

**Table 1S.** Data computed from the MSA containing 47 sequences of human TFPDs.

Case	AA-residues	Conservation/Divergence/Similarity			Comments
1	L,C,K(50-52)	0.61	0.55	0.64	β-strand 1 (F1)
2	T,S,I,C(74-77)	0.53	0.60	0.51	β-strand 2 (F1)
3	V,C,V,A,V,W,R,K(83-90)	0.50	0.56	0.34	β-strand 3 (F2)
4	I,T,L,E,T,V,C,H(95-102)	0.51	0.53	0.32	β-strand 4 (F2)
4	C,I,M,K,E(121-126)	0.48	0.65	0.44	β-strand 5 (F3)
5	T,F,F,M,C,S,C(131-138)	0.55	0.51	0.45	β-strand 6 (F3)
6	C,S,S,D,E,C,N(138-144)	0.70	0.38	0.47	C-terminal
7	C51	1.00			Cys-1 (Db1)
8	C54	0.82			Cys-1 (Db1a)
9	C71	0.82			Cys-2 (Db1a)
8	C77	1.00			Cys-1 (Db2)
9	C84	1.00			Cys-2 (Db1)
10	C101	1.00			Cys-2 (Db2)
11	C121	1.00			Cys-1 (Db3)
12	C136	0.88			Cys-2 (Db3)
13	C138	0.77			Cys-1 (Db4)
14	C143	1.00			Cys-2 (Db4)
15	C143,N144	1.00			C-terminal CN

The sequence conservation was calculated using the sequence of NP\_003233, (TGF-beta type II receptor isoform B precursor, Homo sapiens) as reference and the Blosum30 matrix. Divergence and similarity scores were calculated using the AAC derived from the human genome database containing 28243 entries.

Magenta - signal sequence, in yellow are the Cys residues in the TFPD, whereas in cyan are β-strands established in the structures of 1M9Z.

123456789012345678901234567890123456789012345678901234567890123456789012345678901234567  
10 20 30 40 50 60 70 80 90  
MGRGLRGLWPLHIVLWTRIAS<sup>T</sup>IPPHVQKSVNNDMIVTDNNGAVKFPQLCKFC<sup>D</sup>DVRFST<sup>C</sup>DNQKSCMSNCSITSI<sup>C</sup>EKPQEV<sup>C</sup>VAVWRKNDENITLET<sup>V</sup>CHDPKLPYHDFILEDASPK<sup>C</sup>IMKEKKKPGET<sup>TF</sup>FMCS<sup>C</sup>SSDEC<sup>N</sup>DNII<sup>F</sup>SEEYNTSNPDLLVIFQVTGISLLPPLGV<sup>A</sup>ISVII<sup>I</sup>FYCYRVNRQQLSSTWETGKTRKLMFSEHCAIILED<sup>R</sup>SDISSTCANINHNTELLPIELDTLVGKGRFAEVYKAKLKQNTSEQFETVAVKIFPYEYASWKT<sup>E</sup>KDIFSDINLKHENILQFLTABERKTEL<sup>G</sup>KQYWLITAFHAKGNLQ<sup>E</sup>YLTRHVISWEDLRKLGSSSLARGIAHLHSDHTPCGRPKMP<sup>I</sup>VHRDLKSSNILVKNDLTCC<sup>L</sup>CD<sup>F</sup>G<sup>L</sup>SLRLDPTLSVDDLANSGQVGTARYMAPEVLES<sup>R</sup>MRNLENVESFKQ<sup>T</sup>DVYSMALVLWEMTSRCNAVGEVKDYEP<sup>P</sup>FGSKVREHPCVESMKDNVLRDRGRPEI<sup>P</sup>PSFWLNHQGIQ<sup>M</sup>V<sup>C</sup>ETL<sup>T</sup>ECWDHDP<sup>E</sup>ARLTAQCVAERFSELEHLDRLSGRSCSEEKIPEDGSLN<sup>T</sup>TK\*