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Supplementary information S1 (table) | **Major features of HUH enzymes**

	Group	Protein (element)	Ys	HUH	Biochemistry	Structure
Reps	Phages	GpA (ϕX174)	Y343 Y347	yes	Y343 and Y347 involved (Van Mansfeld et al., 1986) Flip-flop mechanism (Hanai and Wang, 1993)	NO
		A (P2)	Y454 Y450	yes	Initiation (Y454) and termination (Y450) Tyr are different (Odegrip and Haggård-Ljungquist, 2001)	NO
		GpII (M13)	Y197	no	No stable covalent complex (Asano et al., 1999)	NO
		SIRV1 Rep	Y108	yes	Stable covalent complex (Oke et al., 2011)	2X3G (Oke et al., 2011) dimer
	Viruses	Rep (AAV5)	Y156	yes	Site-specific endonuclease activity (Im and Muzyczka, 1990)	1M55 (Hickman et al., 2002) 1RZ9 (Hickman et al., 2004)
		Rep (TYLCV)	Y103	yes	Cleavage and joining domain (Heyraud-Nitschke et al., 1995)	1L2V (Campos-Olivas et al., 2002)
		Rep (FBNYV)	Y79	HUQ	In vitro endonuclease activity (Vega-Rocha et al., 2007b)	2HWT (Vega-Rocha et al., 2007b)
		Rep (PCV)	Y96	HUQ	In vitro endonuclease activity (Vega-Rocha et al., 2007a)	2HW0 (Vega-Rocha et al., 2007a)
	Plasmids	RepB pMV158	Y99	Yes	Chiral phosphorothioate (Moscoso et al., 1997)	3DKY (Boer et al., 2009)
		RepA pC194	Y214 E210	yes	Termination hydrolysis by Glu (Noirot-Gros et al., 1994) Flip-flop with E210Y (Noirot-Gros and Ehrlich, 1996)	NO

		RepC pT181	Y191	No	Short oligonuclotide inactivation (Rasooly and Novick, 1993)	NO
Mobs	MOB_F	TrwC (R388)	Y18 Y26	yes	Initiation and termination Tyr (Grandoso et al., 2000) Intramolecular reaction (Gonzalez-Perez et al., 2007) TrwC transfer to the recipient (Draper et al., 2005) Termination reaction in the recipient (Garcillán-Barcia et al., 2007)	1OMH (Guasch et al., 2003)
		TraI (F)	Y16 Y17		Two contiguous catalytic Tyr (Street et al., 2003) Differential metal affinity (Larkin et al., 2005)	1P4D, (Datta et al., 2003)
		TraI (pCU1)	Y18-19 Y26-27	yes	Tyrosine partners (Nash et al., 2011)	3L57 (Nash et al., 2010)
	MOB_Q	MobA (RSF1010)	Y25	yes	In vitro SC and SS DNA cleavage (Scherzinger et al., 1992)	2NS6 (Monzingo et al., 2007)
	MOB_P	TraI (RP4)	Y22	Yes	Three motifs (Pansegrau et al., 1994)	NO
		MbeA (ColE1)	Y19	HEN	Divergent HUH motif (Varsaki et al., 2003)	NO
	MOB_V	MobM (pMV158)	?	yes	In vitro relaxase activity (Guzmán and Espinosa, 1997)	NO
	MOB_C	MobC (CloDF13)	?	No	No covalent complex (Núñez and De La Cruz, 2001)	NO
	MOB_H	TraI (Neisseria chromosome)	Y93 Y201	HHH	Covalent intermediate (Salgado-Pabón et al., 2007)	NO

Tpases	TnpA	IS608 (H. pylori)	Y127	HUH	Covalent intermediate (Ton-Hoang et al., 2005)	2A6M, 2A60 (Ronning et al., 2005) dimer 2VIH (TnpA/LE26), 2VIC (TnpA/LE26+Mn^{2+}), 2VHG (TnpA/RE31), 2VJU (TnpA/RE35) and 2VJV (TnpA/LE26/D6) (Barabas et al., 2008) dimer
	TnpA	ISDra2 (D. radiodurans)	Y132	HUH	Covalent intermediate (Hickman et al., 2010)	2XM3 (TnpA/LE27/T5), 2XMA (TnpA/RE34), 2XO6 (TnpA/Cd) and 2XQC (TnpA/Zn) (Hickman et al., 2010) dimer
		IS1476 (S. solfataricus) Incomplete IS	?	HUH		ISfinder S. solfataricus genome 2F4F, 2F5G (Lee et al., 2006) dimer
REP	$TnpA_{REP}$	E.coli		HUH	Covalent intermediate (Ton Hoang et al., 2012)	(Messing et al., 2012) monomer
	Tpase	IS91		HUH		NO
	Tpase	ISCR		HUH		NO

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