SM1 Simulation model

Type	Label
Description	Simulation model of ERK signaling pathway regulated by RKIP
Reference	https://www.ebi.ac.uk/biomodels/BIOMD0000000647
Study	Cho et al. 2003

RQ1 Research question

Type	Label
Description	"Analyse the role of the positive feedback between the Wnt and ERK pathway and show that it might crucially contribute to cellular transformation"
Study	Kim et al. 2007

QM1 Qualitative model

Type	Label
Description	Reaction scheme for connected Wnt and ERK signaling pathway (via positive feedback)
Reference	Figure 1
Species	Wnt, Dsh, GSK3, APC, β-catenin, Axin, TCF, Ras, Raf-1, MEK, ERK, RKIP, X
Compartments	Cytosol, nucleus
Study	Kim et al. 2007

Back to the provenance graph

A1 Assumption

Type	Label
Description	"β-catenin synthetic rate (v12) increases in the Wnt pathway and the maximal velocity of the MEK phosphatase (V_max4) and ERK phosphatase (V_max5) decreases in the ERK pathway, respectively"
Category	Kinetic constant (9)
Study	Kim et al. 2007

A2 Assumption

Type	Label
Description	"the total concentrations of Ras, Raf-1, MEK, ERK, RKIP, Dishevelled (Dsh), APC, TCF, GSK-3β and all phosphatases are assumed to be constant over the whole simulation periods"
Category	Concentration Conservation Law (362)
Study	Kim et al. 2007

A3 Assumption

Type	Label
Description	For crosstalk: "we have followed general kinetic rules by employing mass action equations (basic chemical reaction kinetics) for the reaction of self-degradation of X (v31); Michaelis–Menten equations (enzyme kinetics) for the reaction of Raf-1 activation by molecule X (v30), GSK-3β phosphorylation by ERKpp (v32) and GSK-3β phosphatase activity (v33); Hill equations (transcriptional activation kinetics) for the reaction of transcriptional synthesis of activator X by β-catenin/TCF (v29)"
Category	Mass action rate law (12)
Study	Kim et al. 2007

A4 Assumption

Type	Label
Description	For crosstalk: "we have followed general kinetic rules by employing mass action equations (basic chemical reaction kinetics) for the reaction of self-degradation of X (v31); Michaelis–Menten equations (enzyme kinetics) for the reaction of Raf-1 activation by molecule X (v30), GSK-3β phosphorylation by ERKpp (v32) and GSK-3β phosphatase activity (v33); Hill equations (transcriptional activation kinetics) for the reaction of transcriptional synthesis of activator X by β-catenin/TCF (v29)"
Category	Henri-Michaelis-Menten rate law (29)
Study	Kim et al. 2007

A5 Assumption

Type	Label
Description	For crosstalk: "we have followed general kinetic rules by employing mass action equations (basic chemical reaction kinetics) for the reaction of self-degradation of X (v31); Michaelis–Menten equations (enzyme kinetics) for the reaction of Raf-1 activation by molecule X (v30), GSK-3β phosphorylation by ERKpp (v32) and GSK-3β phosphatase activity (v33); Hill equations (transcriptional activation kinetics) for the reaction of transcriptional synthesis of activator X by β-catenin/TCF (v29)"
Category	Hill-type rate law (192)
Study	Kim et al. 2007

WD1 Data

Type	Label
Description	"The effect of pharmacological perturbations on β-catenin and ERKpp levels"
Reference	Figure 4
Type of experiment	In vitro
Organism	Human
Cell line	HEK 293 cells (ATCC CRL-1573)
Study	Kim et al. 2007

WD2 Data

Type	Label
Description	"TOPFLASH /FOPFLASH reporter gene assay for β-catenin transcriptional activity"
Reference	Figure 5
Type of experiment	In vitro
Organism	Human
Cell line	HEK 293 cells (ATCC CRL-1573)
Study	Kim et al. 2007

BSM1 Building simulation model

Type	Label
Description	"All these parameters were selected from two published models (Cho et al., 2006, 2003)"
Study	Kim et al. 2007

SM1 Simulation model

Type	Label
Description	Wnt and ERK pathway model with interactions between them (positive feedback)
Reference	https://www.ebi.ac.uk/biomodels/BIOMD0000000149
Study	Kim et al. 2007

ASM1 Analyzing simulation model

Type	Label
Description	Simulation model analysis
Study	Kim et al. 2007

SE1 Experiment

Type	Label
Description	"From additional simulations over a range of parameters, we have confirmed that any small change of the parameters does not affect our hypothesis (data not shown)"
Reference	Not available
Category	Sensitivity analysis
Study	Kim et al. 2007

SD1 Data

Type	Label
Description	Simulation results of SE1
Reference	Not shown
Related to	SE1
Study	Kim et al. 2007

SE2 Experiment

Type	Label
Description	"The effect of parameter perturbations on β-catenin and ERKpp levels"
Reference	Not available
Category	Perturbation
Study	Kim et al. 2007

SD2 Data

Type	Label
Description	Simulation results of SE2
Reference	Figure 3
Related to	SE2
Study	Kim et al. 2007

SE3 Experiment

Type	Label
Description	"The simulation results under conditions of normal and mutated Wnt signaling"
Reference	Not available
Category	Perturbation
Study	Kim et al. 2007

SD3 Data

Type	Label
Description	Simulation results of SE3
Reference	Figure 6
Related to	SE3
Study	Kim et al. 2007

SE4 Experiment

Type	Label
Description	"Comparison of the Wnt and ERK signaling dynamics with and without crosstalk"
Reference	Not available
Category	Perturbation
Study	Kim et al. 2007

SD4 Data

Type	Label
Description	Simulation results of SE4
Reference	Figure 7
Related to	SE4
Study	Kim et al. 2007