

Supporting Information

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Tdp1.hs	1	MSQEGDYGRWITSSSDESEEEKPKDPKSTSSLLCARQGAANEPRYTCEAQKAAHKRKRISPVKF	65
Tdp1.chicken	1	MLQEGAHGRWTVSSSEDSTEENSSEKSTSSLLSAPRSEASGPQYPCSEARKVAHKRKASPLRF	65
Tdp1.dm	1	-MKCEPYG-----EKCYRKNPIHFGEFSAHLDAIYAKGNESGDYEIPAN---YSSEM	49
Tdp1.sc	1	MSRETNFN-----GTKRKRSDVAEKVAQRWKSVR-----	29
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Tdp1.hs	66	SNTDS--VLPPKRQKSGSQEDLGWCLSSSDELOPEMPQKQAEKVVIKKEKDISAPNDGTAQRTE	128
Tdp1.chicken	66	SDTHLPAQTTPAEKQRPQGEGLGWCLSSSDE--EPEDREKHTRKETLKEEK-----CDAPREQPQ	123
Tdp1.dm	50	IHTQLKLEKLFPKQATNKEQEAHSSSSKPAVTAPVAGSSSSGSLDTPNSGSSASGPAASQDTS	114
Tdp1.sc	30	-----YSAEMENMAPVNSNNSDDCVIVSESKIIDL TNQEQLSE	69
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Tdp1.hs	129	NHGAPACHRLKEEEDYEYTSGEQDIWMDLKGPNPFQFYLTRVSGVKPKYNS--GALHIKIDILSPL	192
Tdp1.chicken	124	SHCKDEHSKNEKAEDYNEVLGEPQDTWLLSGGNPFGFFLTKVRGIEQSYNS--GALHIKIDILSPL	187
Tdp1.dm	115	NLAKKQKLNAKNIRDYIPVVIKGGMAKLERAAPYNMFLTAITDSKPTHSEPLSITLQELDES	179
Tdp1.sc	70	RIETNDTAKGAVFKLMKSDFYEREDFMGEVED-----MITLKDIFG--	110
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Tdp1.hs	193	FGTLVSSAQFNFCFVDVWLVKQYP--PEFRKKPILLVHGDKR--EAKAHLHAQAKPYENISLCQAK	254
Tdp1.chicken	188	FGTLVSSAQFNFCIDVAWLVRQYP--QEYRKKPLLVHGEKR--ESKAELLAQARPFENISFCQAK	249
Tdp1.dm	180	LGEIESTVQINFMVDIGWLLGHYYFAGILDKPLLLYGD-----SPELLSIGKFKQQTVAIRVK	239
Tdp1.sc	111	TETLKRSLFSFQYELDFLLRQFH--QNVENITIVGQKGTIMPIEARAMDATLAVILKVKVLIET	174
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Tdp1.hs	255	LDIAFGTHHTKMMLLLYEEG--LRVVIHTSNLIHADWHQKTQGIWLSPLYPRIADG--THKSGESPT	317
Tdp1.chicken	250	LDIAFGTHHTKMMLLLYEEG--LRVVIHTSNLIAEDWHQKTQGIWLSPLYPRLPQSSDSAGESET	313
Tdp1.dm	240	MPTPFATSHTKMMLLGYSDGSMRVVISTANLYEDDWHNRQTGLWISPKLPALPVDADTGAGESLT	304
Tdp1.sc	175	MP--PFASHHTKLIINFYDNGECKIFLPSNMFSTMETNLQQVCWCSPLLKIGKEG-----LPV	231
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Tdp1.hs	318	HFKADLISYLMAYNAPSLKEWIDVIHKHD--LSETNVYLIGSTPG--RFQGSQKDNWGHFRLKLL	378
Tdp1.chicken	314	NFKSDLISYLMAYSSPVLKEWIDLIREHD--LSETRVYLLGSTPG--RYQIDKEKKGWHLKRLK	374
Tdp1.dm	305	GFKQDLMLYLVEYKISLQQPWIARIRNSD--FSAINVFFLGSVPGHREGSVRGHWPGHARLASL	367
Tdp1.sc	232	PFKRSLE YLNSYHLKDIDELITKSVVEVNFAPLSELEFVYSTPS--KFQSSGLLSF--YNKLEKL	293
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Tdp1.hs	379	LKDHAASSPNAESWPVVGQFSSVGLGADGSKW---LCSEFKESMLTLGKESKTPGKSSVP----	436
Tdp1.chicken	375	LKDHAASSIPAQESWPVVGQFSSIGSLGADGSKW---LCSEFQESLVAAGSVAALLKCDVP----	432
Tdp1.dm	368	LAKHAA--PIDDRIPVVCSSSISLGANVQAW---IQQDFVNSLKKD-STPVGKLRQMP-----	422
Tdp1.sc	294	SAGTSASDTAKHYLCQTSSIGTSLSRARDENLWTHLMIPLFTGIMSPPAKDTAGRKKAEILPTNS	358
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Tdp1.hs	437	-----LYLIYPSVENVRTSLEGYPAGGSLPYSIQTAE-----KQNLWHSYFHKWSAET	484
Tdp1.chicken	433	-----IHLVYPTVSNVRQSLLEGYPAGGSLPYSIQTAQ-----KQLWLSYFHKWSAEV	480
Tdp1.dm	423	-----FKMIYPSYGNVAGSHDGMGGGCLPYGKNTND-----KQPWLKDYLQQWSSD	470
Tdp1.sc	359	LINEYSQRKIKPYIIFPTEQEFVTSPLKWSSSGWFHFQYLQKKSYYEMLRNKFKYFVQDPAMVT	423
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Tdp1.hs	485	SGRSNAMPHIKTYMRPSD-----FSKIAWFLVTSANLSKAAWGALEKNG---TQLMIRS	536
Tdp1.chicken	481	SGRSHAMPHIKTYMRPSHD-----FQKIAWFLVTSANLSKAAWGALEKNG---TQLMIRS	532
Tdp1.dm	471	RFRSRAMPHIKSYTRFNLE-----DQSVYWFVLTSAANLSKAAWGCFNKNSNIQPCLRIAN	525
Tdp1.sc	424	RRRGTTPAHSKFMHCATNSAGPCDASQVFKLEWCLYTSANLSQTAWGTVSRKP-----RN	480
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Tdp1.hs	537	YELGVLFLPSAFGLDS--FKVKQKFFAGSQEPMATFP---VPYDLPELYGSKDRPWIWNIPYV	595
Tdp1.chicken	533	YELGVLFLPSAFGLDKGYFHVKGNMLSEGKDSATSF---VPFDLPPERYGSKDQPWIWNIPYT	593
Tdp1.dm	526	YEAGVFLPRFVTGED-----TFPLGNRDGVPAPF---LPYDVPLTPYAPDDKPFLLMDYLQG	580
Tdp1.sc	481	YEAGVLYSRRLANTR---KVTCTRTFDRRRCAGNPHTHAVVPTFLPVIPYDLAEDECFLARHE	542
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Tdp1.hs	596	KAPDTHGNMWVPS	608
Tdp1.chicken	594	SAPDTHGNMWVPS	606
Tdp1.dm	581	-----	580
Tdp1.sc	543	ND-----	544

Fig. S1. Amino acid sequence alignment of *Drosophila* (red), yeast *Saccharomyces cerevisiae*, and human and chicken TDP1 polypeptides. Identical residues are shown in red with asterisks underneath. Conserved residues are indicated by dots underneath. Catalytic residues are highlighted in yellow (1, 2) and conserved residues in contact with the nucleic acid substrate (1) are in pink.

- Pommier Y, et al. (2014) Tyrosyl-DNA-phosphodiesterases (TDP1 and TDP2). *DNA Repair (Amst)* 19:114–129.
- Davies DR, Interthal H, Champoux JJ, Hol WG (2002) The crystal structure of human tyrosyl-DNA phosphodiesterase, Tdp1. *Structure* 10(2):237–248.