Supplemental Table 9. Analysis of published NHR structures with experimentally observed structural disorder. Where predicted disorder for each residue with PONDR VL3H has a probability > 50%.

Family	Name	Experimentally observed disordered region	Agreement in observed and predicted disorder domain from this study	Reference
1A1	**TR α**	D domain (hinge, R152 – T161) is disordered in TRα (only a fraction of the areas could be seen in the electron density). In contrast this area in TRβ is an α-helix. Authors suggest it could either fold into segments of an extended DBD and LBD or unfold to form true unstructured hinge that would facilitate rotational flexibility between LBD and DBD	Yes	[1]
1A2	TR β	No disorder mentioned		[2]
1B1	**RAR α**	Mouse- Helix H2 and the connection between H2 and H3 could not be modeled due to poor electron density		[3]

		in this region.		
		Mouse- D-region and the last 30 residues of the F-region in RARβ, could not be modeled due to poor electron density in these regions. Electron density was observed for only 10 residues (out of 40) of the	Yes	[4]
1B2	**RAR β**	RARβ C-terminal F region.		
1B3	RAR γ	No mention of disorder		[5]
1C1	**PPAR α**	No mention of disorder		[6]
		NMR studies on PPAR-α indicate that the LBD is a flexible protein fold that does not have a well defined structure until a ligand occupies the binding site.	No	[7]
1C2	PPAR β/δ	No mention of disorder		[8]
		Could not get reliable structure for the loop between H2 and H3 of	Yes	[9]
1C3	**PPAR γ**	PPARγ		
1D1	Rev-Erb α	No crystal structures found		
1D2	Rev-Erb β	No crystal structures found		
1F1	**ROR α**	Most RORα amino acids had well-	Yes	[10]

		defined electron density, except for amino acids 461– 464 in loop L9-10, which had the highest B factors.		
		Rat- a residue (D403) located in loop 9-10 is partially disordered according to the electron density map	Not tested	[11]
1F2	**ROR β**	No mention of disorder		[12]
1F3	ROR γ	No crystal structures found		
		Tobacco budworm: Disorder in 321-323, 389, 482, 517-518	Yes (4 of 6 residues)	[13]
1H1	**EcR**	Sweet potato whitefly: no mention of disorder		[14]
		Drosophila -A-box (residues 78-91) of EcR DBD disordered in EcR-USP complex but not EcR-RXR complex	Yes (13 of 14 residues)	[15]
		Red flour beetle EcR: no mention of disorder		[16]
		Crystal structure of amino acids 207-447 - - Helix 2 (230-247) and loop after strand 2 in beta sheet (315-317) not resolved due to lack of interpretable electron density	Yes (helix 2 residues 230-247) and No for residues 315-317	[17]
1H3	**LXRα**			
1H2	**LXRβ**	Amino acids 214-461 crystallized		[18]

		could not get apo structures, structure may change in absence of ligand – no mention of disorder		
		Hairpin loop area displays disorder and differences even between receptor molecules bound to the same ligand. The weak electron density of H12 is comparable with the density of the ligand, suggesting that H12 is flexible in solution when there is no ligand bound.		[19]
		Amino acid residues 205-218 at the N terminal end of the LBD and a stretch of 11 residues between helix 1 and helix 3 (residues 238–248) are disordered.	Yes (residues 205-218) and 4 of 11 residues in between helix 1 and 3	[20]
		15 residue insertion (270-285)	Yes (9 of 15 residues)	[21]
1H4	**FXR**	between helices 1 and 3 is disordered		
		Rat– no mention of disorder		[22]
		Amino acid residues 165-215, part of the long flexible loop between helices	Yes	[23]
1I1	**VDR**	1 and 3, were deleted because their		

		present prevented stable crystal formation. This loop does not contribute to ligand interaction.		
		Large disordered insertion domain at the N-terminal part of the LBD	Yes	[24]
		All PXR structures previously showed residues 178-197 were disordered and 198-210 form a pseudo helix in this structure formed an α-helix through residue 205 – this is unique to PXR.	Yes 17 of 20 residues (178-197) yes all residues from 198-210	[25]
1I2	**PXR**	CD data shows stability with ligand and SRC-1 binding.		
		Rifampicin induces structural disorder at 178-209, 229-235, 310-317, all regions at the base of the LBD. The 2 additional areas were observed in other structures but had high thermal displacement indicative of structural mobility. 192-198-202 pseudo helix changes position and accommodates ligand binding	Residues 229-235 and 310-317 are predicted as ordered	[26]
		No discussion of disorder		[27]

		No discussion of disorder		28
1I3	CAR	Mouse– No discussion of disorder		29
		No discussion of disorder		30
		Electron density is apparent for all residues except those at the amino (133–140) and carboxyl (368–382) termini of the domain and within the loop between helices 1 and 3 (the 1/3 loop, residues 157–165).	Yes (residues 133-140) and for 5 residues in 368-382 and 8 out of 9 for residues 157-165	31
2A1	**HNF4A**			
2A2	HNF4A γ	No crystal structures found		
		Tobacco budworm USP: Disorder in 206-207, 304, 315-318	Yes (residues 206-207), No (304), yes (315-318)	13
2B	**USP/RXR**			
		Drosophila USP -No mention of disorder		15
		Red flour beetle USP: no mention of disorder		16
		Has an additional helix 2 in the same position that FXR has disorder which becomes disordered on ligand binding		32
2B1	**RXR α**			
		No mention of disorder		33

		Residues Arg182 to Cys187 form a distorted helix in the X-ray structure that is not seen in the mean NMR structure. The disorder observed in the D-box of RXR, residues 172 to 176, may well arise from an inherent lack of NOEs because the protein is flexible and undergoes conformational fuctuations.	Yes	[34]
2B2	RXR β	No crystal structures found		
2B3	RXR γ	No mention of disorder		[35]
2C1	TR2	No crystal structures found		
2C2	TR4	No crystal structures found		
2E1	TLX	No crystal structures found		
2E3	PNR	No crystal structures found		
2F1	COUP TFI	No crystal structures found		
2F2	COUP TFII	No crystal structures found		
2F6	EAR 2	No crystal structures found		
		Residues 301-304 and 549-553 are	Yes (301-304) No	[36]
3A1	**ER α**	disordered	(549-553)	
		Residues K416-M421 and Y526-L536 are disordered	No	[37]
		15 residues in DBD disorder		[38]

		ERα-NTD unstructured in solution	Yes	[39]
		H12 (486-) and Met336 are	Yes (486) No (336)	[40]
3A2	**ER β**	disordered		
		H12 disordered in presence of ICI	No	[41]
		ligand. Met 479 disordered.		
		ER beta-N terminal unstructured in	Yes	[39]
		solution		
		Residues P309-P319 and R462-E470	Yes (309-319)	[42]
		disordered	Residues 462-470 not	
3B1	**ERR α**		determined	
		NMR structure of DBD residues	Yes	[43]
3B2	**ERR β**	R182, Y185, and 187-194 disordered		
3B3	ERR γ	No mention of disorder		[44]
		No mention of disorder.		[45]
3C1	**GR**	No mention of disorder.		[46]
		No mention of disorder.		[47]
		NTD AF-1 region shown to be	Yes	[48]
		unstructured in solution using NMR		
		and circular dichroism		
3C2	MR	No mention of disorder.		[49]
		DBD: residues L562, 640-648	Yes 7 of 9 residues	[50]
		disordered.	(640-648) No (residue	
3C3	**PR**		562)	

		No mention of disorder.		[51]
		NTD sensitive to rapid degradation in limited proteolysis experiments indicated disorder	Yes	[52]
		H9-H10 interloop (844-849) disordered	Yes	[53]
3C4	**AR**	Rat LBD: N-terminal 664-671 disordered	No	[54]
		DBD residues 533-536, 612-637 disordered	Yes (612-637) No (533-536)	[55]
		Human N-terminal domain residues 142-485 (AF1) disordered	Yes	[56, 57]
4A1	Nur77	No mention of disorder		[58]
4A2	Nurr1	No mention of disorder		[59]
4A3	NOR-1	No crystal structures found		
5A1	SF1	No mention of disorder		[60]
		No mention of disorder (crystal structures of both SF-1 and LRH-1)		[61]
		No mention of disorder (crystal structures of both SF-1 and LRH-1)		[62]
5A2	FTZ-F1β	No mention of disorder (crystal structures of both SF-1 and LRH-1)		[61]
		No mention of disorder.		[63]

		No mention of disorder (crystal structures of both SF-1 and LRH-1)	62
		DBD of LRH-1: no mention of disorder	64
		LBD: no mention of disorder	65
6A1	GCNF	No crystal structures found	
0B1	DAX1	No crystal structures found	
0B2	SHP	No crystal structures found	

DBD = DNA-binding domain, NTD = N-terminal domain, and LBD = ligand binding domain, NHR in bold show disorder or no density in X-ray/NMR.

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