Crystal structure of human Evectin-2 PH domain, and its complex structure with O-phospho-L-serine

Seiji Okazaki¹, Yasunori Uchida², Ryuichi Kato¹, Takao Inoue², Yusuke Yamada¹, Tomohiko Taguchi^{3,4}, Hiroyuki Arai², Soichi Wakatsuki¹ ¹ Structural Biology Research Center, Photon Factory, Institute of Materials Structure Science, High Energy Accelerator Research Organization (KEK), ² Department of Health Chemistry, Graduate School of Pharmaceutical Sciences, University of Tokyo, ³ Department of Biochemistry, Graduate School of Medicine, Osaka University, ⁴ Institute for Molecular Bioscience, University of Oueensland

Evectin-2, a pleckstrin homology (PH)-domain–containing protein, is implicated to be a regulator of the retrograde transport from plasma membrane to Golgi. Furthermore, it is implicated that Evectin-2 PH domain plays an important role in the retrograde transport by binding to phosphatidylserine (PS) on Recycling Endsomes.

To clarify the detailed binding mode between human Evectin-2 PH domain and PS, the crystal structures of the native and O-phospho-L-serine complex were determined at 1.75 and 1.00 Å resolutions, respectively. The overall structure follows the standard PH domain fold. O-phospho-L-serine binds to positively charged pocket near $\beta 1/\beta 2$ loop, and this binding mode confers the structural basis of the phosphor lipid binding specificity. Based on these structures, potential functional implications of human Evectin-2 PH domain are discussed.