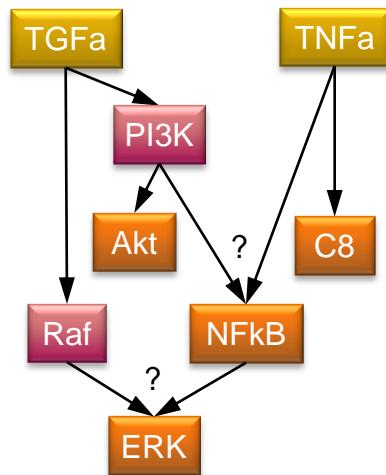


A Model structure of the original Toy model (adapted from Saez-Rodriguez *et al.*, doi: 10.1038/msb.2009.87)

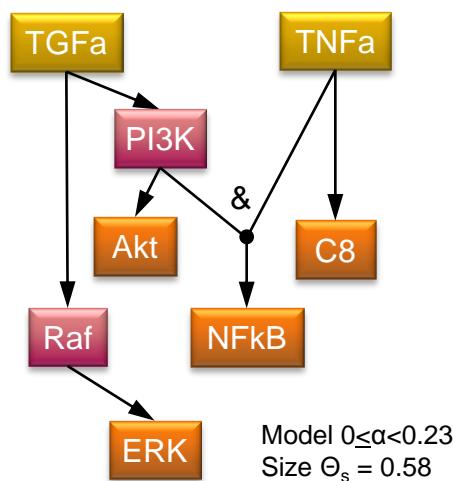


Exp	Input			
	TGFα	TNFα	PI3Ki	Rafi
A	1	0	-	-
B	0	1	-	-
C	1	1	-	-
D	1	0	+	-
E	1	1	+	-
F	1	0	-	+

Exp	Output			
	NFkB	ERK	C8	Akt
A	0	1	0	1
B	0	0	1	0
C	1	1	1	1
D	0	1	0	0
E	0	1	1	0
F	0	0	0	1

B CellNOpt results adapted from the original article of Saez-Rodriguez *et al.* (doi: 10.1038/msb.2009.87)

C Result from the optimization with optPBN toolbox in discrete optimization mode; Left: NFκB, Right: ERK



Exp	NFκB				
		&	PI3K	TNFα	\emptyset
All	$\times(0)$	$\checkmark(1)$	$\times(0)$	$\times(0)$	$\times(0)$

Exp	ERK				
		&	Raf	NFkB	\emptyset
All	$\checkmark(0.5)$	$\times(0)$	$\checkmark(0.5)$	$\times(0)$	$\times(0)$