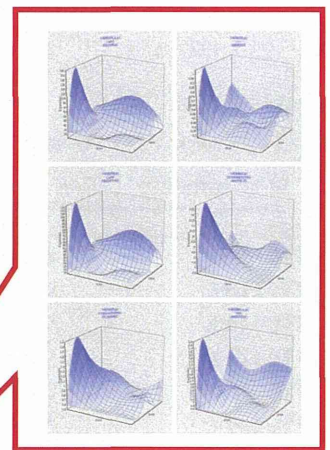
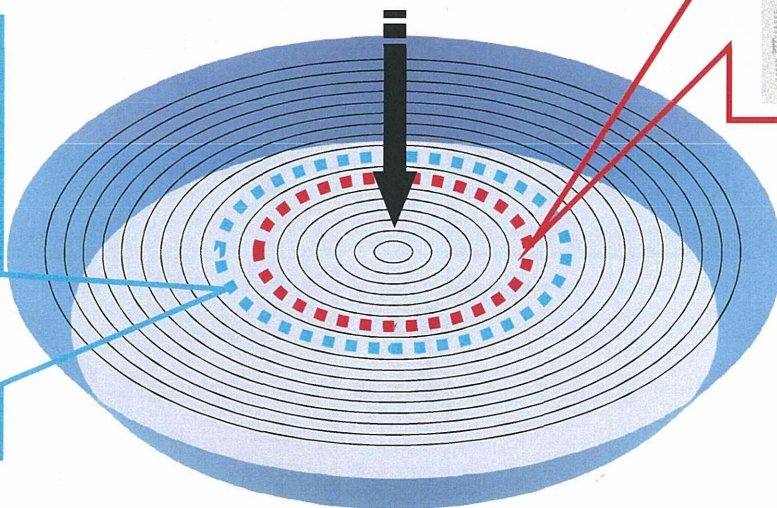
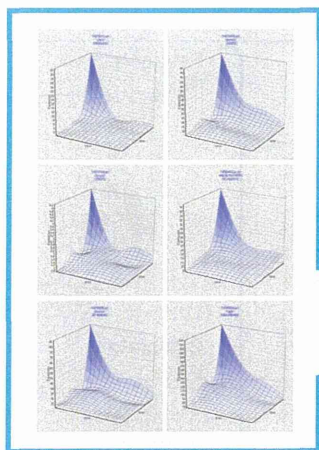


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• Single exposure experiment

- Gene Network = water surface
- Test Chemical = stone
- Alteration in gene expression = ripples

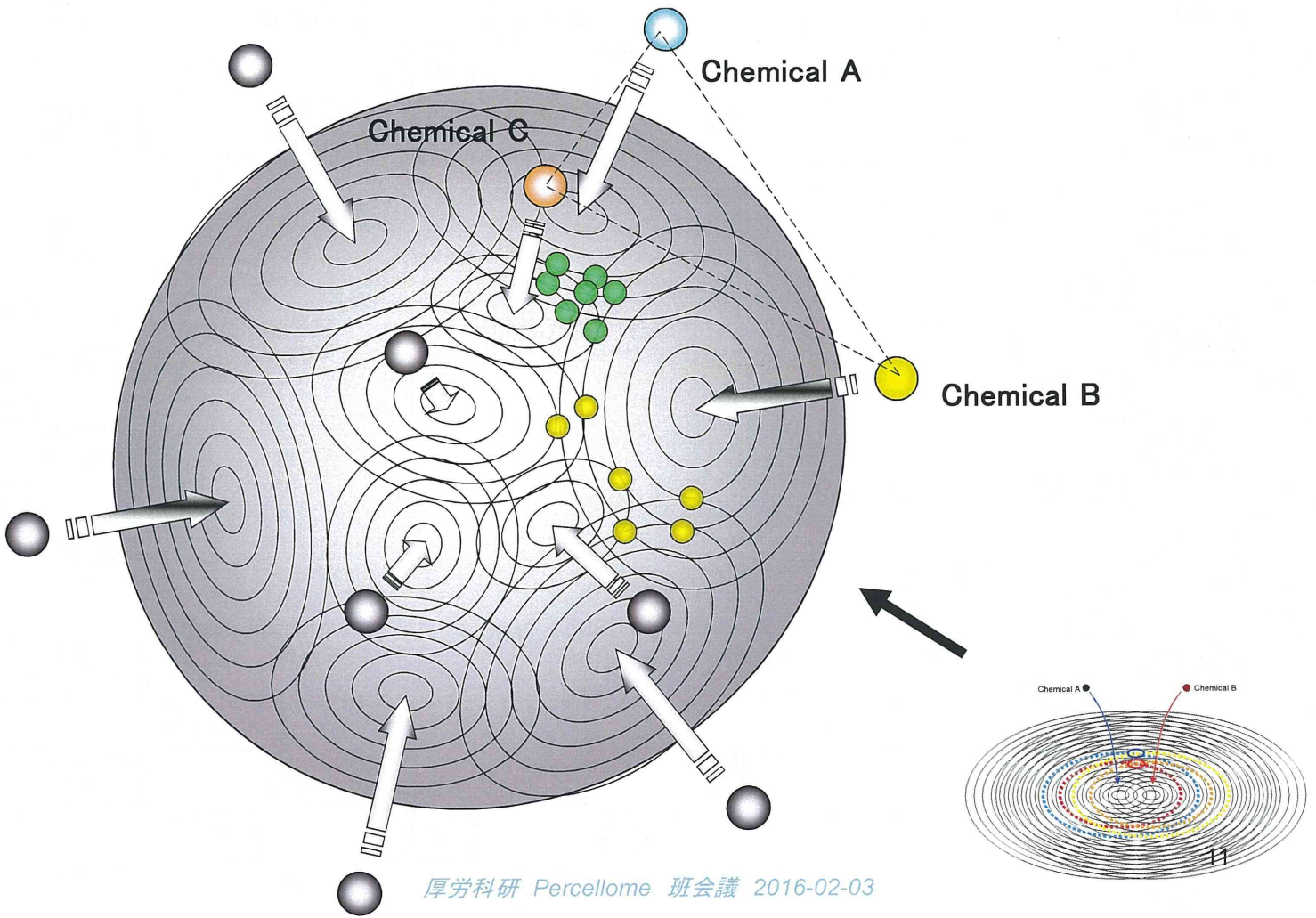


→ Protein etc. → Gene → Protein → Gene → Protein → .....

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231	TTG146-L	Forskolin	974	(MEMO)	(MEMO)	C:VMFDB
232	TTG147-G	Estragole	162	(MEMO)	(MEMO)	C:VMFDB
233	TTG147-L	Estragole	720	(MEMO)	(MEMO)	C:VMFDB

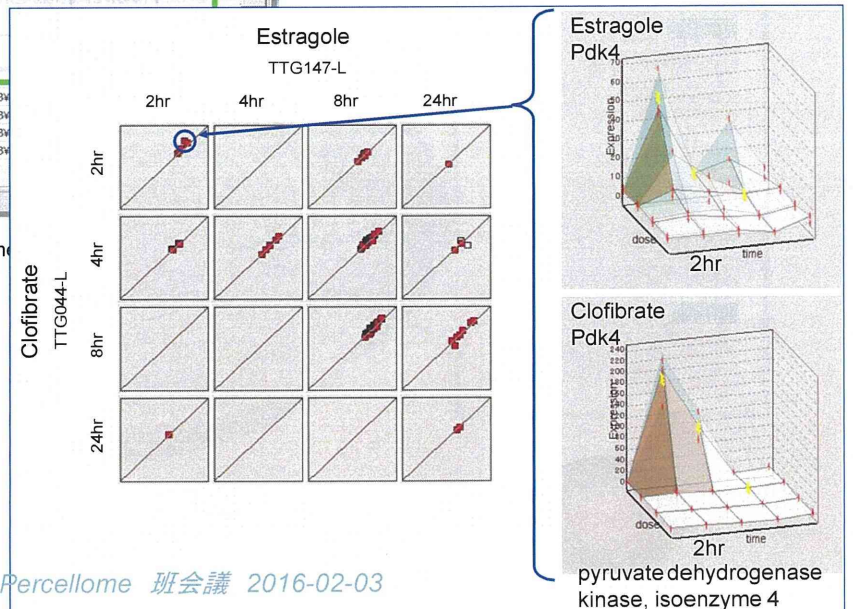
Matching List  
vs TTG147-L // Estragole

Name	Condition	Num	Cor	GL
TTG147-L	Estragole	720	13.889	(MEMO)
TTG118-L	Clofibrate x Clofibrate*	69	0.732	(MEMO)
TTG044-L	Clofibrate	81	0.688	(MEMO)
TTG129-L	CCH x Clofibrate*	63	0.68	(MEMO)
TTG098-L	DEHP			
TTG104-L	MEHP			

TTG104-L	MEHP	114	0.642	(MEMO)	C:VMFDB	Surfa	C:VMFDB
TTG021-G	Tetradecane (2hr x 1day)*	7	0.617	(MEMO)	C:VMFDB	Surfa	C:VMFDB
TTG134-L	Nerolidol	18	0.61	(MEMO)	C:VMFDB	Surfa	C:VMFDB
TTG141-L	Tributyltin x Clofibrate*	88	0.602	(MEMO)	C:VMFDB	Surfa	C:VMFDB

Stand by.....

\*: Perform

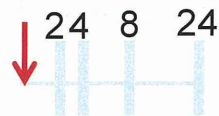


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# 反復投与の意味の考察

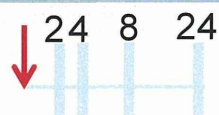
## ヒント: 遺伝子改変動物の反応を解析する

野生型マウス



単回投与

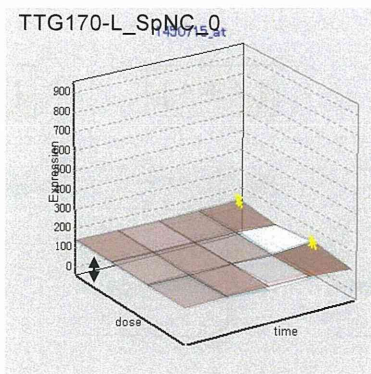
遺伝子改変マウス



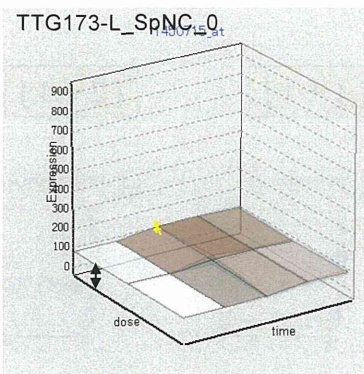
単回投与

AhR KO mouse

TCDD

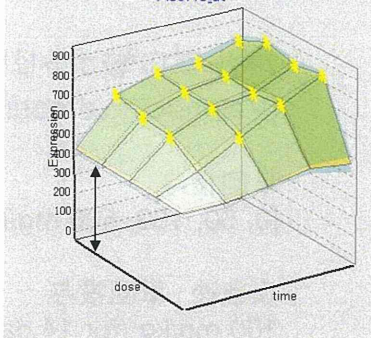


3-MC

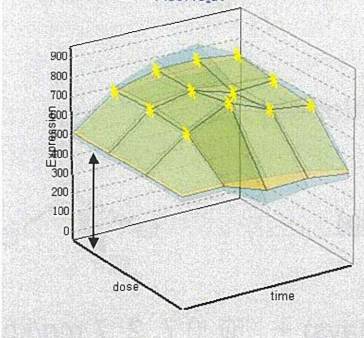


Wild type mouse

TTG020-L\_SpNC\_0



TTG056-L\_SpNC\_0



Cyp1a2  
 NM\_009993  
 cytochrome P450, family 1, subfamily a, polypeptide 2



# 単回投与 vs 反復投与後の反応

(TTG119-G)

(TTG130-G)

単回投与後の反応 (“TTG1 type”) [0+1]



単回投与

反復投与後の反応 (“TTG2 type”) [14+1]



反復投与 (全群単一用量)

[0 + 1]

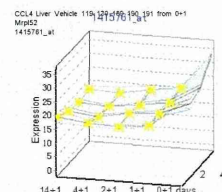
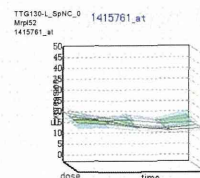
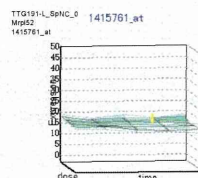
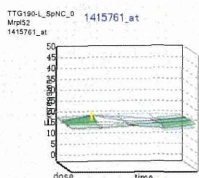
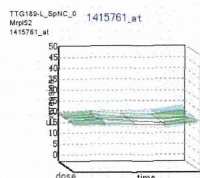
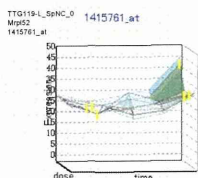
[1 + 1]

[2 + 1]

[4 + 1]

[14 + 1]

Vehicle



## 四塩化炭素

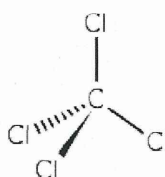
[Carbon tetrachloride]

単回投与

[0, 0.7, 2, 7 mg/kg]

反復後 単回投与

5 mg/kg (for 14 days) + [0, 0.7, 2, 7 mg/kg]



## バルプロ酸ナトリウム

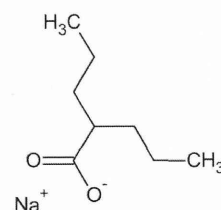
[Valproic acid sodium salt]

単回投与

[0, 50, 150, 500 mg/kg]

反復後 単回投与

100 mg/kg (for 14 days) + [0, 50, 150, 500 mg/kg]



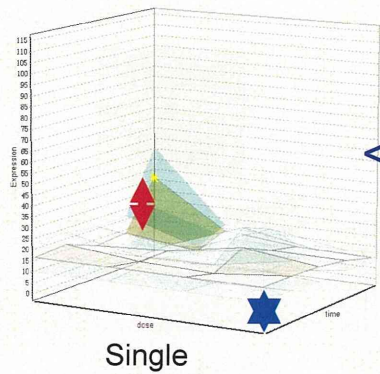
●反復投与が毎回の投与による反応に大きな影響を与える物質

用語定義 Definition

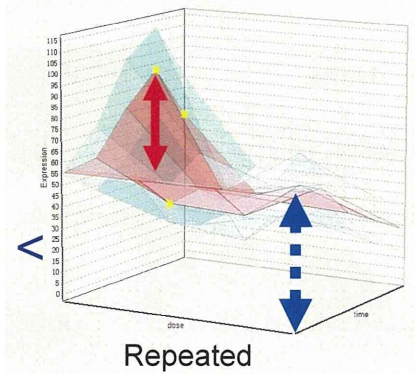
↑↓  
Transient Response  
(T-Res)  
過渡反応

↑  
↓  
Baseline Response  
(B-Res)  
基線反応

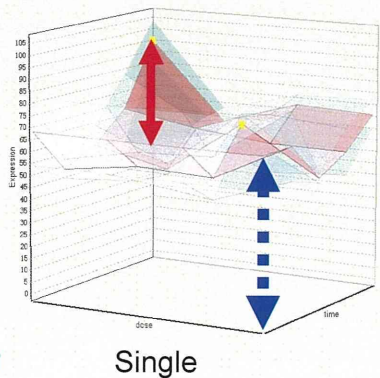
TTG119-L\_SpNC\_0\_439817\_at



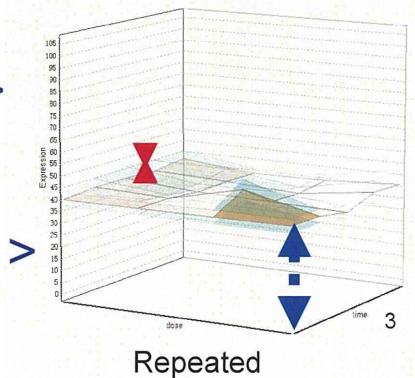
TTG130-L\_SpNC\_0\_439817\_at



TTG119-L\_SpNC\_0\_439817\_at



TTG130-L\_SpNC\_0\_439817\_at



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★組み合わせデータの解析

- ・CCl<sub>4</sub> & CCl<sub>4</sub>、Clrof、PB、
- ・VPA & VPA \*、Asp、Thalidomide
- ・Clofibrate & Clrof、PCN、ATRA
- ・TBT & TBT、PB、Clrof

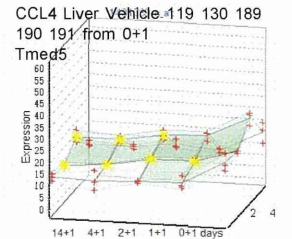
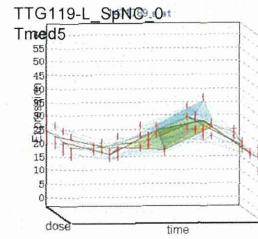
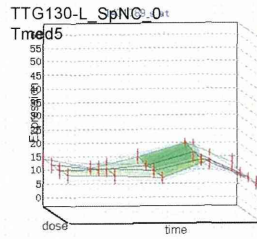
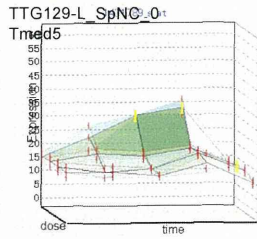
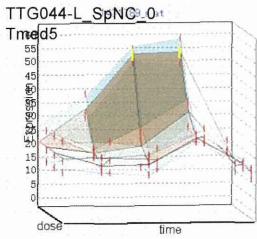
None  
+  
Clofibrate 1

CCl<sub>4</sub> 14  
+  
Clofib 1

CCl<sub>4</sub> 14  
+  
CCl<sub>4</sub> 1

None  
+  
CCl<sub>4</sub> 1

CCl<sub>4</sub> Vehicle



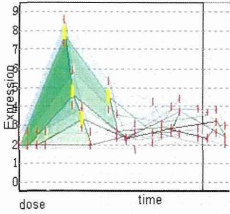
[14+1]  
TBT + Clofibrate  
CCl<sub>4</sub> + Clofibrate



[14+1] TBT + Clofibrate  
 [14+1] CCl<sub>4</sub> + Clofibrate

Clofib x1

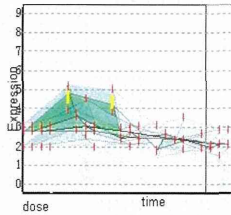
TTG044-L\_SpNC<sub>4</sub>0  
 Clofibrate  
 Cblb



Casitas B-lineage lymphoma b

TBT x14 + Clofib x1

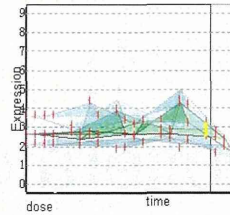
TTG141-L\_SpNC<sub>4</sub>0  
 Tributyltin chloride x Clofibrate  
 Cblb



Casitas B-lineage lymphoma b

TBT x1

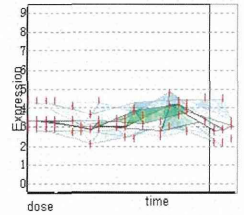
TTG085-L\_SpNC<sub>4</sub>0  
 Tributyltin  
 Cblb



Casitas B-lineage lymphoma b

TBT x14 + TBT x1

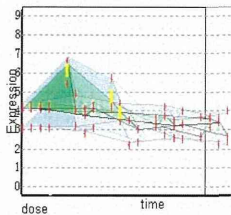
TTG145-L\_SpNC<sub>4</sub>0  
 Tributyltin chloride x Tributyltin chloride  
 Cblb



Casitas B-lineage lymphoma b

CCl<sub>4</sub> x14 + Clofib x1

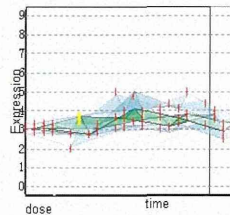
TTG129-L\_SpNC<sub>4</sub>0  
 CCl<sub>4</sub> x Clofibrate  
 Cblb



Casitas B-lineage lymphoma b

CCl<sub>4</sub> x1

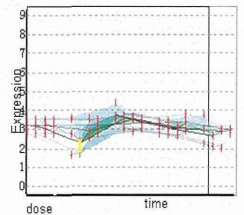
TTG119-L\_SpNC<sub>4</sub>0  
 Carbon tetrachloride  
 Cblb



Casitas B-lineage lymphoma b

CCl<sub>4</sub> x14 + CCl<sub>4</sub> x1

TTG130-L\_SpNC<sub>4</sub>0  
 CCl<sub>4</sub> x CCl<sub>4</sub>  
 Cblb

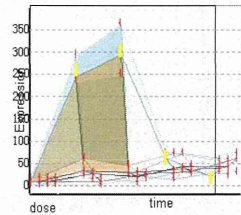


Casitas B-lineage lymphoma b

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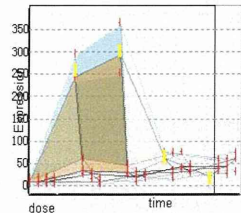
7

TTG044-L\_SpNC<sub>4</sub>0  
 Clofibrate  
 G0s2



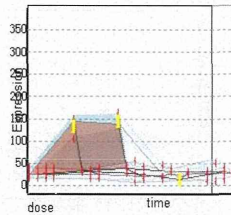
G0/G1 switch gene 2

TTG044-L\_SpNC<sub>4</sub>0  
 Clofibrate  
 G0s2



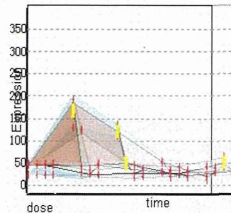
G0/G1 switch gene 2

TTG141-L\_SpNC<sub>4</sub>0  
 Tributyltin chloride x Clofibrate  
 G0s2



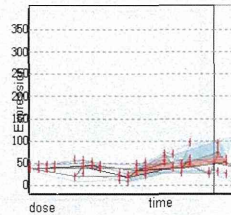
G0/G1 switch gene 2

TTG129-L\_SpNC<sub>4</sub>0  
 CCl<sub>4</sub> x Clofibrate  
 G0s2



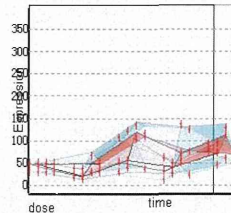
G0/G1 switch gene 2

TTG085-L\_SpNC<sub>4</sub>0  
 Tributyltin  
 G0s2



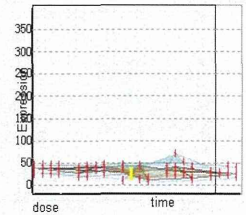
G0/G1 switch gene 2

TTG119-L\_SpNC<sub>4</sub>0  
 Carbon tetrachloride  
 G0s2



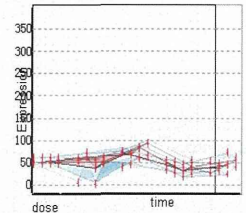
G0/G1 switch gene 2

TTG145-L\_SpNC<sub>4</sub>0  
 Tributyltin chloride x Tributyltin chloride  
 G0s2



G0/G1 switch gene 2

TTG130-L\_SpNC<sub>4</sub>0  
 CCl<sub>4</sub> x CCl<sub>4</sub>  
 G0s2



G0/G1 switch gene 2

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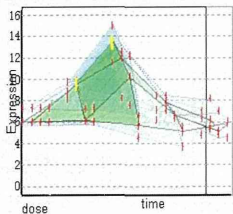
8

# [14+1] Clofibrate + PCN

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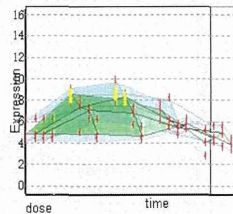
9

TTG090-L\_SpNC\_0  
Pregnenolone Carbonitrile  
Pik3ap1



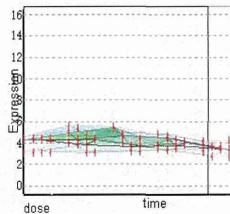
phosphoinositide-3-kinase adaptor protein 1

TTG120-L\_SpNC\_0  
Clofibrate x PCN  
Pik3ap1



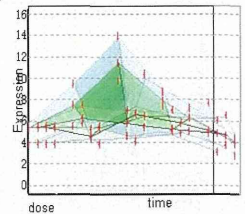
phosphoinositide-3-kinase adaptor protein 1

TTG118-L\_SpNC\_0  
Clofibrate x Clofibrate  
Pik3ap1



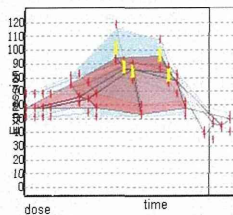
phosphoinositide-3-kinase adaptor protein 1

TTG044-L\_SpNC\_0  
Clofibrate  
Pik3ap1



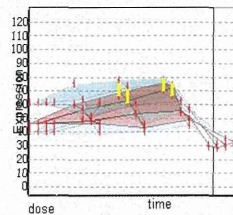
phosphoinositide-3-kinase adaptor protein 1

TTG090-L\_SpNC\_0  
Pregnenolone Carbonitrile  
AtI2



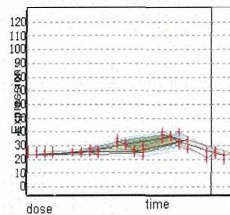
atlastin GTPase 2

TTG120-L\_SpNC\_0  
Clofibrate x PCN  
AtI2



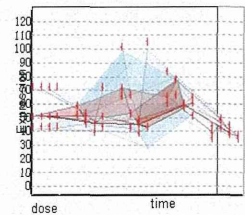
atlastin GTPase 2

TTG118-L\_SpNC\_0  
Clofibrate x Clofibrate  
AtI2



atlastin GTPase 2

TTG044-L\_SpNC\_0  
Clofibrate  
AtI2



atlastin GTPase 2

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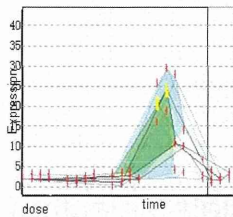


# [14+1] VPA+Thalidomide

11

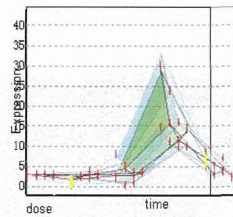
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TTG126-L\_SpNC<sub>0</sub>  
Thalidomide  
Acot3



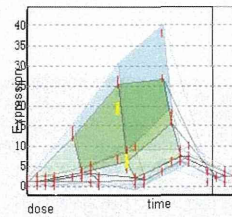
acyl-CoA thioesterase 3

TTG150-L\_SpNC<sub>0</sub>  
Valproic acid sodium salt x Thalidomide  
Acot3



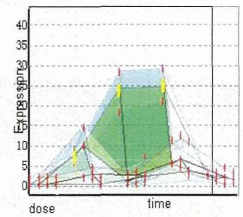
acyl-CoA thioesterase 3

TTG151-L\_SpNC<sub>0</sub>  
Valproic acid sodium salt x Valproic acid  
sodium salt  
Acot3



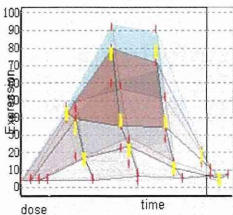
acyl-CoA thioesterase 3

TTG157-L\_SpNC<sub>0</sub>  
Valproic acid sodium salt  
Acot3



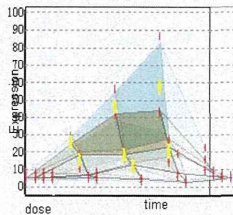
acyl-CoA thioesterase 3

TTG126-L\_SpNC<sub>0</sub>  
Thalidomide  
Cyp2b10



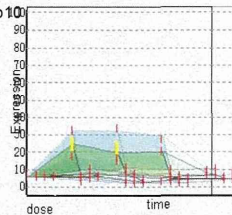
cytochrome P450, family 2, subfamily b,  
polypeptide 10

TTG150-L\_SpNC<sub>0</sub>  
Valproic acid sodium salt x Thalidomide  
Cyp2b10



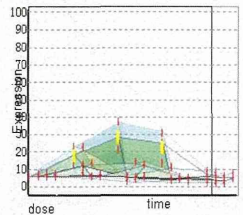
cytochrome P450, family 2, subfamily b,  
polypeptide 10

TTG151-L\_SpNC<sub>0</sub>  
Valproic acid sodium salt x Valproic acid  
sodium salt  
Cyp2b10



cytochrome P450, family 2, subfamily b,  
polypeptide 10

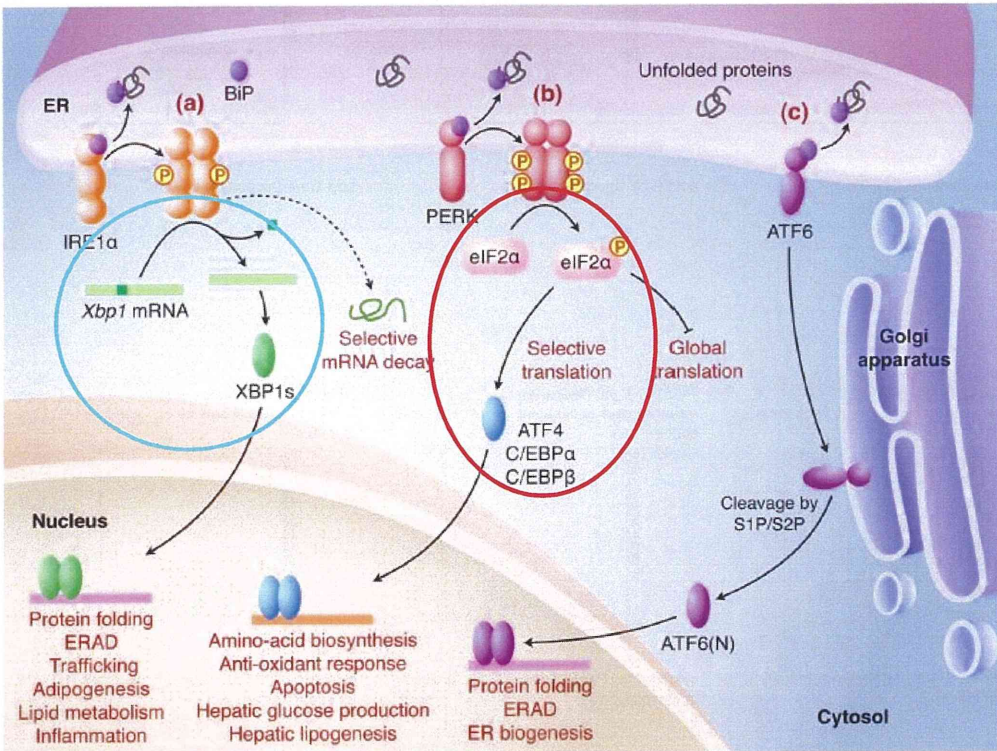
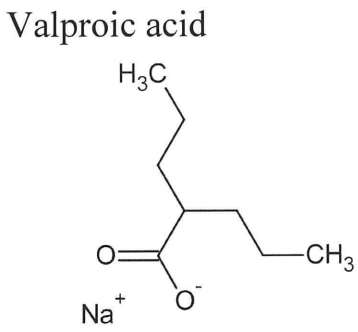
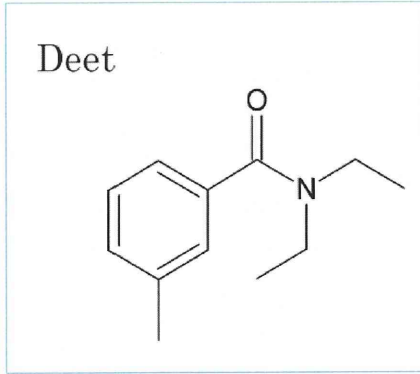
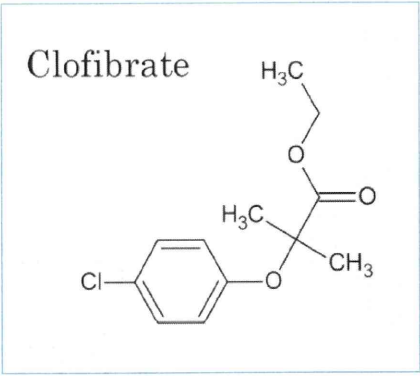
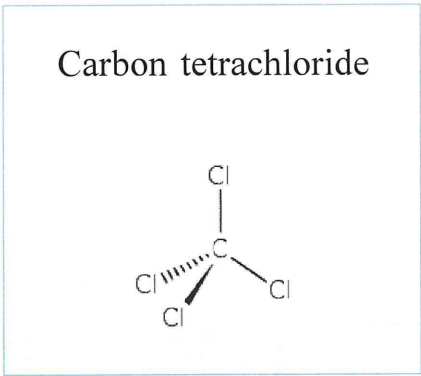
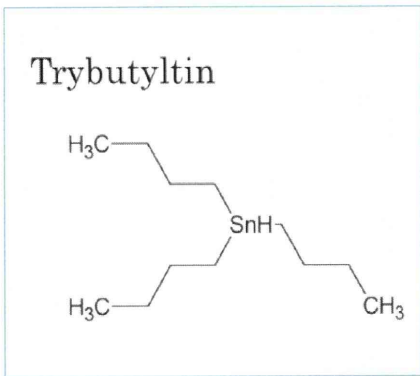
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Valproic acid sodium salt  
Cyp2b10



cytochrome P450, family 2, subfamily b,  
polypeptide 10

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厚劳科研 Percellome 班会議 2016-02-03



Possible selection of ER stress pathways by readiness of the gene ?

Tachyphylaxis  
"Brady"phylaxis