Supplementary materials

REVIEW

Human carboxylesterases: a comprehensive review

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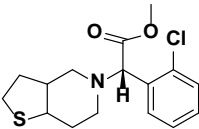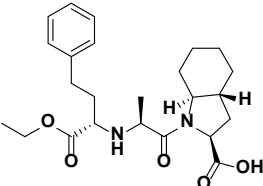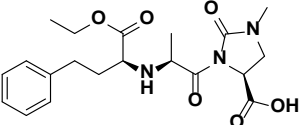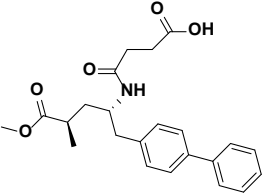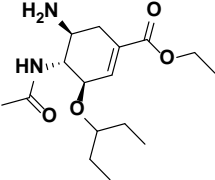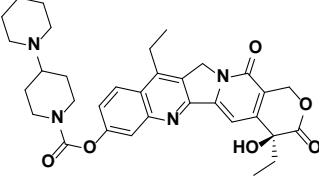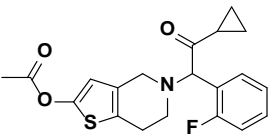
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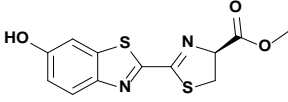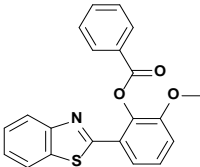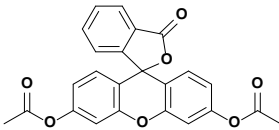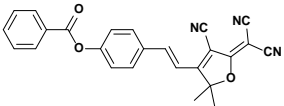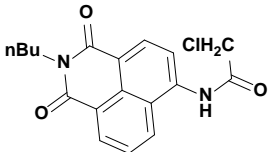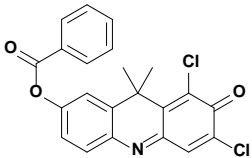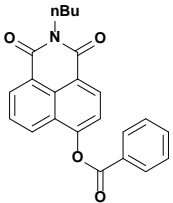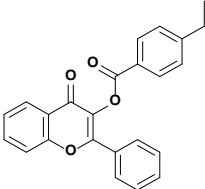[†]These authors made equal contribution to this work.

Table S1 Enzyme kinetic parameters of typical drug substrate of CES.

Substrate	Structure	Enzyme source	Kinetic parameter		Ref.
			K_m (µmol/L)	V_{max} (nmol/min/mg)	
Clopidogrel		HLM	62.7	3.56	10
Trandolapril		HLM	1734	624	50
Imidapril		HLM	245	2.4	4
Sacubitril		HLM	767.2	557.5	55
Oseltamivir		HLM	380	145	11
CPT-11		CES2	3.4	2.5	24
Prasugrel		CES2	49.8	54839	54

HLM: human liver microsomes.

Table S2 Optical probe substrates for high-throughput screening of CES inhibitors.

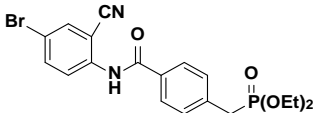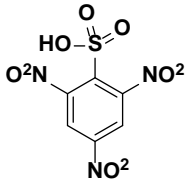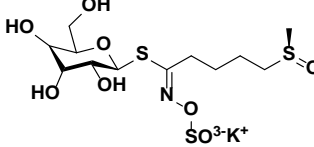| Substrate	Structure	Enzyme source	Kinetic parameter		Method and detection condition	Ref.
			K_m (µmol/L)	V_{max} (nmol/min/mg)		
DME		CES1	4.51	1208,000	Bioluminescence $\lambda_{em} = 560$ nm	49
		HLM	3.60	1441,000		
BMBT		CES1	12.18	93070	Fluorescence $\lambda_{ex}/_{em} = 304/488$ nm	61
FD		CES2	4.82	14,600	Fluorescence $\lambda_{ex}/_{em} = 483/525$ nm	51
		HLM	4.87	18,500		
		HIM	4.04	39,050		
TCFB		CES2	3.06	5.84	Fluorescence $\lambda_{ex}/_{em} = 560/612$ nm	58
		HLM	2.19	14.7		
		HIM	2.14	12.8		
NCEN		CES2	8.58	34.87	Fluorescence $\lambda_{ex}/_{em} = 430/542$ nm	60
		HLM	6.13	4.52		
		HIM	8.12	5.08		
DDAB		CES2	1.92	20.4	Fluorescence $\lambda_{ex}/_{em} = 600/662$ nm	63
		HLM	1.83	16.5		
		HIM	0.95	8.88		
BNN		CES2	ND	ND	Fluorescence $\lambda_{ex}/_{em} = 452/564$ nm	62
EBHF		CES2	162	17.84	Fluorescence $\lambda_{ex}/_{em} = 346/528$ nm	59

HLM: human liver microsomes; HIM: human intestine microsomes. The detection conditions are depicted for the corresponding hydrolytic metabolite.

Table S3 The regulatory effects of some inducers of CES.

Substrate	Structure	Cell line	n-Folds of induction (mRNA)		Ref.
			CES1	CES2	
NO-1886		Human primary hepatocytes	1.4	2.6	136
Trinitrobenzene sulfonate		Human dermal fibroblasts	2.6	ND	133
		HT1080	3.1	ND	133
		Human primary hepatocytes	1.5	ND	133
		Huh 7	3.7	ND	133
Sulforaphane		Human dermal fibroblasts	3.8	ND	133
		HT1080	2.1	ND	133
		Human primary hepatocytes	2.7	ND	133
		Huh 7	3.9	ND	133