Table S3. Tubulin fragment-binding sites identified by X-ray crystallography.

β-Tubulin

sID [1]	SS [2]	ResID [3]	Fragment ID [4]	V_f [5] (Å^3)	PDB ID [6]	Notes
βI	βH6 βH9 βH9-βS8	βAsp 211 βIle 212 βArg 215 βThr 216 βLys 218 βSer 298 βLys 299	01 53	173	5S4L 5S61	Unknown ligand-binding site Residue substitutions in human β-tubulin isotypes: β2a/β2b, A298S; β1/β6, K299R; β8, R215K
βII	βH1 βH7 βS7 βM βS8 βS9-βS10 βS10	βVal 23 βGlu 27 βHis 229 βAla 233 βThr 234 βSer 236 βGly 237 βPhe 272 βPro 274 βArg 320 βPro 360 βArg 369 βLeu 371 βSer 374 βThr 376	02 03	207	5S4M 5S4N	Taxane site Residue substitutions in human β-tubulin isotypes: β1, V23M, A233L, A374S; β4a/β5/β6, S374A
βIII	βN-ter βH1' βT7	αThr 73 βMet 1 βLeu 46 βGlu 47 βArg 48 βIle 49 βAsn 50 βVal 51 βAla 250 βAsp 251	04	179	5S4O	Unknown ligand-binding site Residue substitutions in human β-tubulin isotypes: β5, E47D, N50S
βIV	αT5 βS1 βH1' βS4 βS5 βS6 βH7 βT7 βH8 βS8 βS9 βS10	αThr 179 αAla 180 αVal 181 βIle 4 βTyr 52 βGln 136 βAsn 167 βPhe 169 βGlu 200 βTyr 202 βVal 238 βThr 239 βCys 241	03 05 06 07 08 09 10 11 12 13 14 15 16	780	5S4N 5S4P 5S4Q 5S4R 5S4S 5S4T 5S4U 5S4V 5S4W 5S4X 5S4Y 5S4Z 5S50	Colchicine site Residue substitutions in human β-tubulin isotypes: β1, E200A, Y202F, V238I, C241S, A317C, V318I, T353V; β2a/β2b, V318I; β3/β6, C241S, A317T, T353V; β8, Y202F, V318I

		βLeu 242 βGln 247 βLeu 248 βAsn 249 βAla 250 βLeu 252 βLeu 255 βAla 256 βAsn 258 βMet 259 βPhe 268 βAla 316 βAla 317 βIle 318 βAsn 350 βLys 352 βThr 353 βAla 354 βIle 378	17 18 19		5S51 5S52 5S53	
βV	αH11' βS4 βH4 βH4-βS5 βS5 βH5 βH5-βS6 βH8 βH8-βS7	αHis 406 αVal 409 αGly 410 αGlu 411 βPhe 135 βIle 154 βIle 157 βArg 158 βTyr 161 βPro 162 βAsp 163 βArg 164 βIle 165 βMet 166 βVal 195 βGlu 196 βAsn 197 βThr 198 βAsp 199 βArg 253 βPro 263 βArg 264 βHis 266	14 20 21 22 23 24 25 26	669	5S4Y 5S54 5S55 5S56 5S57 5S58 5S59 5S5A	Unknown ligand-binding site Residue substitutions in human β-tubulin isotypes: β1, I154L, V195I, T198A; β3, I157V; β4a/β6, Y161F; β8, I154M, M166I, V195I, T198A

β1α2-Tubulin

sID [1]	SS [2]	ResID [3]	Fragment ID [4]	V_f [5] (Å^3)	PDB ID [6]	Notes
βαI	αH8-αS7 αH12 βH11-βH11'	αTyr 262 αPro 263 αArg 264 αIle 265 αAsp 431 αGlu 434 αVal 435 βArg 400 βArg 401 βLys 402	27 28 29	511	5S5B 5S5C 5S5D	Unknown ligand-binding site Residue substitution in human β-tubulin isotypes: β1, R400K
βαII	αH3-S4 αS4 αH4-αS5 αS6 αH8 βT3 βH3' βT5 βH11'	αCys 4 αGln 133 αGly 134 αPhe 135 αLeu 136 αSer 165 αLeu 167 αAsp 199 αCys 200 αPhe 202 αLeu 242 αLeu 252 αThr 253 αGln 256 αThr 257 αLeu 259 βGly 100 βAsn 101 βAsn 102 βLys 105 βVal 182 βTrp 407 βTyr 408 βGlu 411	04 11 30 31 32 33 34 35 36 37 38 39 40 41 42 43	632	5S4O 5S4V 5S5E 5S5F 5S5G 5S5H 5S5I 5S5J 5S5K 5S5L 5S5M 5S5N 5S5O 5S5P 5S5Q 5S5R	Unknown ligand-binding site Located between the maytansine and pironetin sites Residue substitution in human β-tubulin isotypes: β6, Y408F
βαIII	αT7 αH8 αH10 αH10-αS9 αS9 βT5 βH5 βH6 βH6-βH7 βH7 βH11	αLeu 248 αVal 250 αAsn 258 αPro 325 αVal 328 αAsn 329 αIle 332 αPro 348 αGly 350 αPhe 351 αLys 352 αVal 353 αGly 354 αIle 355 βPro 173	03 05 07 15 22 26 29 30 38 44 45 46 47 48 49	1139	5S4N 5S4P 5S4R 5S4Z 5S56 5S5A 5S5D 5S5E 5S5M 5S5S 5S5T 5S5U 5S5V 5S5W 5S5X	Vinblastine site Residue substitution in human β-tubulin isotypes: β1, Q394H

		βSer 174 βPro 175 βLys 176 βVal 177 βSer 178 βAsp 179 βThr 180 βVal 181 βGlu 183 βPro 184 βTyr 210 βThr 221 βPro 222 βThr 223 βTyr 224 βLeu 227 βGln 394	50 51 52 53 54 55 56		5S5Y 5S5Z 5S60 5S61 5S62 5S63 5S64	

α-Tubulin

sID [1]	SS [2]	ResID [3]	Fragment ID [4]	V_f [5] (Å^3)	PDB ID [6]	Notes
αI	αH6 αM αH9	αArg 215 αAsn 216 αPro 274 αVal 275 αLys 280 αLeu 286 αAla 294	05	185	5S4P	Unknown ligand-binding site Residue substitutions in human α-tubulin isotypes: α8, V275I, A294S
αII	αH1 αH2 αH2-αS3 αH7	αGln 15 αAsn 18 αAla 19 αTrp 21 αGlu 22 αGlu 77 αVal 78 αGly 81 αThr 82 αTyr 83 αPhe 87 αThr 225 αAsn 228 αArg 229	02 25 53	364	5S4M 5S59 5S61	Unknown ligand-binding site Residue substitutions in human α-tubulin isotypes: α4a, V78I, T82P

Crystal contact/binding partner of T_2R-TTL

sID [1]	SS [2]	ResID [3]	Fragment ID [4]	V_f [5] (Å^3)	PDB ID [6]	Notes
X1	αH1-αS2	αThr 41 αIle 42 αGly 43 αGly 44 αGly 45 αAsp 46	26 39 57	-	5S5A 5S5N 5S65	Site involving a crystal contact formed by a neighboring α-tubulin monomer
X2	αH2- αS3 αH3	αHis 88 αGlu 90 αGln 91 αArg 121 αLys 124 αLeu 125	05	-	5S4P	Site involving a crystal contact formed by a neighboring TTL molecule
X3	αH4-αS5 αH5 βH11’	αSer 158 αGly 162 αLys 163 αLys 166 αGlu 196 αHis 197 αSer 198 αAsp 199 βGly 410	58 59	-	5S66 5S67	Site involving residues of RB3

[1]Fragment site identifiers. X1, X2 and X3 refer to sites that involve either a crystal contact (X1 and X2) or a tubulin-binding partner of the T_2R-TTL complex (X3).
[2]Secondary structural elements involved in site formation.
[3]Residues that are in contact with the identified fragments (maximal distance of 4 Å).
[4]Fragment ID according to the deposited structures in the RCSB Protein Data Bank.
[5]Total fragment volume.
[6]PDB IDs for the deposited structures in the RCSB Protein Data Bank.