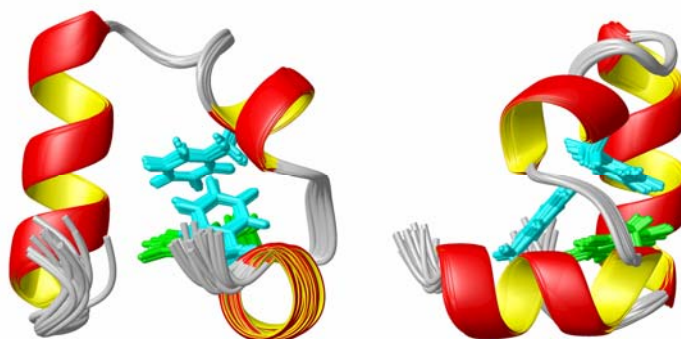


Center for Eukaryotic Structural Genomics

Protein Structure Data Summary

CESG ORF No.	GO.102026	
Organism	<i>Gallus gallus</i>	
Gene Designator	cVHP	
PDB Entry	2JM0	Deposition: 06-Sep-2006
BMRB Entry	15000	Deposition: 06-Sep-2006
Function	chicken villin headpiece	
Produced From	N/A	
Structure by NMR	Restraints/Residue: 21.8	Subunits/Molecule: 1
	No. of Residues: 35	Molecular Weight: 4.2 kDa
	Backbone RMSD(14-120,126-152): 0.23 Å	All Heavy Atoms RMSD(14-120,126-152): 0.80 Å
Data Collected At	Nuclear Magnetic Resonance Facility at Madison (NMRFAM)	
Authors	Cornilescu, C.C., Cornilescu, G., Hadley, E.B., Gellman, S.H., Markley, J.L.	



Structural Features

We report the first high-resolution structure of a protein containing a more heavily fluorinated side chain (bearing at least three F atoms). Recently we carried out a systematic evaluation of phenylalanine to pentafluorophenylalanine (Phe --> F(5)-Phe) mutants for the 35-residue chicken villin headpiece subdomain (c-VHP), the hydrophobic core of which features a cluster of three Phe side chains (residues 6, 10, and 17). Phe --> F(5)-Phe mutations are interesting because aryl-perfluoroaryl interactions of optimal geometry are intrinsically more favorable than either aryl-aryl or perfluoroaryl-perfluoroaryl interactions, and because perfluoroaryl units are more hydrophobic than are analogous aryl units. Only one mutation, Phe10 --> F(5)-Phe, was found to provide enhanced tertiary structural stability relative to the native core (by approximately 1 kcal/mol, according to guanidinium chloride denaturation studies). The NMR structure of this mutant, described here, reveals very little variation in backbone conformation or side chain packing relative to the wild type. Thus, although Phe --> F(5)-Phe mutations offer the possibility of greater tertiary structural stability from side chain-side chain attraction and/or side chain desolvation, the constraints associated with the native c-VHP fold apparently prevent the modified polypeptide from taking advantage of this possibility. Our findings are important because they complement several studies that have shown that fluorination of saturated side chain carbon atoms can provide enhanced conformational stability.

References: (1) Cornilescu, G., Hadley, E.B., Woll, M.G., Markley, J.L., Gellman, S.H., Cornilescu, C.C. (2007) Solution structure of a small protein containing a fluorinated side chain in the core. *Protein Sci* 16(1):14-9.

Percent Identity with Nearest PDB Structure at Time Solved	85% over 35 aa (1QQV)
Pfam Cluster	VHP
Sequence Family Size	100

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