BSE321 Assignment
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Given PDB ID: 8RSW

1. Protein Name, Function, and Significance

Protein Name: Pacsin 2 SH3 domain

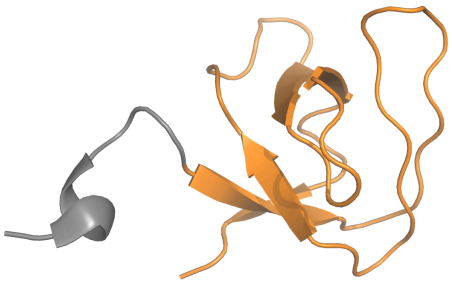
PACSIN 2 (syndapin II) is a cytosolic adaptor protein with an N-terminal F-BAR domain and a C-terminal SH3 domain. 8RSW contains the SH3 domain from chicken PACSIN2 (also called focal adhesion 52 kDa protein). SH3 domains recognize proline-rich motifs; PACSIN2's SH3 binds partners like dynamin, N-WASP or N-cadherin, coordinating actin assembly and endocytosis. PACSIN2 regulates membrane trafficking (e.g. caveolae dynamics) and cell migration, so its structure helps explain how it modulates cytoskeleton-linked signaling and receptor internalization.

2. Structure Determination Details (conditions, method, resolution etc.)

The structure was solved by solution NMR spectroscopy. Data were collected on Varian Inova 600 MHz and 800 MHz instruments in aqueous buffer (pH 6.8, 293 K). A suite of multi-dimensional NMR experiments (1H–15N HSQC, 3D NOESY, HNCA, etc.) provided structural restraints. The final PDB entry includes 20 conformer models (out of ~300 computed). 8RSW was deposited Jan 25, 2024 and released Feb 12, 2025. (No diffraction "resolution" applies for NMR.)

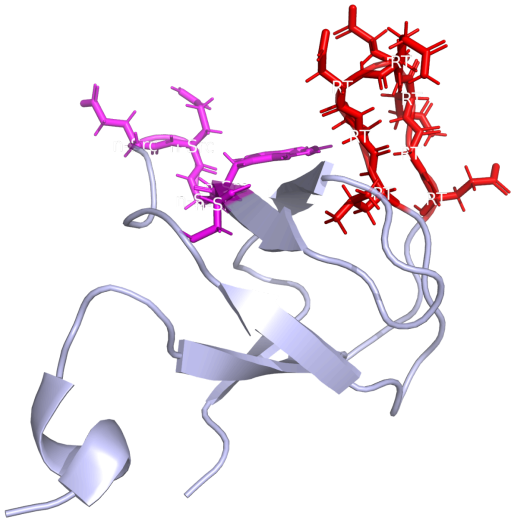
3. Overall Structural Features (oligomeric state, ligand bound or apo-state etc.)

The model covers the SH3 domain (residues 1–58 of the construct) with an N-terminal expression tag (residues –8–0). The SH3 fold is a five-stranded β-barrel (as expected) with the typical RT- and n-Src loops exposed for peptide binding. Since it is monomeric and apo, no specific residues can be pointed to in a ligand-binding or dimerization interface.
Overall Structure Snapshot:

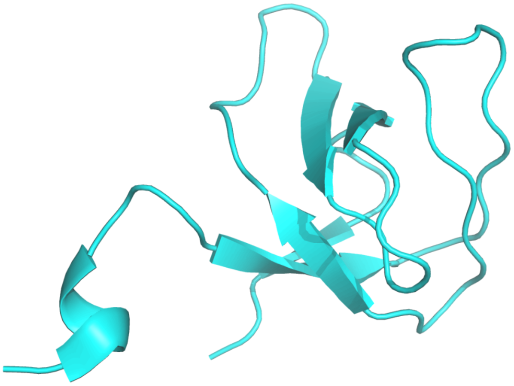


- **Assembly:** Monomeric. The asymmetric unit contains a single polymer chain (A) of 67 residues.

- **Residues involved in ligand binding:** Apo form – no peptide or small molecule ligand is present. The canonical PXXP-binding groove is empty. RT and n-Src Loops of SH3 Domain are part of the canonical PXXP-binding groove, even though no ligand is present (apo form).



- **Residues involved in oligomerization:** No oligomeric interfaces; no self-association is observed because 8RSW is monomeric in both the asymmetric unit and biological assembly. There are no inter-chain contacts, so no residues mediate oligomerization.



- **Residues involved in intermolecular interaction:** Not part of a larger complex in this entry because the structure does not represent a protein complex. Only one chain (A) is present in the structure. No hetero-oligomeric partners or protein-protein interfaces exist in 8RSW.

4. Anything else that stands out in the structure

A distinct feature is the engineered N-terminus: chain A begins with a 9-residue expression tag (Gly–8 through Ser 0) preceding the native SH3 sequence. Otherwise, the domain is canonical. It exhibits no insertions or unusual motifs beyond a standard SH3 architecture. No non-standard residues or covalent modifications are present. Because the structure is an NMR ensemble (20 models), it implies some flexibility in the loop regions even though the fold is well-defined. To our knowledge, 8RSW is the first structural model of Pacsin2's SH3 domain, providing a basis for future ligand-bound studies. (For example, docking peptides from N-cadherin or dynamin onto this structure could map the interaction surface.)

5. Overall Conclusion

This analysis confirms that the Pacsin 2 SH3 domain adopts the conserved β-barrel fold and is ready to engage proline-rich partners, consistent with its role in endocytosis and actin regulation. The high-quality NMR ensemble (no steric clashes) provides atomic detail on the peptide-binding surface in the absence of ligand. This sets the stage for designing mutagenesis or inhibitor studies to probe PACSIN2 function. Overall, the structure complements existing knowledge of PACSIN family proteins, underscoring how SH3-mediated interactions link membrane curvature events to cytoskeletal dynamics. Future work (e.g. co-structures with bound peptide) will further illuminate how Pacsin2 orchestrates cellular remodeling.