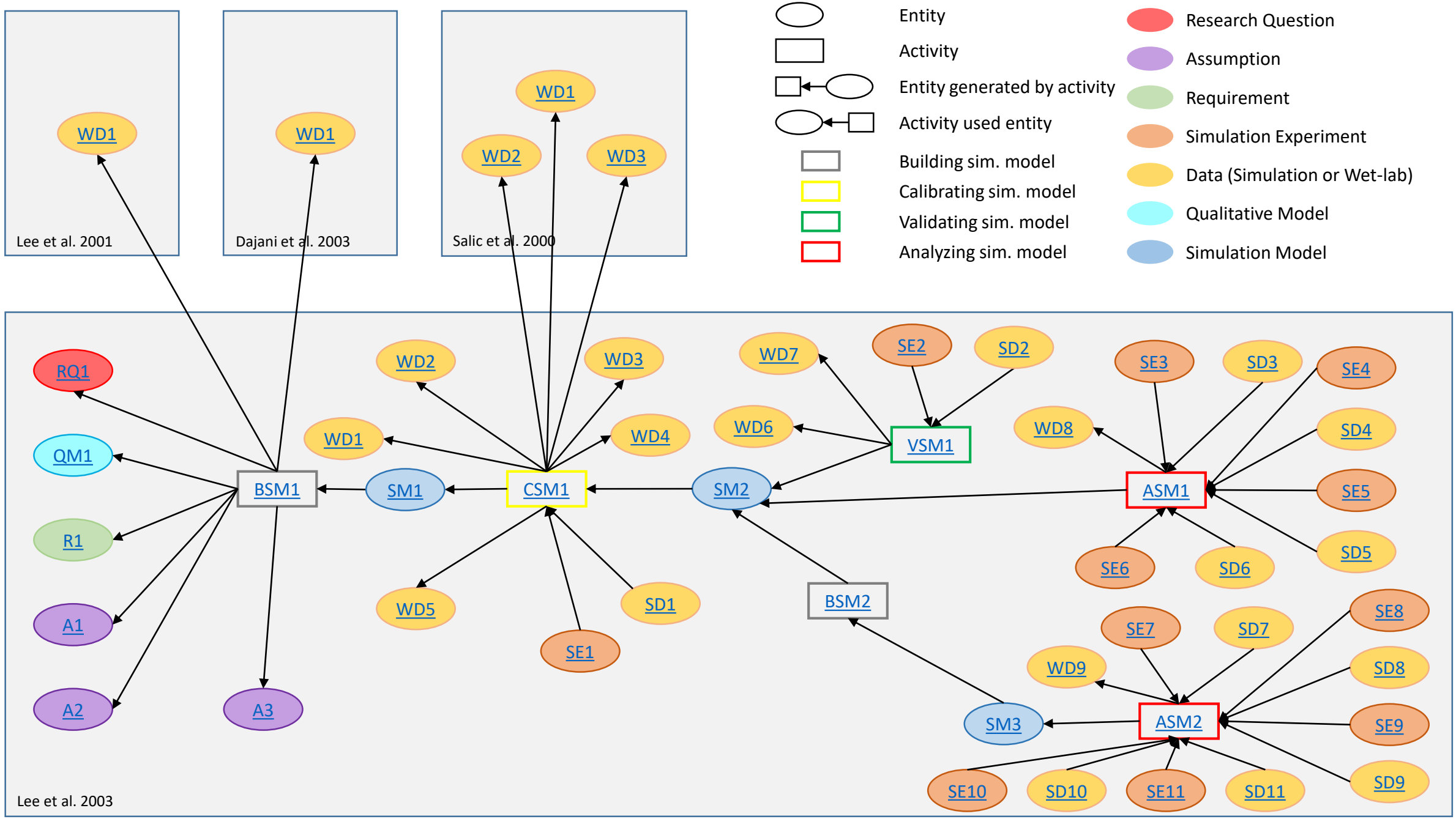
Entity
Activity
Entity generated by activity
Activity used entity
Building sim. model
Calibrating sim. model
Validating sim. model
Analyzing sim. model
Research Question
Assumption
Requirement
Simulation Experiment
Data (Simulation or Wet-lab)
Qualitative Model
Simulation Model
Lee et al. 2001
WD1
Dajani et al. 2003
WD1
Salic et al. 2000
WD1
WD2
WD3
Lee et al. 2003
RQ1
QM1
R1
A1
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A3
BSM1
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WD4
SM1
CSM1
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SE1
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VSM1
SM2
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SE3
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SD4
ASM1
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WD9
SM3
ASM2
SE9
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SD10
SE11
SD11

WD1 Wet-lab Data

Type	Label
Description	“TCF reduces the rate of β-catenin degradation”
Reference	Figure 1
Type of experiment	In vitro
Organism	Xenopus
Cell line	Egg extract
Study	Lee et al. 2001

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WD1 Wet-lab Data

Type	Label
Description	“axin stimulates the phosphorylation of β-catenin by GSK3b at least 24,000-fold”
Reference	Figure 5
Type of experiment	In vitro
Organism	Xenopus
Cell line	Egg extract
Study	Dajani et al. 2003

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WD1 Wet-lab Data

Type	Label
Description	“β-catenin has a 10-fold lower affinity for nonphosphorylated compared to phosphorylated APC”, “ratio K_{17} / K_{8}=10”
Reference	Not available
Type of experiment	In vitro
Organism	Xenopus
Cell line	Egg extract
Study	Salic et al. 2000

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WD2 Wet-lab Data

Type	Label
Description	“experimentally determined rate of β-catenin degradation”
Reference	Figure 1
Type of experiment	In vitro
Organism	Xenopus
Cell line	Egg extract
Study	Salic et al. 2000

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WD3 Wet-lab Data

Type	Label
Description	“experiments to determine the rate of APC and axin dephosphorylation”
Reference	Figure 6h
Type of experiment	In vitro
Organism	Xenopus
Cell line	Egg extract
Study	Salic et al. 2000

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RQ1 Research question

Type	Label
Description	“Why are two scaffold proteins, APC and axin, both necessary? Do their roles differ?”
Study	Lee et al. 2003

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QM1 Qualitative model

Type	Label
Description	Reaction scheme for Wnt signaling pathway
Reference	https://doi.org/10.1371/journal.pbio.0000010.g001
Species	Wnt, Dsh, GSK3, Axin, APC, β-catenin, TCF
Compartments	Cell extract (cytosol)
Study	Lee et al. 2003

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R1 Requirement

Type	Label
Description	“axin stimulates the phosphorylation of β-catenin by GSK3β at least 24,000-fold” (Dajani et al. 2003)
Related to	WD1 (Dajani et al. 2003)
Main species	Axin, β-catenin, GSK3β
Type	Quantitative
Study	Lee et al. 2003

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A1 Assumption

Type	Label
Description	“Dsh, TCF, and GSK3b are degraded very slowly, we assume that their concentrations remain constant throughout the timecourse of a Wnt signaling event”
Category	Concentration conservation law (362)
Study	Lee et al. 2003

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A2 Assumption

Type	Label
Description	“Unimolecular reactions are assumed to be irreversible and are described by linear rate equations”
Category	Mass action rate law for first order irreversible reactions (44)
Study	Lee et al. 2003

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A3 Assumption

Type	Label
Description	“reversible binding steps between axin, β-catenin, APC, and TCF are very fast, such that the corresponding protein complexes are in rapid equilibrium”
Category	Equilibrium or steady-state constant (193)
Study	Lee et al. 2003

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BSM1 Building simulation model

Type	Label
Description	Development of provisional reference state model
Study	Lee et al. 2003

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SM1 Simulation model

Type	Label
Description	Provisional reference state model: “seven ordinary differential equations coupled to four conservation equations and four relationships for binding equilibria”
Reference	Not available
Study	Lee et al. 2003

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CSM1 Calibrating simulation model

Type	Label
Description	Development of calibrated reference state model which includes a large number of experimental data
Study	Lee et al. 2003

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WD1 Wet-lab Data

Type	Label
Description	“turnover of GSK3b, Dsh, and TCF is relatively slow”
Reference	Not available
Type of experiment	In vitro
Organism	Xenopus
Cell line	Egg extract
Study	Lee et al. 2003

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WD2 Wet-lab Data

Type	Label
Description	“total concentrations of Dsh, TCF, GSK3b, axin, β-catenin, and APC in Xenopus egg extract were determined experimentally using Western blot analysis”
Reference	Not available
Type of experiment	In vitro
Organism	Xenopus
Cell line	Egg extract
Study	Lee et al. 2003

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WD3 Wet-lab Data

Type	Label
Description	“phosphorylated β-catenin dissociates from axin more rapidly (reaction 10) than nonphosphorylated β-catenin”
Reference	Not available
Type of experiment	In vitro
Organism	Xenopus
Cell line	Egg extract
Study	Lee et al. 2003

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WD4 Wet-lab Data

Type	Label
Description	“steady state flux v_{11} for the degradation of β-catenin via the Wnt pathway and the flux ratio v_{13}/v_{11} describing the extent to which β-catenin is degraded via non-Wnt mechanisms”
Reference	Not available
Type of experiment	In vitro
Organism	Xenopus
Cell line	Egg extract
Study	Lee et al. 2003

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WD5 Wet-lab Data

Type	Label
Description	“rate of axin degradation were determined directly from experiments performed in Xenopus egg extracts”
Reference	Not available
Type of experiment	In vitro
Organism	Xenopus
Cell line	Egg extract
Study	Lee et al. 2003

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SE1 Simulation Experiment

Type	Label
Description	“number of parameters were set such that the results of the model were in agreement with previous experimental data, specifically with the experimentally determined rate of β-catenin degradation (Salic et al. 2000; Lee et al. 2001)”
Reference	Not available
Category	Optimization
Study	Lee et al. 2003

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SD1 Simulation Data

Type	Label
Description	“number of parameters were set such that the results of the model were in agreement with previous experimental data, specifically with the experimentally determined rate of β-catenin degradation (Salic et al. 2000; Lee et al. 2001)”
Reference	Not available
Related to	SE1
Study	Lee et al. 2003

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SM2 Simulation model

Type	Label
Description	Calibrated reference state model
Reference	https://www.ebi.ac.uk/biomodels/BIOMD0000000658
Study	Lee et al. 2003

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VSM1 Validating simulation model

Type	Label
Description	Model validation
Study	Lee et al. 2003

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WD6 Wet-lab Data

Type	Label
Description	“Preincubation of Dsh in Xenopus egg extracts abolishes the lag in Dsh activity”
Reference	https://doi.org/10.1371/journal.pbio.0000010.g003
Type of experiment	In vitro
Organism	Xenopus
Cell line	Egg extract
Study	Lee et al. 2003

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WD7 Wet-lab Data

Type	Label
Description	“Kinetics of β-catenin degradation”, “tested the results using the previously described biochemical system (Salic et al. 2000; Lee et al. 2001), adding purified proteins or compounds at t=0”
Reference	https://doi.org/10.1371/journal.pbio.0000010.g002
Type of experiment	In vitro
Organism	Xenopus
Cell line	Egg extract
Study	Lee et al. 2003

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SE2 Simulation Experiment

Type	Label
Description	“we ran through a series of simulations, all of which used the same set of parameters. From these we calculated simulated timecourses for β-catenin degradation under a range of different conditions (increased axin concentration, increased Dsh a concentration, inhibition of GSK3b, increased TCF concentration)”
Reference	Not available
Category	Parameter scan
Study	Lee et al. 2003

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SD2 Simulation Data

Type	Label
Description	Simulation results of SE2 (validation successful)
Reference	https://doi.org/10.1371/journal.pbio.0000010.g002
Related to	SE2
Study	Lee et al. 2003

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ASM1 Analyzing simulation model

Type	Label
Description	Analyzing reference state model
Study	Lee et al. 2003

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WD8 Wet-lab Data

Type	Label
Description	“we studied experimentally the dose-dependent effects of Dsh, GSK3β, and axin on β-catenin degradation”
Reference	https://doi.org/10.1371/journal.pbio.0000010.g004
Type of experiment	In vitro
Organism	Xenopus
Cell line	Egg extract
Study	Lee et al. 2003

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SE3 Simulation Experiment

Type	Label
Description	“Effect of Dsh versus Axin or GSK3β on the half-life of β-catenin in Xenopus extracts”
Reference	Not available
Category	Parameter scan
Study	Lee et al. 2003

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SD3 Simulation Data

Type	Label
Description	Simulation results of SE3
Reference	https://doi.org/10.1371/journal.pbio.0000010.g004
Related to	SE3
Study	Lee et al. 2003

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SE4 Simulation Experiment

Type	Label
Description	“theoretical effect of APC on the concentrations of both β-catenin and axin”
Reference	Not available
Category	Perturbation
Study	Lee et al. 2003

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SD4 Simulation Data

Type	Label
Description	Simulation results of SE4
Reference	https://doi.org/10.1371/journal.pbio.0000010.g005
Related to	SE4
Study	Lee et al. 2003

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SE5 Simulation Experiment

Type	Label
Description	“simulated the effects of changes in the rate of β-catenin (v_{12}) and axin (v_{14}) synthesis on both β-catenin and axin levels”
Reference	Not available
Category	Parameter scan
Study	Lee et al. 2003

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SD5 Simulation Data

Type	Label
Description	Simulation results of SE5
Reference	https://doi.org/10.1371/journal.pbio.0000010.sg003
Related to	SE5
Study	Lee et al. 2003

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SE6 Simulation Experiment

Type	Label
Description	“transient Wnt stimulation by an exponential decay” with different rates of axin synthesis and degradation”
Reference	Not available
Category	Parameter scan
Study	Lee et al. 2003

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SD6 Simulation Data

Type	Label
Description	Simulation results of SE6
Reference	https://doi.org/10.1371/journal.pbio.0000010.g006
Related to	SE6
Study	Lee et al. 2003

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BSM2 Building simulation model

Type	Label
Description	Model extension (including the formation of the β-catenin/axin complex)
Study	Lee et al. 2003

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SM3 Simulation model

Type	Label
Description	Extended model with added reactions 18 and 19
Reference	Not available
Study	Lee et al. 2003

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ASM2 Analyzing simulation model

Type	Label
Description	Analyzing extended model
Study	Lee et al. 2003

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WD9 Wet-lab Data

Type	Label
Description	“Effects of increasing axin concentration on β-catenin degradation”
Reference	https://doi.org/10.1371/journal.pbio.0000010.g007
Type of experiment	In vitro
Organism	Xenopus
Cell line	Egg extract
Study	Lee et al. 2003

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SE7 Simulation Experiment

Type	Label
Description	“Effects of increasing axin concentration on β-catenin degradation”
Reference	Not available
Category	Parameter scan
Study	Lee et al. 2003

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SD7 Simulation Data

Type	Label
Description	Simulation results of SE7
Reference	https://doi.org/10.1371/journal.pbio.0000010.g007
Related to	SE7
Study	Lee et al. 2003

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SE8 Simulation Experiment

Type	Label
Description	“Effects of APC concentrations on β-catenin degradation”
Reference	Not available
Category	Parameter scan
Study	Lee et al. 2003

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SD8 Simulation Data

Type	Label
Description	Simulation results of SE8
Reference	https://doi.org/10.1371/journal.pbio.0000010.g008
Related to	SE8
Study	Lee et al. 2003

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SE9 Simulation Experiment

Type	Label
Description	“effect of these alternative pathways [with and without regulatory loop Eq. 5] becomes much more prominent when the APC concentration is lowered”
Reference	Not available
Category	Perturbation
Study	Lee et al. 2003

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SD9 Simulation Data

Type	Label
Description	Simulation results of SE9
Reference	https://doi.org/10.1371/journal.pbio.0000010.g009
Related to	SE9
Study	Lee et al. 2003

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SE10 Simulation Experiment

Type	Label
Description	“Sensitivity analysis (control coefficients) of model regarding reaction rate constants”
Reference	Not available
Category	Sensitivity analysis
Study	Lee et al. 2003

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SD10 Simulation Data

Type	Label
Description	Simulation and calculation results of SE10
Reference	https://doi.org/10.1371/journal.pbio.0000010.t003
Related to	SE10
Study	Lee et al. 2003

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SE11 Simulation Experiment

Type	Label
Description	“Sensitivity analysis (control coefficients) of model regarding concentration”
Reference	Not available
Category	Sensitivity analysis
Study	Lee et al. 2003

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SD11 Simulation Data

Type	Label
Description	Simulation and calculation results of SE11
Reference	https://doi.org/10.1371/journal.pbio.0000010.t004
Related to	SE11
Study	Lee et al. 2003

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