

Serendipitous Discovery and X-Ray Structure of a Human Phosphate Binding Apolipoprotein

Eric Chabriere^{7,3}, Renaud Morales¹, Anne Berna², Philippe Carpentier¹, Carlos Contreras-Martel¹, Frédérique Renault³, Murielle Nicodeme⁴, Marie-Laure Chesne-Seck², François Bernier², Christine Schaeffer⁶, Hélène Diemer⁶, Alain Van-Dorsselaer⁶, Juan C. Fontecilla-Camps¹, Patrick Masson³, Daniel Rochu³, ¹Laboratoire de Cristallogénèse et Cristallographie des Protéines, Institut de Biologie Structurale JP EBEL, 38027 Grenoble, France. ²Institut de Biologie Moléculaire des Plantes du CNRS, Université Louis Pasteur, 67083 Strasbourg Cedex, France. ³Unité d'Enzymologie, Département de Toxicologie, Centre de Recherches du Service de Santé des Armées, 38702 La Tronche, France. ⁴Laboratoire des Biosciences de l'Aliment, Université Henri Poincaré-Nancy 1, 54506 Vandoeuvre-lès-Nancy, France. ⁵Laboratoire de Cristallographie Macromoléculaire, Institut de Biologie Structurale JP EBEL, 38027 Grenoble, France. ⁶Laboratoire de Spectrométrie de Masse Bio-Organique, ECPM, 67087 Strasbourg, France. ⁷Laboratoire de Cristallographie et Modélisation des Matériaux Minéraux et Biologiques, CNRS-Université Henri Poincaré, 54506 Vandoeuvre-lès-Nancy, France. E-mail: eric.chabriere@lcm3b.uhp-nancy.fr

Solute-binding proteins¹ (SBPs), ubiquitous in archaea and bacteria, play a central role in the substrate uptake mechanism of ATP binding cassette transmembrane transporters² (ABC transporters). Despite the existence of ABC transporters in eukaryotes, no SBPs have been characterized or predicted from genome database analyses in this kingdom. Here, we report the discovery of a HDL-associated, phosphate SBP in human plasma and provide the first X-ray structural determination of a eukaryotic SBP. In addition, we conclusively demonstrate that phosphate SBPs are ubiquitous in all taxa including the domain eukaryota. The systematic absence from genome databases of genes associated with eukaryota phosphate SBP, and an astonishing 90% conservation at the nucleotide level of these genes between distant species raise new intriguing questions related to the peculiar features of these genes. Although phosphate is essential to metabolism, this protein is the first identified transporter capable of binding phosphate ions in plasma. This phosphate SBP is similar to another unpredicted human protein, namely the Crystal Adhesion Inhibitor, that could prevent development of kidney stones³. Thus these results provide new insights into phosphatemia and related pathologies such as atherosclerosis⁴.

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