

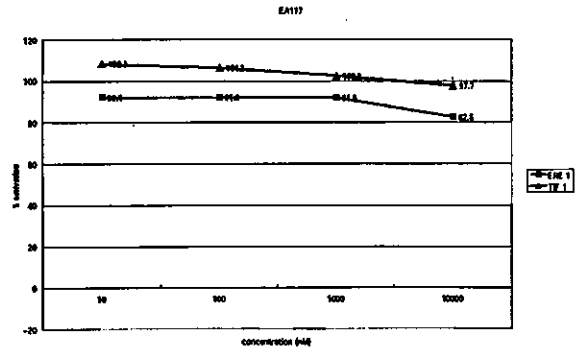
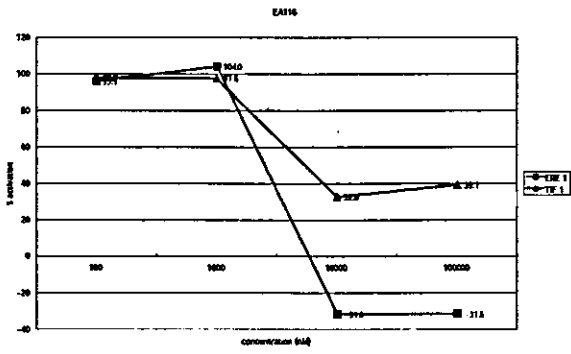
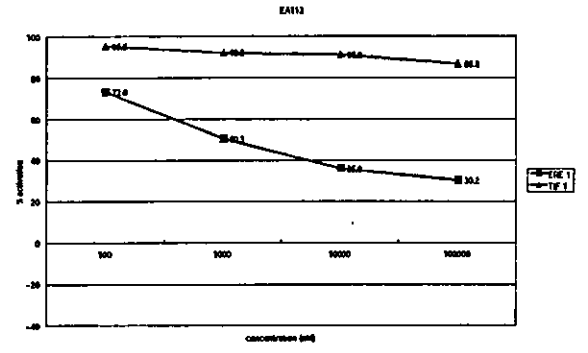
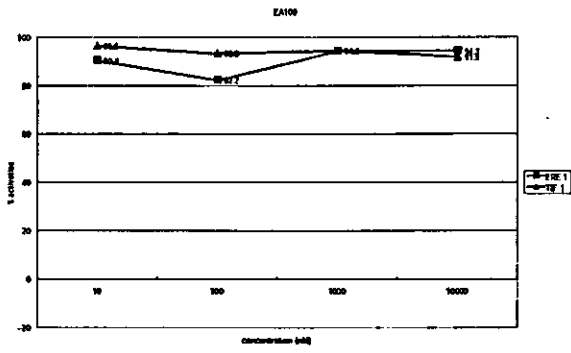
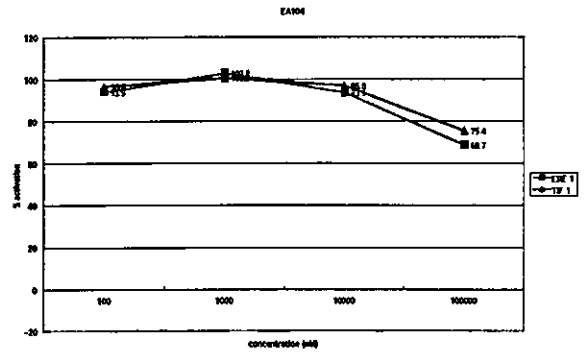
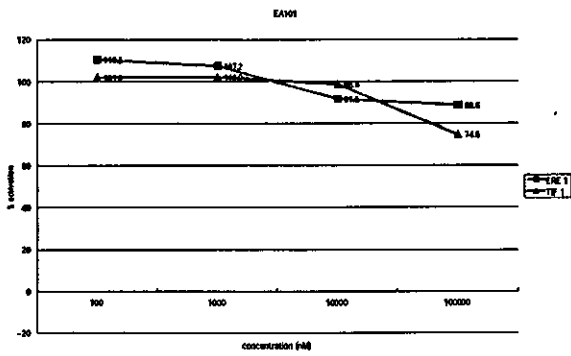
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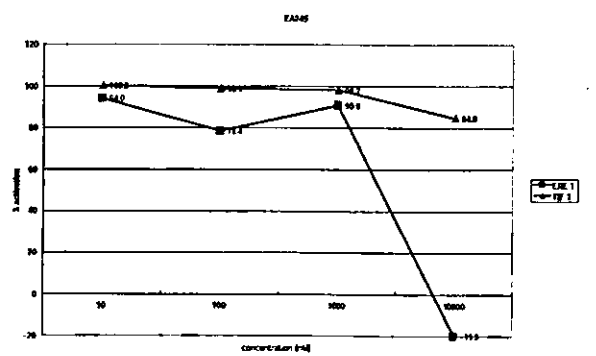
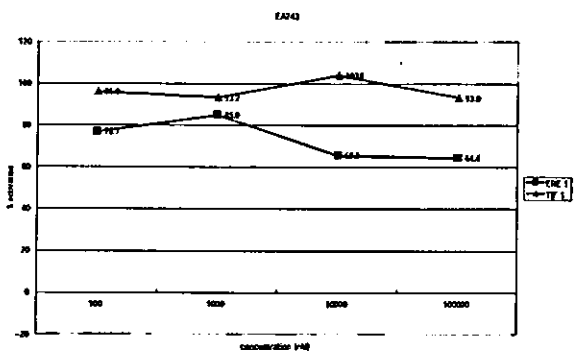
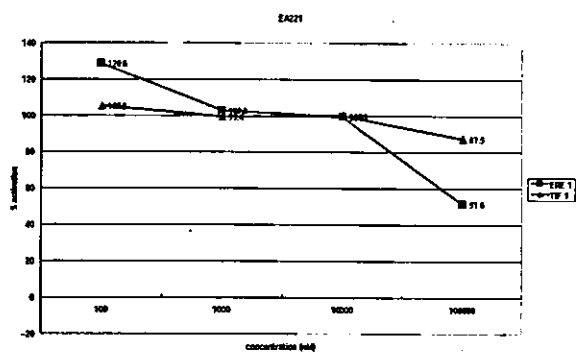
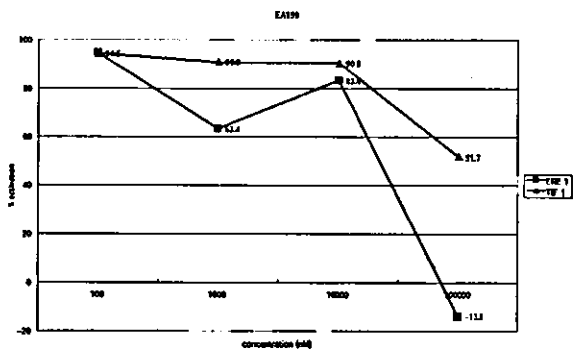
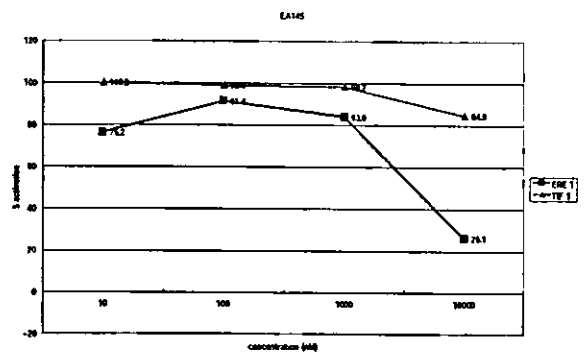
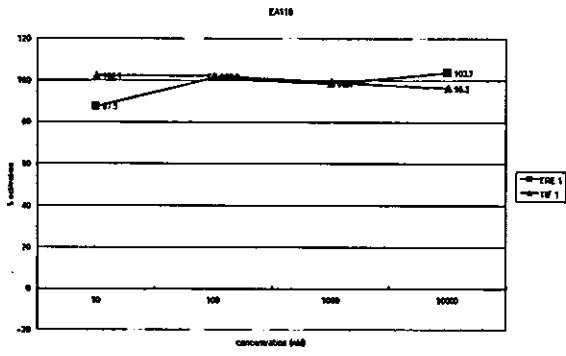
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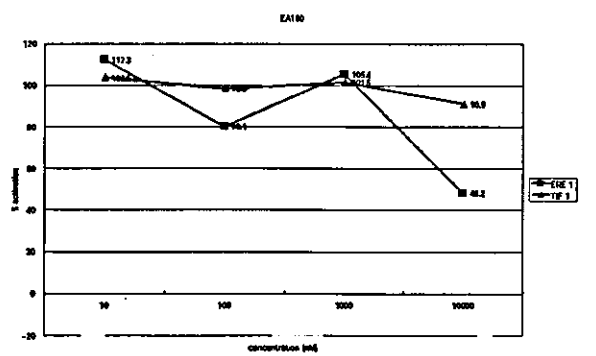
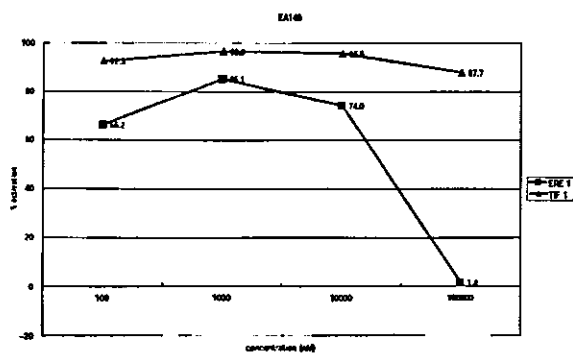
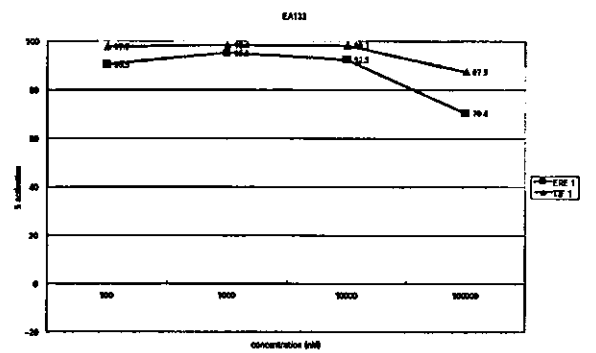
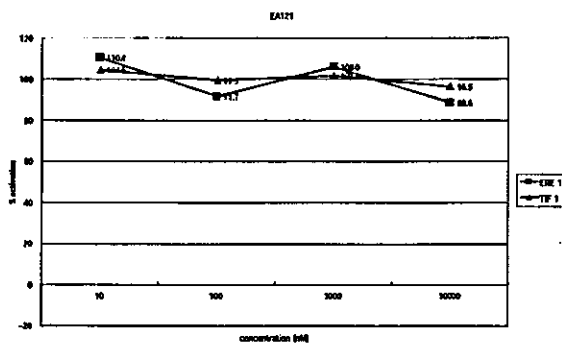
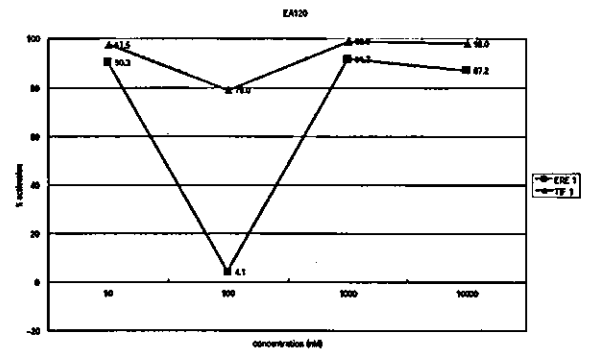
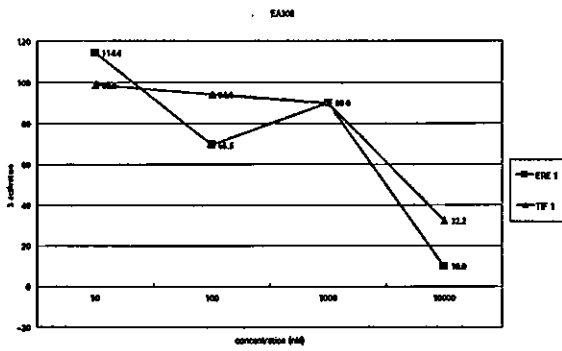
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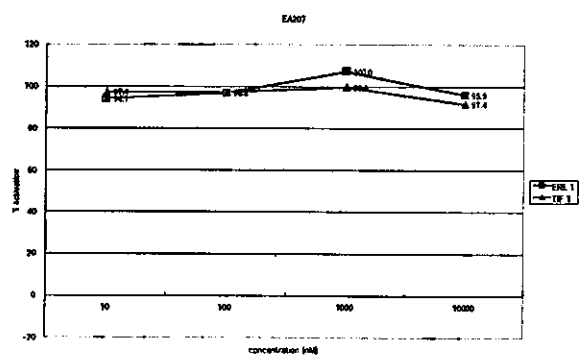
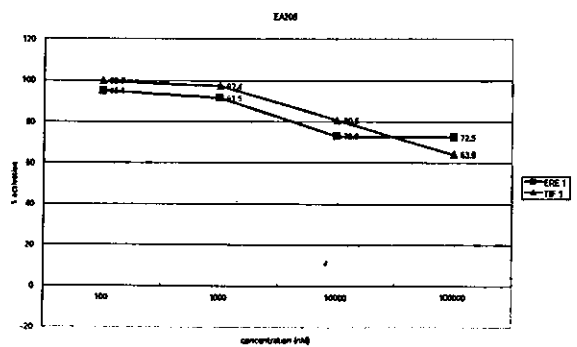
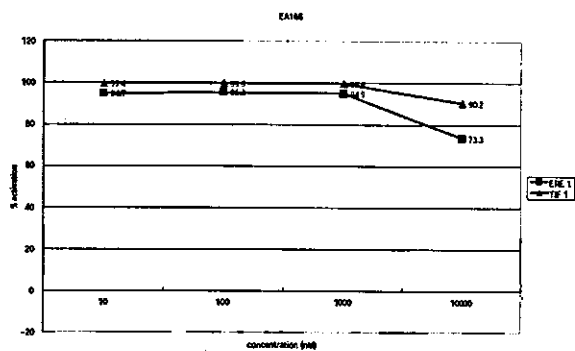
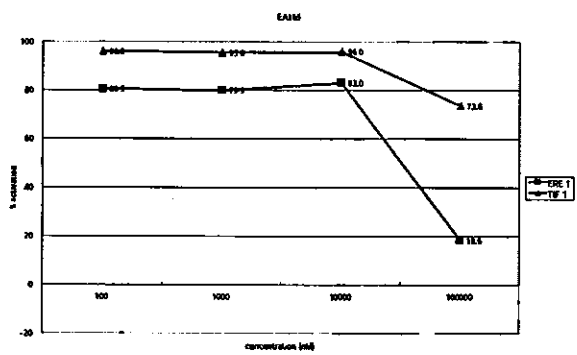
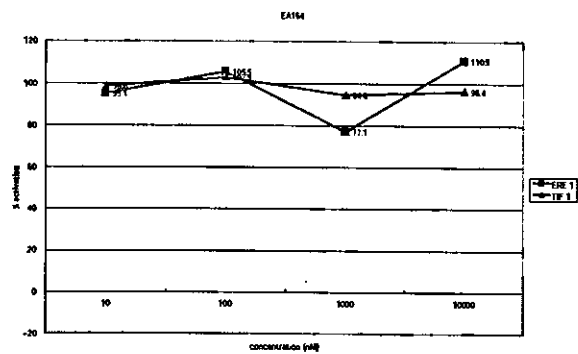
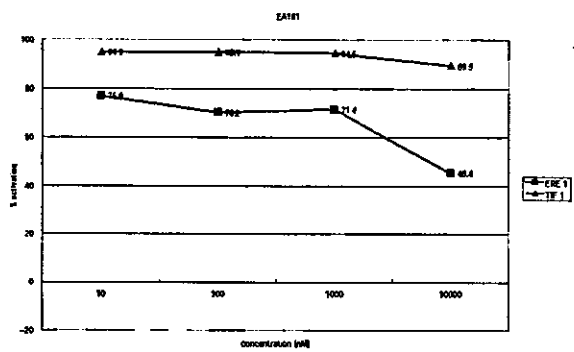
図6 競合試験

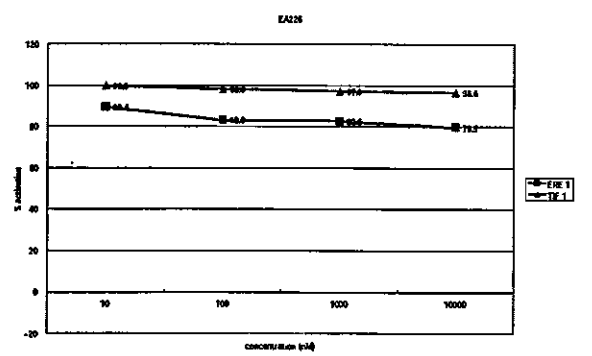
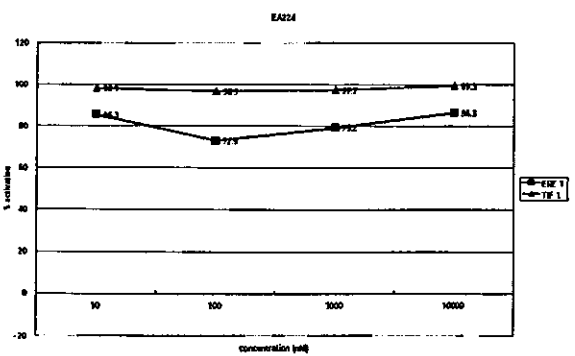
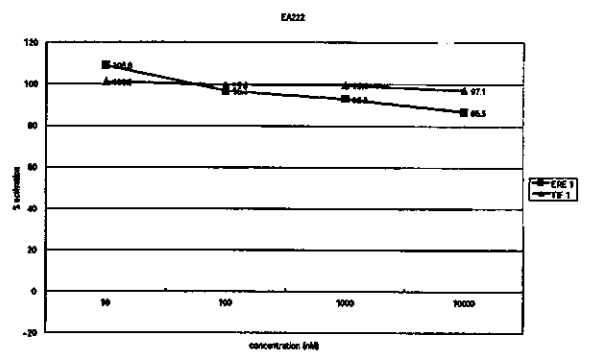
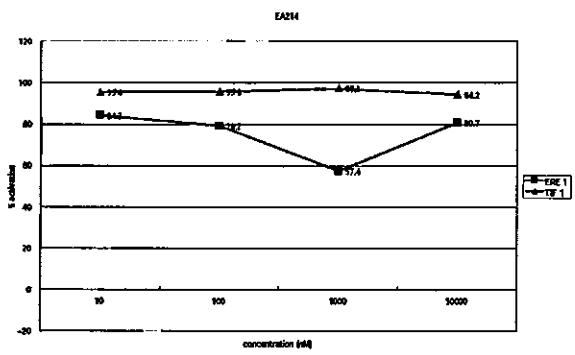
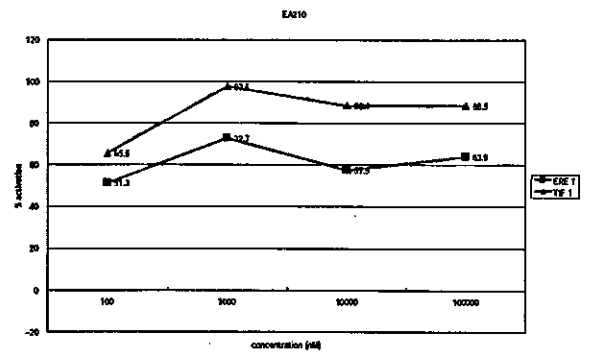
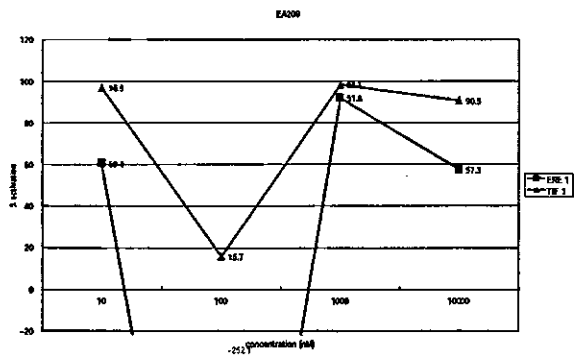
平成14年度の35化合物の競合試験
EREアッセイとTIFアッセイの競合試験の結果を示す

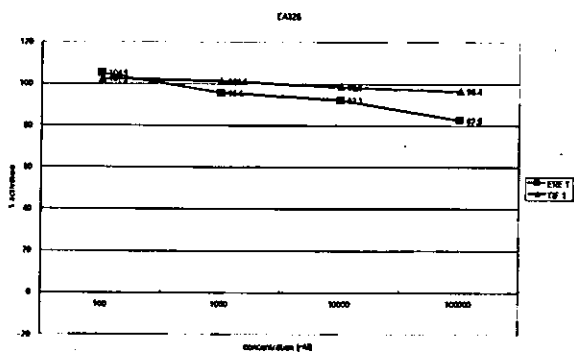
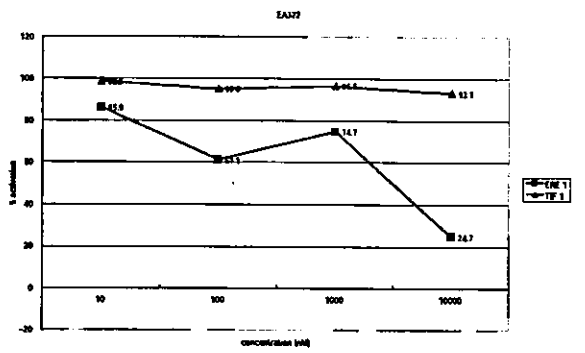
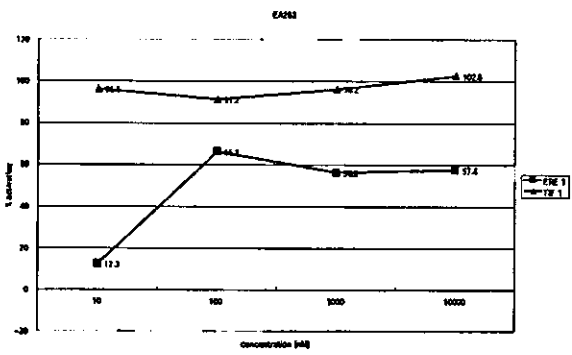
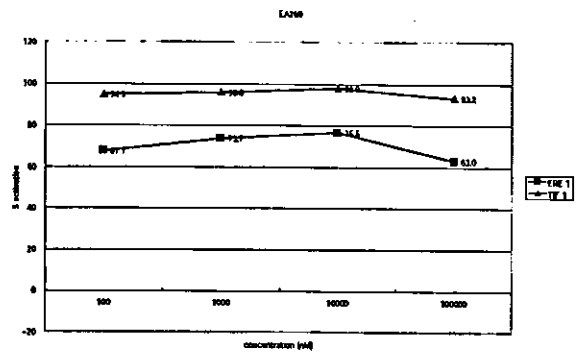
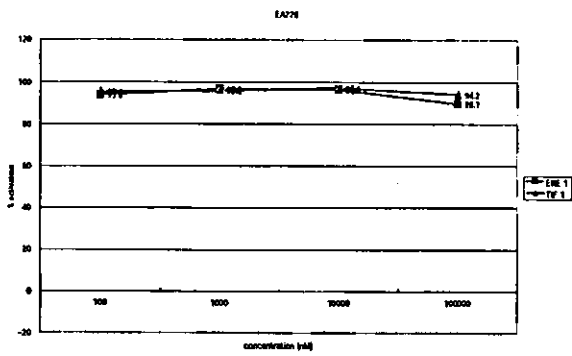




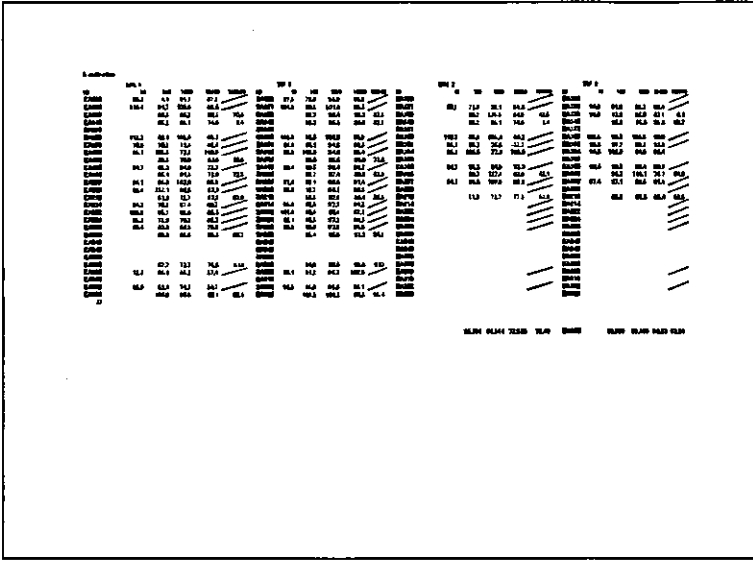








ENE 1		TF 1		ENE 1		TF 1	
Conc	Act	Conc	Act	Conc	Act	Conc	Act
100	97.7	100	97.7	100	97.7	100	97.7
1000	98.6	1000	98.6	1000	98.6	1000	98.6
10000	98.4	10000	98.4	10000	98.4	10000	98.4
100000	96.2	100000	96.7	100000	96.2	100000	96.7



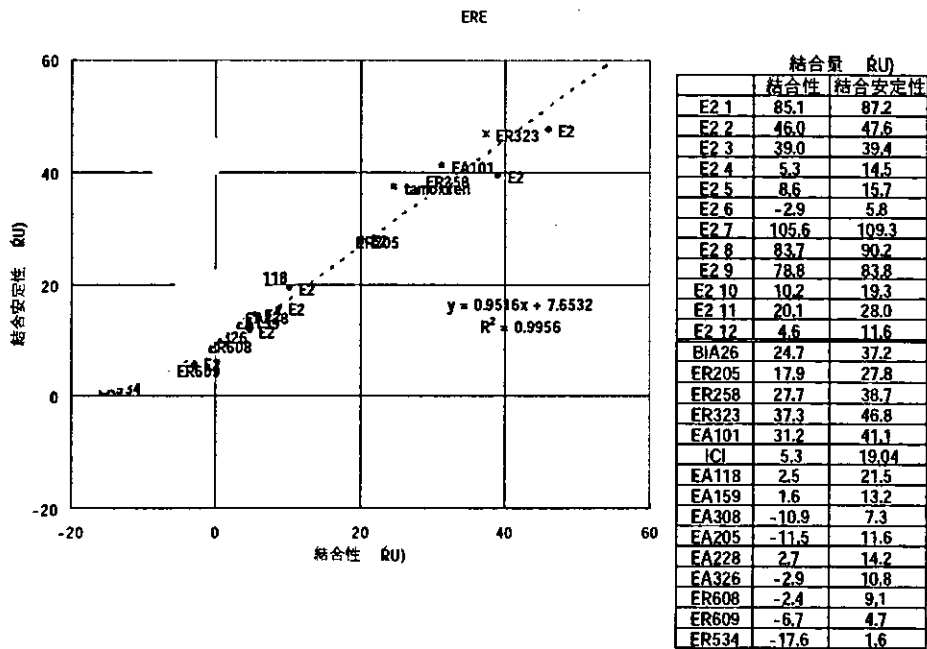
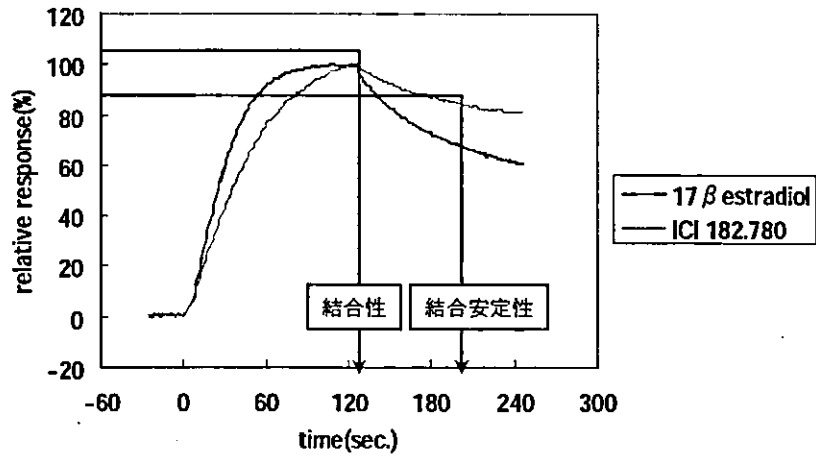


図5 カイネティクス解析

ID	CAS-No.	Name	Chemical Structure	%activation of 10 μ M			
				ERE assay		TIF assay	
ER608	000131-55-5	2,2',4,4'-Tetrahydroxy benzophenone		102.53	H	61.60	H
ER609	000131-56-6	2,4-Dihydroxy benzophenone		55.22	H	6.83	L
ER607	000131-54-4	2,2'-Dihydroxy-4,4'-dimethoxy benzophenone		3.68	L	1.01	N
ER610	000131-57-7	2-hydroxy-4-methoxy-benzophenone,		6.93	L	-0.33	N

ERE assay High responder 50% Low responder 20-50% Non responder <20%	TIF assay High responder 50% Low responder 10-50% Non responder <10%
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図7 化学物質の構造とER活性との相関

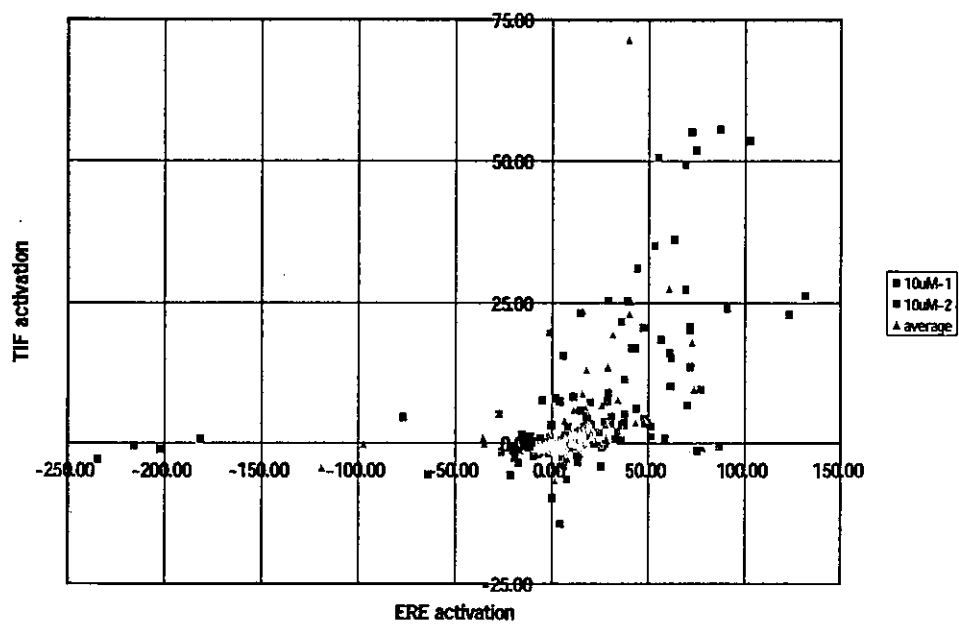


図8 平成15年度の89化合物のスクリーニング結果

2回のスクリーニング結果のうち10 μ Mの化学物質濃度
 におけるERE、TIFアッセイの結果をプロットした。
 0.1、1、10 μ Mの結果の平均スコアもプロットした。

平成16年度 スクリーニングデータ

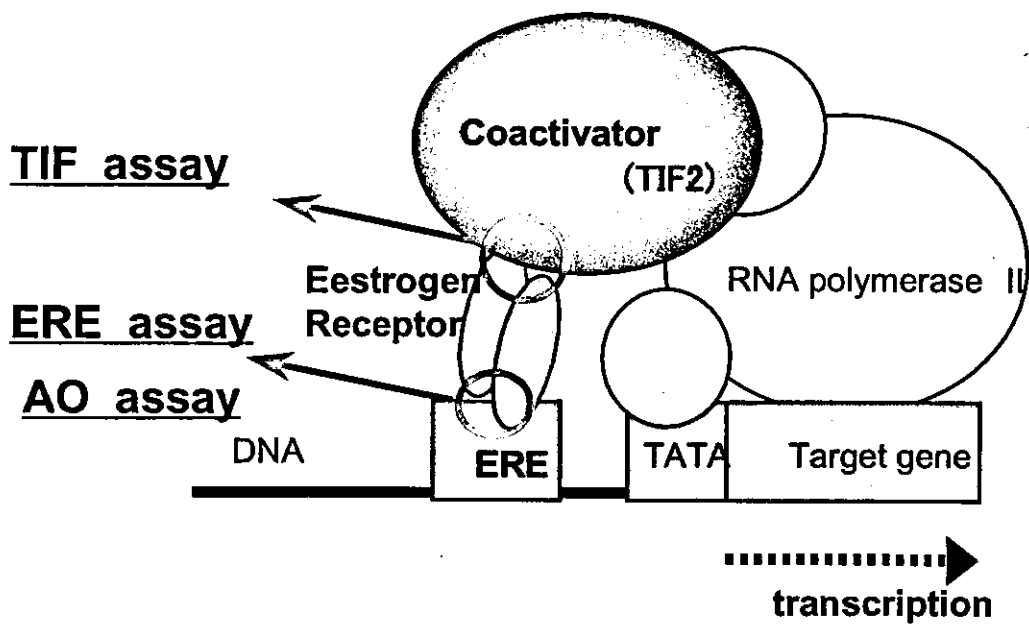


図1 表面プラズモン共鳴スクリーニング法の概要

エストロゲンレセプターの作用機構と3種類のアッセイ

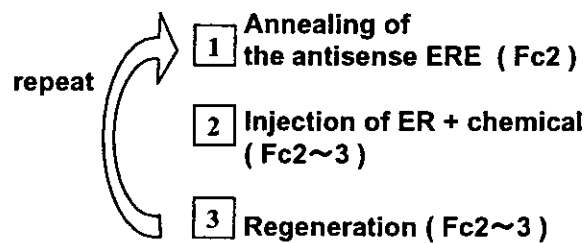
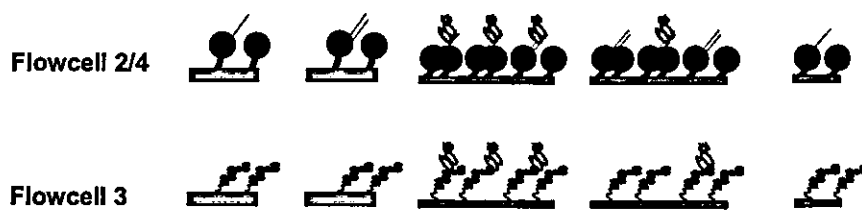
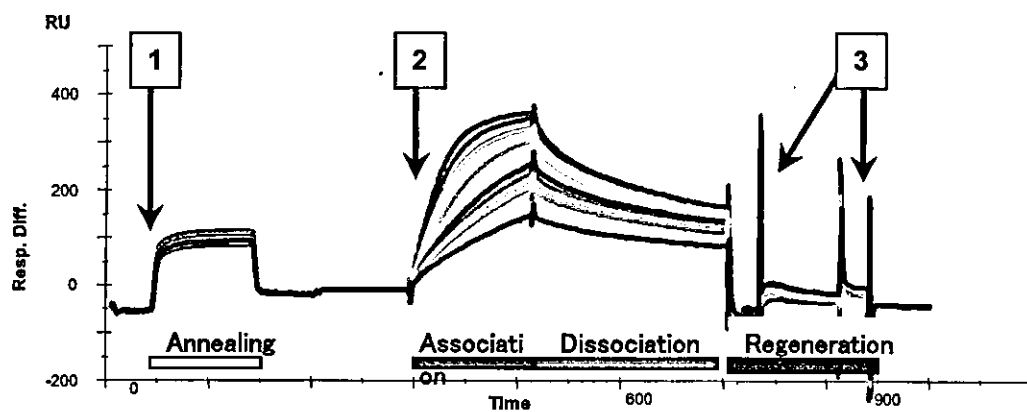
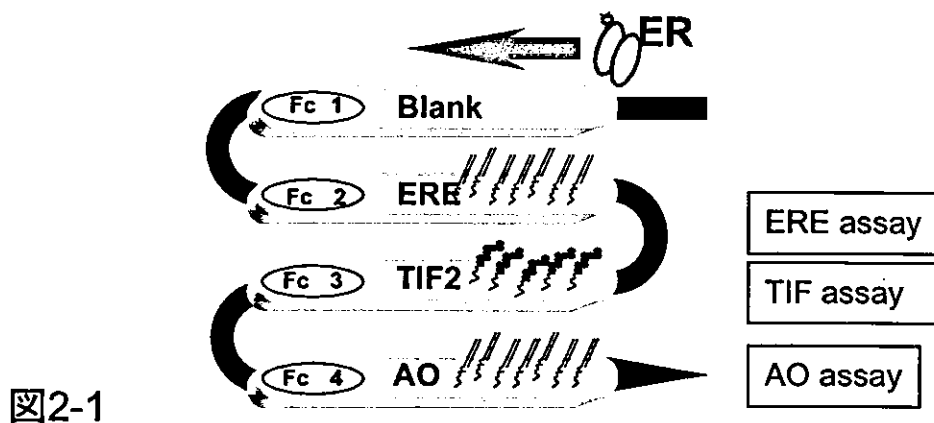
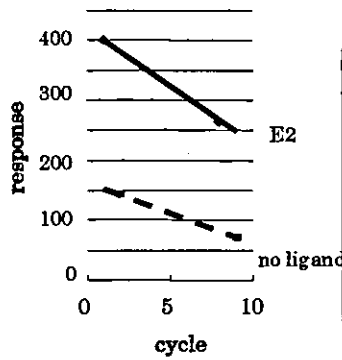
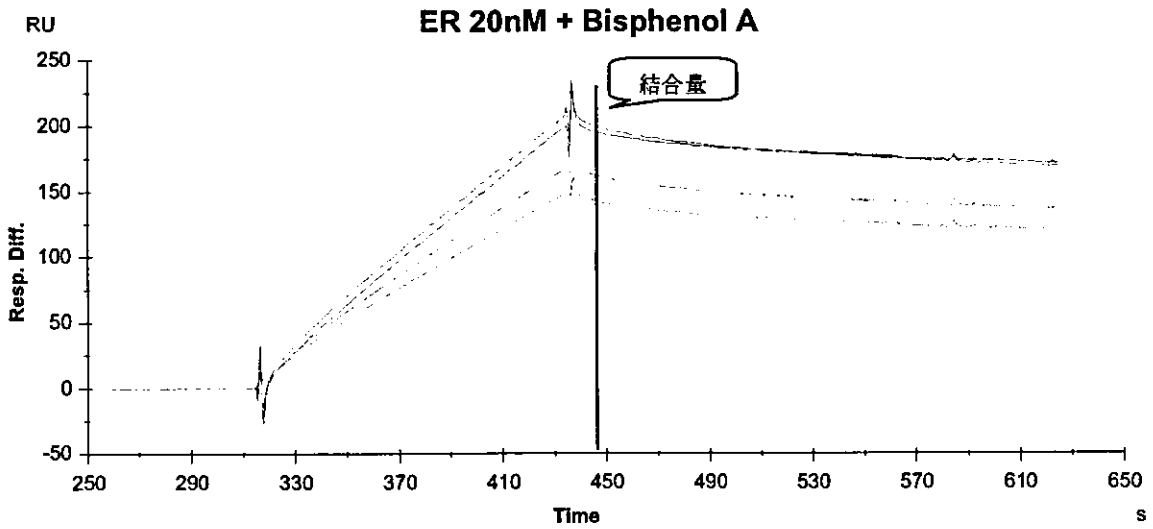
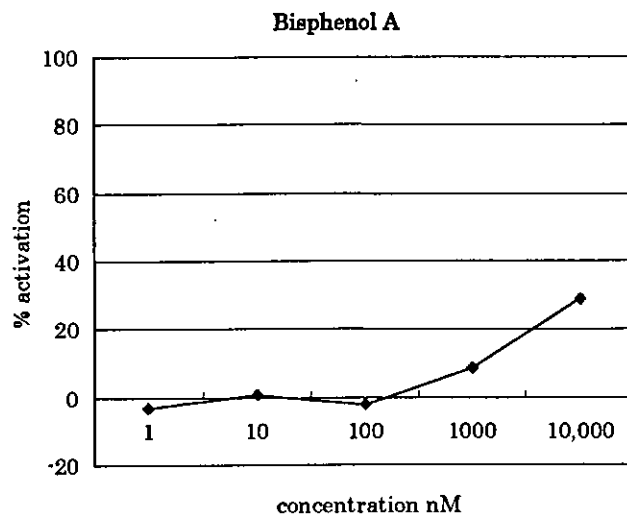


図2-2

図2 表面プラズモン共鳴センサーのアッセイ
 図2-1 センサーチップ上でのアッセイの構築
 図2-2 アッセイの流れとセンサーグラム



cycle	bisphenol A		BLA9		drug activation	E2 activation	%activation
	conc nM	RelRes	E2cal	nolig cal			
2	0	141.4	380.75	141.40	0.00	239.36	0.00
9	0	70.8	246.05	70.80	0.00	175.26	0.00
7	1	84.8	284.54	90.97	-6.17	193.57	-3.19
6	10	92.1	284.54	90.97	1.13	193.57	0.58
5	100	97.2	303.78	101.05	-3.85	202.73	-1.90
4	1000	129	323.03	111.14	17.86	211.89	8.43
3	10,000	185.5	342.27	121.23	64.27	221.04	29.08
1	100	400	400.00	151.48	248.52	248.51	100.00
8	100	265.3	265.30	80.88	184.42	184.41	100.00



$$\% \text{ activation} = \frac{(\text{化学物質存在下での結合量} - \text{ネガティブコントロールでの結合量})}{(\text{100 nM E2存在下での結合量} - \text{ネガティブコントロールでの結合量})} \times 100$$

図3 ERアッセイのデータ解析法