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We isolated and solved the structure of a plasma phosphate carrier (human). Surprisingly, despite the high importance of phosphate, none plasma phosphate carrier has been described so far. Due to the difficulty to obtain heavy atom derivative, we solved the structure at very-low resolution (25 Å) using a new direct method requiring neither heavy atom derivative nor model [1]. The atomic structure was finally solved at 1.8 Å resolution by classical SIRAS structure determination with one heavy atom derivative, which was obtained using a new family of molecule specially designed to produce better heavy atom derivatives (Kahn *et al.*, in preparation). The structure revealed two globular domains with a fold very similar to the phosphate binding proteins of *E. coli* and *M. tuberculosis* [2]-[3], primary ABC phosphate carriers. ABC carriers have been found in eukaryote kingdom but no primary ABC carrier has been described in this kingdom.

We showed that this protein is associated to paraoxonase in human plasma. Paraoxonase is a lipoprotein associated to HDL ("good cholesterol"). This phosphotriesterase is involved in protection against atherosclerosis development. Knowing that hyperphosphatemia is a risk factor in atherosclerosis, the human phosphate binding protein could be a preclinic marker of cardiovascular pathologies.

[1] Fokine A, Morales R, Contreras-Martel C, Carpentier P, Renault F, Rochu D, Chabriere E. (2003). *Acta Cryst. D* **59**,2083-7.

[2] Luecke H, Quiocho FA. (1990). *Nature* **347**,402-6.

[3] Vyas NK, Vyas MN, Quiocho FA. (2003). *Structure* **11**,765-74.