# *In silico* identification of potential druggable binding sites on CIN85 SH3 domain

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**Table of content:**

**Table S1** List of the residues forming the identified binding sites in CIN85 SH3A and corresponding amino acids in the other CIN85 SH3 domains obtained from 3D alignment.

| Binding site | CIN85 SH3A | CIN85 SH3B | CIN85 SH3C |
|---|---|---|---|
| **P1** | Tyr10, Glu17, Leu18, Ile20, Trp36, Leu47, Phe48, Pro49, Phe52 | Tyr109, Glu116, Leu117, Leu119, Trp135, Met146, Phe147, Pro148, Phe151 | Tyr278, Glu285, Leu286, Ile288, Trp306, Val317, Phe318, Pro319, Phe322 |
| **P2** | Val2, Glu3, Ala4, Ile29, Trp37, Asp50, Val53, Arg54, Glu55 | Arg101, Arg102, Cys103, Val127, Trp136, Ser149, Ile52, Lys153, Glu154 | Asp270, Tyr271, Cys272, Leu296, Trp307, Asp320, Val323, Lys324, Leu325 |
| **CS1** | Tyr10, Asp16, Glu17, Leu18, Ile20, Trp36, Leu47, Phe48, Pro49, Phe52 | Tyr109, Asp115, Glu116, Leu117, Leu119, Trp135, Met146, Phe147, Pro148, Phe151 | Tyr278, Asp284, Glu285, Leu286, Ile288, Trp306, Val317, Phe318, Pro319, Phe322 |
| **CS2** | Glu3, Ala4, Ile25, Ile26, Thr27, Gln40, Ile41, Asn42, Lys57 | Arg102, Cys103, Ile124, Ile125, Glu126, Val139, Leu140, Asn141, Ser156 | Tyr271, Cys272, Ile293, Val294, Thr295, Glu310, Leu311, Asn312, Pro327 |
| **CS3** | Asp16, Glu17, Leu18, Glu38, Gly39, Arg44, Arg45, Gly46, Leu47 | Asp115, Glu116, Leu117, Glu137, Gly138, Lys143, Thr144, Gly145, Met146 | Asp284, Glu285, Leu286, Glu308, Gly309, Arg314, Arg315, Gly316, Val317 |
| **CS4** | Leu18, Thr19, Ile20, Ser21, Glu24, Ile41, Asn42, Arg44 | Leu117, Glu118, Leu119, Lys120, Asp123, Leu140, Asn141, Lys143 | Leu286, Thr287, Ile288, Lys289, Asp292, Leu311, Asn312, Arg314 |
| **CS5** | Glu7, Phe8, Trp37, Asp50, Asn51, Phe52, Val53, Arg54, Glu55 | Ala106, Phe107, Trp136, Ser149, Asn150, Phe151, Ile152, Lys153, Glu154 | Ile275, Phe276, Trp307, Asp320, Asn321, Phe322, Val323, Lys324, Leu325 |
| **CS6** | Gly34, Gly35, Trp36, Pro49, Asp50, Asn51 | Glu133, Gly134, Trp135, Pro148, Ser149, Asn150 | Val304, Gly305, Trp306, Pro319, Asp320, Asn321 |
| **CS7** | Asp15, Glu17, Leu18, Thr19, Arg44, Arg45 | Asp114, Glu116, Leu117, Glu118, Lys143, Thr144 | Asp283, Glu285, Leu286, Thr287, Arg314, Arg315 |

**FigureS1** Superimpositions between some of the NMR derived models contained in 2K9G and some of the MD derived conformers.
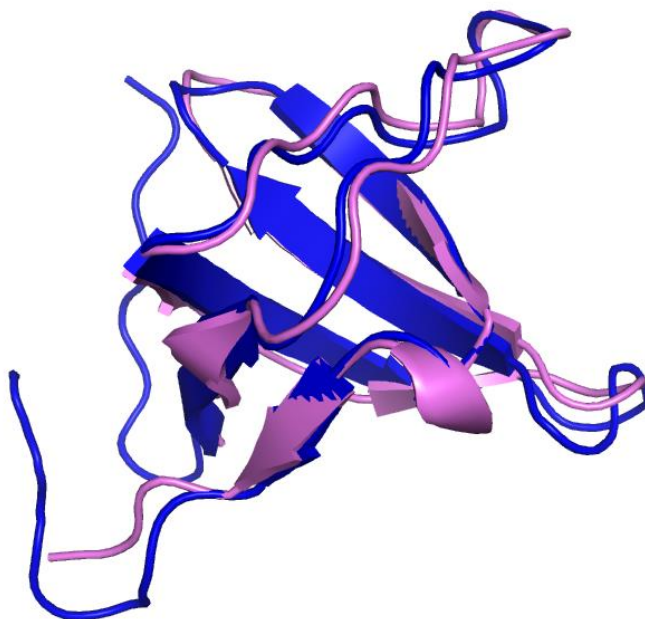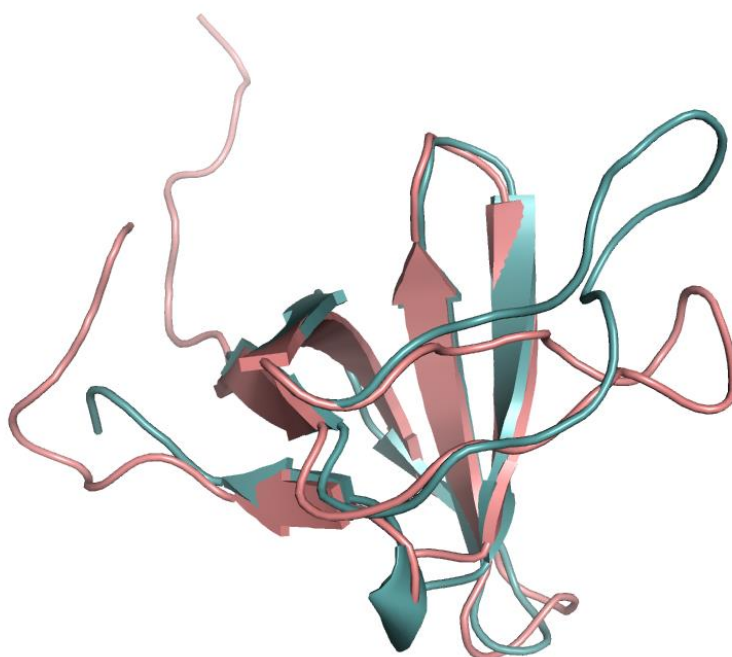


A) Model 1 of 2K9G (blue) superimposed to the representative frame of C2 (violet) (RMSD= 1.090 Å)
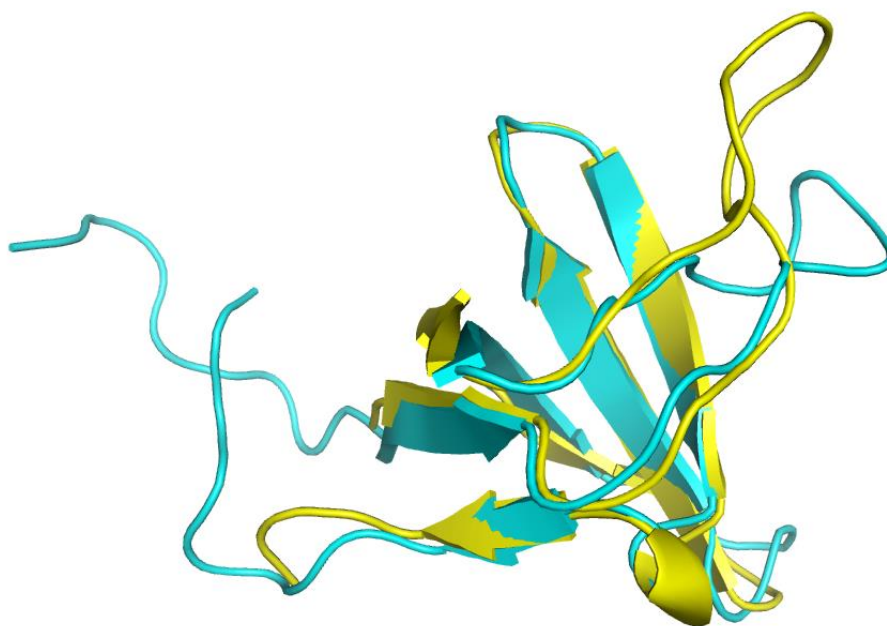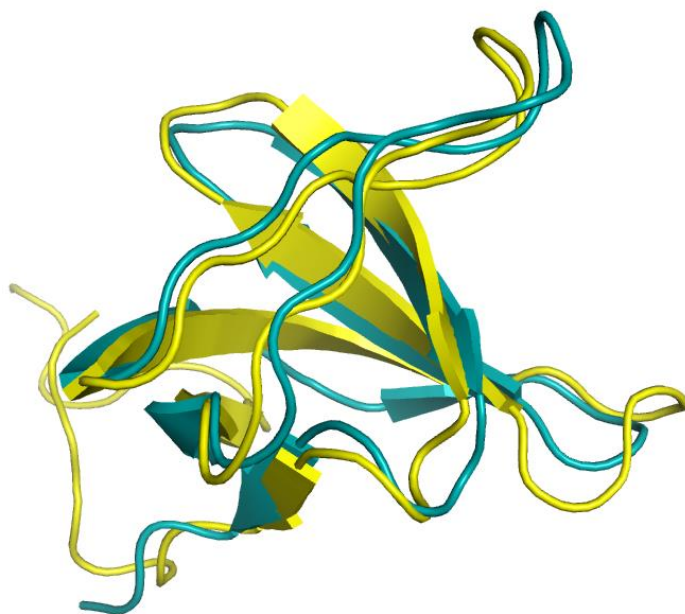


B) Model 2 of 2K9G (cyan) overlapped to the representative frame of C27 (yellow) (RMSD= 1.507 Å)
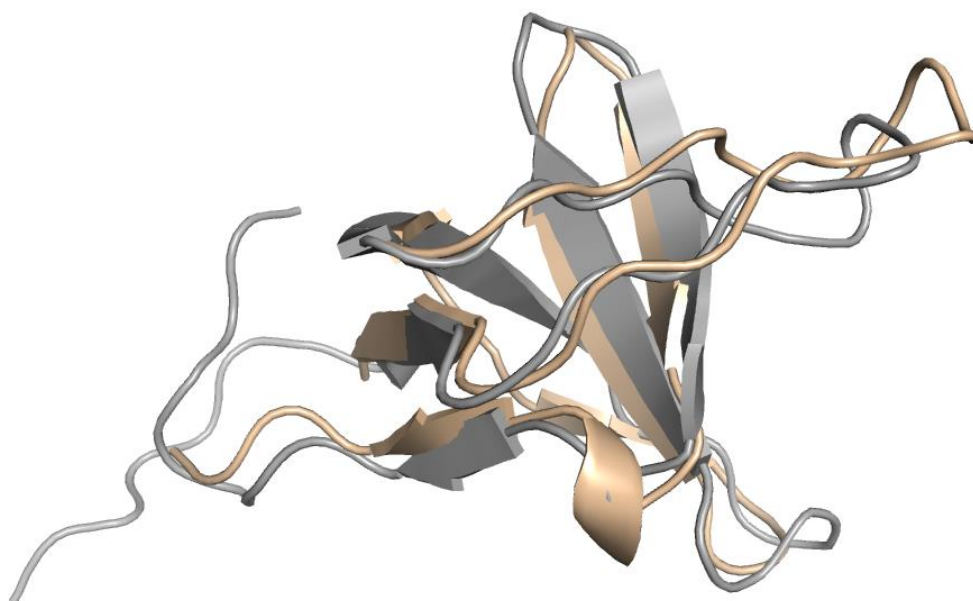
C) Model 3 of 2K9G (green) superimposed to the representative frame of C1 (green) (RMSD= 1.163 Å)
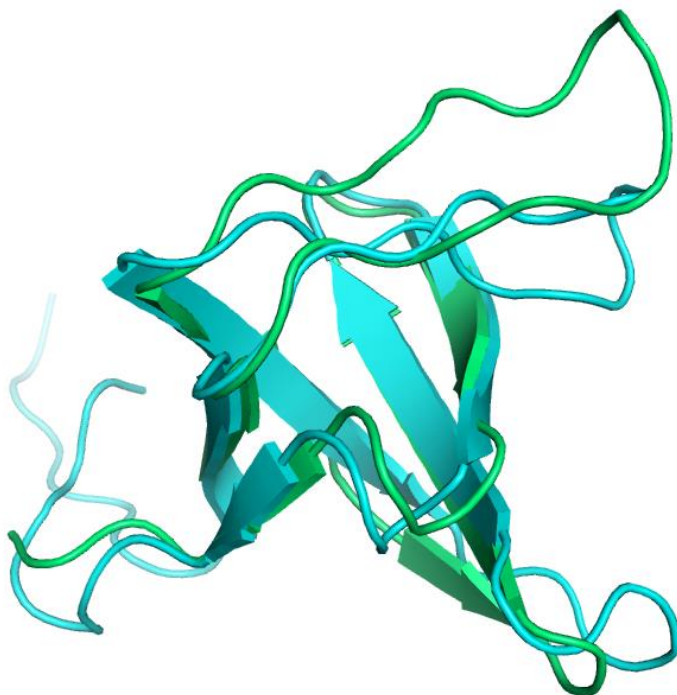


D) Model 5 of 2K9G (pink) superimposed to the representative frame of C26 (palecyan). (RMSD= 1.612Å)
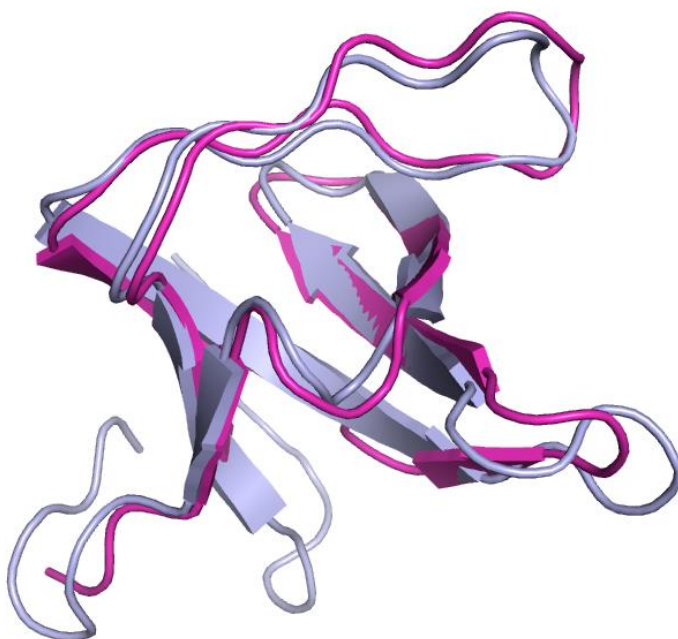
E) Model10 of 2K9G (giallo) superimposed to the representative frame of C10 (deepteal) (RMSD= 1.931 Å).



F) Model14 of 2K9G (grey) superimposed to the representative frame of C12 (wheat). (RMSD= 2.498Å)

G) Model16 of 2K9G (cyan) superimposed to the representative frame of C17 (green) (RMSD = 1.777 Å)



H) Model20 of 2K9G (lightblue) superimposed to the representative frame of C6 (magenta) (RMSD = 0.914).