found that soluble inorganic pyrophosphatase from yeast has an Asp-119 residue situated close to bound metal near the reactive phosphate of enzyme-bound PPi. Recently, Fry *et al.*[15] described a similarly situated Asp-119 residue in adenylate kinase, where the free carboxylate group of the Asp may be coordinated to Mg^{2+} bound to oxygen atoms of the two terminal phosphate residues of the enzyme-bound ATP. In order to find out whether this is an indication that similarities between nucleotide-binding proteins may be extended to include also PPi-binding proteins, we have compared some amino acid sequences in the region of the apparently functionally relevant Asp residue.

Walker *et al.*[16] found two regions of homology between the adenylate kinase sequence and those of several ATPases. According to Fry *et al.*[15] there is a third homologous region in several of these and other proteins. This region, "segment 3", is located in adenylate kinase at or near the MgATP binding site (within 11 Å), as are the two other homologous regions. Since segment 3, which in adenylate kinase comprises the amino acids 114–119, is visualized as flanking the triphosphate chain of MgATP (including the reaction centre) and is a hydrophobic strand of parallel β-pleated sheet terminated by the above-mentioned Asp-119, it may serve to exclude water and minimize hydrolysis.[15]

The soluble PPase from yeast shows a remarkable similarity in sequence to both α- and β-subunits of ATP synthases, especially those from photosynthetic bacteria (Table 1), and it is tempting to assume that this similarity has functional significance. One may tentatively predict that the Asp ("D") residue of the sequences given is involved, as well as metal ion, in the binding and/or function of the respective phosphate residues of the substrates. Whether the sequence similarities indicate divergent or convergent evolution is still

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Table 1. Similarities between amino acid sequences in soluble PPase from yeast and some nucleotide binding polypeptides.

113 – G – D – N – N – P – I – D – 119	Yeast soluble PPase[a]
– G – L – G – N – P – I – D	*R. rubrum* α-ATPase[b]
– A – L – G – N – P – I – D	*R. blastica* α-ATPase[b]
– T – L – G – A – P – I – D	*E. coli* α-ATPase[b]
– V – V – G – E – P – I – D	*R. blastica* β-ATPase[b]
– V – I – G – E – P – V – D	*R. rubrum* β-ATPase[b]
– V – L – G – E – P – V – D	*E. coli* β-ATPase[b]
113 – T – L – L – L – Y – V – D – 119	Rabbit muscle adenylate kinase[c]

[a]Ref. 17. [b]Ref. 18. [c]Ref. 15.

an open question. Nevertheless, when taken together, the similarities between pyrophosphate-binding and nucleotide-binding polypeptides would appear to support a concept of "molecular co-evolution" for phosphate compounds and polypeptides. This concept is somewhat analogous to that of Williams,[19] who has recently discussed the symbiosis of metal and protein functions.

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