- the evaluation of the probability of twinned 2D nucleation on the (010) faces will be discriminating to understand the complex genetic mechanism of penetration twins.

Keywords: gypsum, twin

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Structure of the whole plakin domain of plectin

Esther Ortega Porterov,[a] Rubén Martínez Buey,[a,b] Jose M[a] de Pereda,[a] *[a]Department of Structural Biology, Instituto de Biología Molecular y Celular del Cáncer, CSIC–USAL, Salamanca, (Spain). [b]Biomolecular Reseach, Structural Biology, The Paul Scherrer Institut, (Switzerland).* E-mail:ortegape@usal.es

Plectin is a member of the plakin family of proteins that cross-links components of the cytoskeleton and link them to membrane-associated structures, such as desmosomes and hemidesmosomes. Plectin (500kDa) exhibits a multi-domain structure. The N-terminal region contains a ~ 1000-residue long sequence conserved between the members of this protein family, termed the plakin domain. The plakin domain of plectin is formed by an array of nine Spectrin Repeats (SR1 to SR9) arranged in tandem and a Src-homology 3 (SH3) domain inserted into the central SR5 [1].

We have combined X-ray crystallography and small angle X-ray scattering (SAXS) to elucidate the structure of the plakin domain. Here, we present the crystal structure of four fragments that correspond to the regions: SR3-SR4, SR4-SR5-SH3, SR7-SR8 and SR7-SR8-SR9. The SR-fold consists on three α-helices (A,B and C) connected by short loops and packed in a helical bundle with a up-down-up topology. In adjacent SRs, the helix-C of the N-terminal repeat and the helix-A of the C-terminal repeat are fused in a single helix that spans both SR, yet there is no conservation in the relative orientation of adjacent SRs. The SH3 domain of plectin shows the canonical SH3 fold, but exhibits alterations in its putative Pro-rich binding-site suggesting that this domain does not bind to Pro-rich motifs as the canonical SH3 domains [2]. Moreover, the SH3 binding-site is occluded by the SR4, making extensive contacts with it. Residues that participate in the SR4-SH3 interaction as the residues of the SH3 pseudo-binding site are conserved in other members of the plakin family. The structure of the plakin domain of plectin presented herein, serves as a structural model for other plakins.

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Conformational Plasticity of Histidine Kinases is Key for Signal Transduction

Alejandro Buschiazzo,[a] Felipe Trajtenberg,[a] Daniela Albanesi,[b] Horacio Botti,[a] Natalia Ruetalo,[a] Julia Forman,[c] Michael Nilges,[c] Diego de Mendoza,[b] Pedro Alzari[d] *[a]Unit of Protein Crystallography, Institut Pasteur de Montevideo, Montevideo (Uruguay). [b]Instituto de Biologia Molecular y Celular de Rosario, Rosario (Argentina).[c]Structural Bioinformatics and [d]Structural Biochemistry Units, Institut Pasteur, Paris (France).* E-mail : alebus@pasteur.edu.uy

DesK is a membrane-bound histidine kinase (HK) from *Bacillus subtilis*, able to sense the order of membrane lipids when cells are subjected to cold shock, ultimately behaving as a molecular thermometer. Although the relevance of sensor HKs in signal transduction is well established, we still do not understand at the molecular level how HKs transduce input signal information to regulate their output catalytic activities. We address this issue by using a combination of structural and biochemical approaches. We have determined eight crystal structures of the intracytoplasmic catalytic core of DesK, including the wild-type, the phosphorylated form, and point mutants that retain particular functional traits.

Structural analyses show that DesK has been trapped in three conformational states that correspond to alternate functions of the protein along the signaling pathway [1]. By comparing the 3D structures of a single HK in different functional configurations, we observe a remarkable plasticity in the central helical domain. Incoming signals induce helix rotations and asymmetric helical bends that modify the accessible surface of the phosphorylation site and the mobility of the ATP-binding domains, ultimately modulating the protein's catalytic activities. The transition between conformational states through helical rotational shifts, was analyzed using Targeted Molecular Dynamics simulations, further supporting their role as a functional signal transduction mechanism.

The central four-helix bundle domain includes coiled-coil structures that reach the histidine phosphorylation site. The trans-membrane sensor region seems to drive the helical rearrangements. Heptad-repeat sequence features allow for the extension or disruption of the coiled-coil towards the N-terminus of the catalytic core, ultimately serving as a signal transmission gear. In correlation with these movements, the flanking ATP-binding domains, remain either rigidly fixed to the 4-helix bundle, or otherwise free to move. We have explored the transient intradimeric autophosphorylation state by semiflexible docking algorithms, leading to a proposed mechanism working in *trans*, one monomer phosphorylating the other. Structure-based cysteine engineering lends support to the working hypotheses, allowing us to trap an intermediate state with disulfide bridges between the two domains [2]. Negative cooperativity leads to phosphorylation of only one monomer within the dimer.

Structure-based mutagenesis and protein engineering experiments *in vitro* and *in vivo*, confirm the importance of the 'coiled-coil'-mediated plasticity in the conserved central phosphotransfer domain. Similar switching mechanisms could operate in a wide range of sensor HKs. Structural studies of the interaction of DesK with its cognate response regulator DesR are currently underway.

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PLZF oncoprotein; An extensive SAXS analysis

Katrine Nørgaard Toft,[a] Mads Gravers Jeppesen,[a] Tine Kragh Nielsen,[b] Gil Prive,[c] Bente Vestergaard,[a] *[a]Department of Medicinal Chemistry, University of Copenhagen (Denmark). [b]NNF Center for Protein Research, University of Copenhagen (Denmark). [c]Department of Biochemistry, University of Toronto (Canada)* E-mail: knt@farma.ku.dk

In Acute Promyelocytic Leukemia (APL) the balance between stem cell differentiation and proliferation is disrupted. The promyelocytic zinc finger protein (PLZF) is a transcriptional repressor, and is one of six