Supplementary Table 1. Quantitative evaluations of ATTECs (1)

TPD technology	Target substrate	Treatment condition			Degradation measurement			Reference
		Model (cell line/animal model)	Compound	Treatment condition	Measurement method	DC50	Dmax	
ATTEC	mHTT	Cultured primary cortical neurons (HdhQ7/Q140)	10O5	100 nM, 48 h	Immunoblotting	N/A	26 %	Z. Li (2019)[1]
			8F20	100 nM, 48 h		N/A	40.1 %	
			AN1	50 nM, 48 h		N/A	35.7 %	
			AN2	75 nM, 48 h		N/A	34 %	
		Primary human HD patient fibroblasts (Q49)	10O5	100 nM, 48 h	HTRF	N/A	44.9 %	
			8F20			N/A	44.6 %	
			AN1			N/A	45.8 %	
			AN2			N/A	54.6 %	
		Primary human HD patient fibroblasts (Q55)	10O5	100 nM, 48 h	HTRF	N/A	34.3 %	
			8F20			N/A	28.7 %	
			AN1			N/A	26.5 %	
			AN2			N/A	39.3 %	
		Primary human HD patient fibroblasts (Q68)	10O5	100 nM, 48 h	HTRF	N/A	20.9 %	
			8F20			N/A	22.9 %	
			AN1			N/A	26.4 %	
			AN2			N/A	18.1 %	

Supplementary Table 1. Quantitative evaluations of ATTECs (2)

TPD technology	Target substrate	Treatment condition			Degradation measurement			Reference
		Model (cell line/animal model)	Compound	Treatment condition	Measurement method	DC50	Dmax	
ATTEC	mHTT	HD patient iPSC-derived neurons (Q47)	10O5	100 nM, 48 h	HTRF	N/A	31.3 %	Z. Li (2019)[1]
			8F20			N/A	28.8 %	
			AN1			N/A	39.2 %	
			AN2			N/A	40.4 %	
		Immortalized patient iPSC-derived neurons (Q47)	10O5	100 nM, 48 h	HTRF	N/A	30.2 %	
			8F20			N/A	21.9 %	
			AN1			N/A	41.9 %	
			AN2			N/A	41.4 %	
		Cortices from icv-injected mice (HdhQ7/Q140)	10O5	2 ul at 25 μM/day for 10 days	Immunoblotting	N/A	43.3 %	
			8F20			N/A	9.1 %	
			AN1			N/A	29.9 %	
			AN2			N/A	30.3 %	
		Cortices from ip-injected mice (HdhQ7/Q140)	10O5	0.5 mg/kg/day for 2 weeks	Immunoblotting	N/A	20.5 %	
			AN2			N/A	37 %	
		Striata from ip-injected mice (HdhQ7/Q140)	10O5	0.5 mg/kg/day for 2 weeks	Immunoblotting	N/A	24.4 %	
			AN2			N/A	26.1 %	

Supplementary Table 1. Quantitative evaluations of ATTECs (3)

TPD Technology	Target substrate	Treatment condition			Degradation measurement			Reference
		Model (cell line/animal model)	Compound	Treatment condition	Measurement method	DC50	Dmax	
ATTEC	mHTT	Transgenic flies expressing full-length HTT(Q128)	10O5	10 μM for 6 days (fed with elav-GAL4)	HTRF	N/A	47.9 %	Z. Li (2019)[1]
			8F20			N/A	78.4 %	
			AN1			N/A	38.3 %	
			AN2			N/A	60 %	
	mutant ATXN3	Primary human SCA3 patient fibroblast	10O5	100 nM, 48 h	Immunoblotting	N/A	71.8 %	
			AN1	100 nM, 48 h		N/A	70.5 %	
			AN2	50 nM, 48 h		N/A	66.2 %	
	polyQ-GFP	Exogenously expressed 38Q-GFP in HEK293T cells	10O5	100 nM, 48 h	Measure GFP intensity through live cell imaging (Incucyte)	N/A	10.7 %	
			AN1	100 nM, 48 h		N/A	25.5 %	
			AN2	50 nM, 48 h		N/A	10.8 %	
		Exogenously expressed 46Q-GFP in HEK293T cells	10O5	100 nM, 48 h		N/A	31 %	
			AN1	100 nM, 48 h		N/A	39.9 %	
			AN2	50 nM, 48 h		N/A	18.3 %	
		Exogenously expressed 72Q-GFP in HEK293T cells	10O5	100 nM, 48 h		N/A	24.8 %	
			AN1	100 nM, 48 h		N/A	24.4 %	
			AN2	50 nM, 48 h		N/A	7.7 %	

Supplementary Table 1. Quantitative evaluations of ATTECs (4)

TPD Technology	Target substrate	Treatment condition			Degradation measurement			Reference
		Model (cell line/animal model)	Compound	Treatment condition	Measurement method	DC50	Dmax	
ATTEC	BRD4	HeLa	10f	20 μM. 24 h	Immunoblotting	N/A	92 %	J. Pei (2021)[2]
		HL60				N/A	86 %	
		MDA-MB-231				N/A	99 %	
		MCF-7				N/A	83 %	
		MDA-MB-436				N/A	90 %	
		MDA-MB-436				N/A	91 %	
	NAMPT	A2780	A3	3 μM, 48 h	Immunoblotting	N/A	91 %	G. Dong (2022)[3]
	CDK9 42	U-2932	Compound 10	1 μM, 24 h	Immunoblotting	N/A	59 %	Y. Zeng (2023)[4]
			Compound 16	1 μM, 24 h		N/A	50 %	
	CDK9 55	U-2932	Compound 10	1 μM, 24 h	Immunoblotting	N/A	54.8 %	
			Compound 16	1 μM, 24 h		N/A	46 %	

Supplementary Table 2. Mass-spectrometry analysis after cells or mice were treated with Ub-independent TPDs

TPD technology	Sample type	Treatment compound		MS data analyzing method	Fold change	p-Value	Number of significantly changed proteins (compared to control)			Reference
		Treatment compound	treatment condition				Total (change/ID)	Up	Down	
ATTEC	HD mouse cortices	10O5	0.5 mg/kg of compound by i.p. injection for 14 days	iBAQ	N/A	< 0.01	181/7191	105	76	Z. Li (2019)[1]
		AN2					73/7245	43	30	
	cultured cortical neurons	10O5	100 nM, 48h				51/7140	27	24	
		AN2	50 nM, 48 h				103/7086	33	70	
	Liver tissues from db/db mice	C3	30 mg/kg/day by i.p. injection for 14 weeks	iBAQ	>|0.7|	< 0.01	39/3393	28	11	Y. Fu (2021)[5]
		C4					35/3337	24	11	
LYTAC	Hella cells	Ab-2	10 nM, 24 h	LFQ	> |2|	< 0.05	26/3877	11	15	S. M. Banik (2020)[6]
KineTAC	MDA-MB-231 cells (surface enriched)	CXCL12-Atz	100 nM, 48 h	SILAC	> |2|	< 0.01	*1/898	0	1	K. Pance (2023)[7]
	MDA-MB-231 cells (whole cell)						*1/4714	0	1	
	Hela cells (surface enriched)	CXCL12-Ctx					*2/1305	0	2	
	Hela cells (whole cell)						*1/4912	0	1	
UID	HEK293-Rpn13-HTP-Flag cells	WJ704	10 uM, 4h	TMT	> |2|	< 0.01	N/A	N/A	N/A	M. Balzarini (2023)[8]
		WJ706					N/A	N/A	N/A	

*The number of significantly changed proteins is defined by significance value (> 20) and more than 2-fold change

Supplementary Table 3. Quantitative evaluations of AUTOTACs (1)

TPD technology	Target substrate	Treatment condition			Degradation measurement			Reference
		Model (cell line/animal model)	Compound	Treatment condition	Measurement method	DC50	Dmax	
AUTOTAC	ERβ	HEK293T	PHTPP-1304	0.001-2.5 μM, 24 h	Immunoblotting	1.48 nM	95.8 %	C. H. Ji (2022)[9]
		ACHN		0.1-5 μM, 24 h		<100 nM	N/A	
		MCF7		0.1-10 μM, 24 h		<100 nM	N/A	
	AR	LNCaP	VinclozolinM2-2204	0.01-10 μM, 24 h		211.08 nM	94 %	
	MetAP2	HEK293T	Fumagilin-105	0.001-10 μM, 24 h		0.701 μM	80.8 %	
		U87-MG	Fumagilin-105	0.5-10 μM, 24 h		~500 nM	N/A	
	Tau	SH-SY5Y-TauP301L	PBA-1105	0.001-10 μM, 24 h		0.71 nM	87.5 %	
			Anle138b-F105	0.001-10 μM, 24 h		2.63 nM	90.4 %	
	Insoluble hTauP301L	i.p. injected TauP301L-BiFC transgenic mice	PBA-1105	20 mg/kg for 4weeks (3 times/week)	Immunoblotting	N/A	56.1 %	
	Total tau oligomer				Quantification of BiFC fluorescence in the cortex	N/A	37.2 %	
	p-tau				Immunostaining -quantification of AT-8 fluorescence in the cortex	N/A	22.4 %	

Supplementary Table 3. Quantitative evaluations of AUTOTACs (2)

TPD technology	Target substrate	Treatment condition			Degradation measurement			Reference
		Model (cell line/animal model)	Compound	Treatment condition	Measurement method	DC50	Dmax	
AUTOTAC	Insoluble hTauP301L	i.p. injected TauP301L-BiFC transgenic mice	PBA-1105	50 mg/kg for 4weeks (3 times/week)	Immunoblotting	N/A	90.4 %	C. H. Ji (2022)[9]
	Total tau oligomer				Quantification of BiFC fluorescence in the cortex	N/A	61.3 %	
	p-tau				Immunostaining-quantification of AT-8 fluorescence in the cortex	N/A	37.3 %	
	RFP-GFP-TauP301L	HeLa	PBA-1105	100 nM, 24 h	Immunostaining – quantification of GFP puncta	N/A	60 %	
	mHTT	HeLa-Htt-NLS-Q97-GFP	PBA-1105 PBA-1106	2.5 μM, 24 h	Immunoblotting	0.1-1 μM	N/A	
		HeLa-Htt-NES-Q97-GFP	PBA-1106 YOK-1106	2.5 μM, 24 h				
	α-synuclein	SH-SY5Y A53T	ATC161	0.01-1 μM, 24 h	Immunoblotting	100 nM	N/A	J. Lee (2023)[10]
		Primary cortex neurons		0.01-1 μM, 24 h		N/A	N/A	

Supplementary Table 4. Quantitative evaluations of LYTACs (1)

TPD technology	Target substrate	Treatment condition			Degradation measurement			Reference
		Model (cell line/animal model)	Compound	Treatment condition	Measurement method	DC50	Dmax	
LYTAC	EGFR	HeLa	Ab-2	10 nM, 24h	Immunoblotting	N/A	80 %	S. M. Banik (2020)[6]
		Hep3B		10 nM, 48h		N/A	69 %	
		BT-474		10-20 nM. 48 h		N/A	83 %	
		HepG2		10-20 nM. 48 h		N/A	61 %	
	CD71	Jurkat	Anti-CD71+Ab-1	50 nM, 24h	Immunoblotting	N/A	81 %	
	PD-L1	MDA-MB-231	Ab-3	50 nM, 24-72 h	Live-cell flow cytometry	N/A	32.5 %	
				50 nM, 48 h	Immunoblotting	N/A	35 %	
		HDLM-2		50 nM, 36 h		N/A	45 %	
		HDLM-2	Atz-M6Pn	25 nM, 48 h	Immunoblotting	N/A	73 %	
	EGFR	Hep3B	Ctx-GalNAc	10 nM, 48h	Live-cell flow cytometry	1 nM	66 %	G. Ahn (2021)[11]
					Immunoblotting	N/A	70 %	
		HepG2				N/A	60.7 %	
		Huh7				N/A	44.7 %	
	HER2	HepG2	Ptz-GalNAc	100 nM, 48 h	Immunoblotting	N/A	75 %	

Supplementary Table 4. Quantitative evaluations of LYTACs (2)

TPD technology	Target substrate	Treatment condition			Degradation measurement			Reference
		Model (cell line/animal model)	Compound	Treatment condition	Measurement method	DC50	Dmax	
LYTAC	Integrin (αvβ5)	HepG2	PIP-GalNAc	100 nM, 44 h	Live-cell flow cytometry	N/A	26.8 %	G. Ahn (2021)[11]
	Integrin (αvβ3)						68.5 %	
	Monoclonal α–DNP antibodies in serum	α–DNP antibodies i.p. injected nude mice	D-MoDE-A	1 mg/kg/day for 3 weeks	ELISA (Relative clearance compared to day 0)	N/A	*97.1 %	D. F. Caianiello (2021)[12]
	Polyclonal α–DNP antibodies in serum			1 mg/kg/day for 9 days		N/A	*93.5 %	
	MIF in serum	Recombinant hMIF i.p. injected nude mice	M-MoDE-A	1-10 mg/kg/day for 3 weeks		N/A	*89.6 %	
	Met	HeLa	D3 (A1-L-A2)	300 nM, 24 h	Immunoblotting	N/A	88 %	Y.Miao (2021)[13]
	PTK-7	CEM	D4 (A1-L-A2)	500 nM, 24 h		N/A	43 %	
	HER2	SKBR3	HER2-LYTAC	500 nM, 24 h	Immunoblotting	N/A	68 %	K. Hamada (2023)[14]
	PDGF	HepG2	GalNAc-AptPDGF	50 nM, 6 h	Immunoblotting	N/A	41.2 %	Y. Wu (2023)[15]
	PTK-7	HepG2	GalNAc-AptPTK-7	500 nM, 24 h		N/A	31 %	
	HER2	BT474	Compound 3	10 nM, 48 h	Immunoblotting	N/A	57 %	X. Zhang (2022)[16]
	EGFR	HepG2	Compound 9	10 nM, 48 h	Immunoblotting	N/A	57 %	
	EGFR	HepG2	Ctx-Gn	30 nM, 48 h	Immunoblotting	N/A	40 %	Y. Zhou (2021)[17]
		Huh7					39 %	

*Dmax is not measured relative to PBS control but compared to day 0.

Supplementary Table 5. Quantitative evaluations of IFLD and DENTACs

TPD technology	Target substrate	Treatment condition			Degradation measurement			Reference
		Model (cell line/animal model)	Compound	Treatment condition	Measurement method	DC50	Dmax	
IFLD	PD-L1	MDA-MB-231	BMS-L1-RGD	25 nM, 8 h	Immunoblotting	N/A	75 %	J. Zheng (2022)[18]
DENTAC/SR	NCL	A549	N-DENTAC	1-100 nM, 48 h	Live-cell flow cytometry	25 nM	60 %	C. Zhu (2023)[19]
				50 nM, 48 h	Immunoblotting	N/A	68 %	
		Hela			Immunoblotting	N/A	48%	
		MCF-7				N/A	49%	
		HepG2				N/A	71%	
		i.t. injected A549 xenograft mice	N-DENTAC	2 mg/kg/2 day (for 14 days)	Immunoblotting	N/A	71%	
	EGFR	A549	E-DENTAC	1-100 nM, 48 h	Live-cell flow cytometry	15 nM	66 %	
				50 nM, 48 h	Immunoblotting	N/A	72%	

Supplementary Table 6. Quantitative evaluations of CXCL12-based KineTACs

TPD Technology	Target substrate	Treatment condition			Degradation measurement			Reference
		Model (cell line/animal model)	Compound	Treatment condition	Measurement method	DC50	Dmax	
KineTAC	PD-L1	MDA-MB-231	CXCL12-Atz	100 nM, 24 h	Immunoblotting	N/A	89.7 %	K. Pance (2023)[7]
		MC38	CXCL12-Atz	100 nM, 24h (treated with mouse IFNg)	Immunoblotting	N/A	62.3 %	
		CT26				N/A	82.3 %	
	HER2	MCF7	CXCL12-Tras	1-100 nM, 24 h	Immunoblotting	N/A	49 %	
		MDA-MB-175VII				N/A	62 %	
		SK-BR-3				N/A	25.5 %	
	EGFR	Hela	CXCL12-Ctx	1-100 nM, 24 h	Immunoblotting	N/A	82.5 %	
		MDA-MB-231				N/A	64.5 %	
		A431				N/A	54 %	
		NCI-H292				N/A	72.5 %	
		A549		100 nM, 24 h	Immunoblotting	N/A	72 %	
		NCI-H358				N/A	79 %	
		HCC-827				N/A	1.5 %	
	PD-1	CD8+ T cells	CXCL12-Nivo	100 nM, 24 h	Live-cell flowcytometry	N/A	82 %	
	CDCP1	Hela	CXCL12-4A06	1-100 nM, 24 h	Immunoblotting	N/A	93 %	
	TROP2	MCF7	CXCL12-sanituzumab	1-100 nM, 24 h	Immunoblotting	N/A	51 %	

Supplementary Table 7. Quantitative evaluations of CIDEs and UIDs

TPD technology	Target substrate	Treatment condition			Degradation measurement			Reference
		Model (cell line/animal model)	Compound	Treatment condition	Measurement method	DC50	Dmax	
CIDE	BRD4	HEK293	L-CIDE	10 μM, 24 h	Immunostaining	0.73 μM	N/A	C. Bashore (2022)[20]
	BRD4L			5 μM, 24 h	Immunoblotting	N/A	79 %	
	BRD4S					N/A	79 %	
	BRD3					N/A	51 %	
UID	BRD2	HEK293-Rpn13(1-128)-HTP-Flag	WJ704	10 μM, 4 h	Immunoblotting	N/A	79 %	M. Balzarini (2023)[8]
			WJ705					
			WJ706					

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