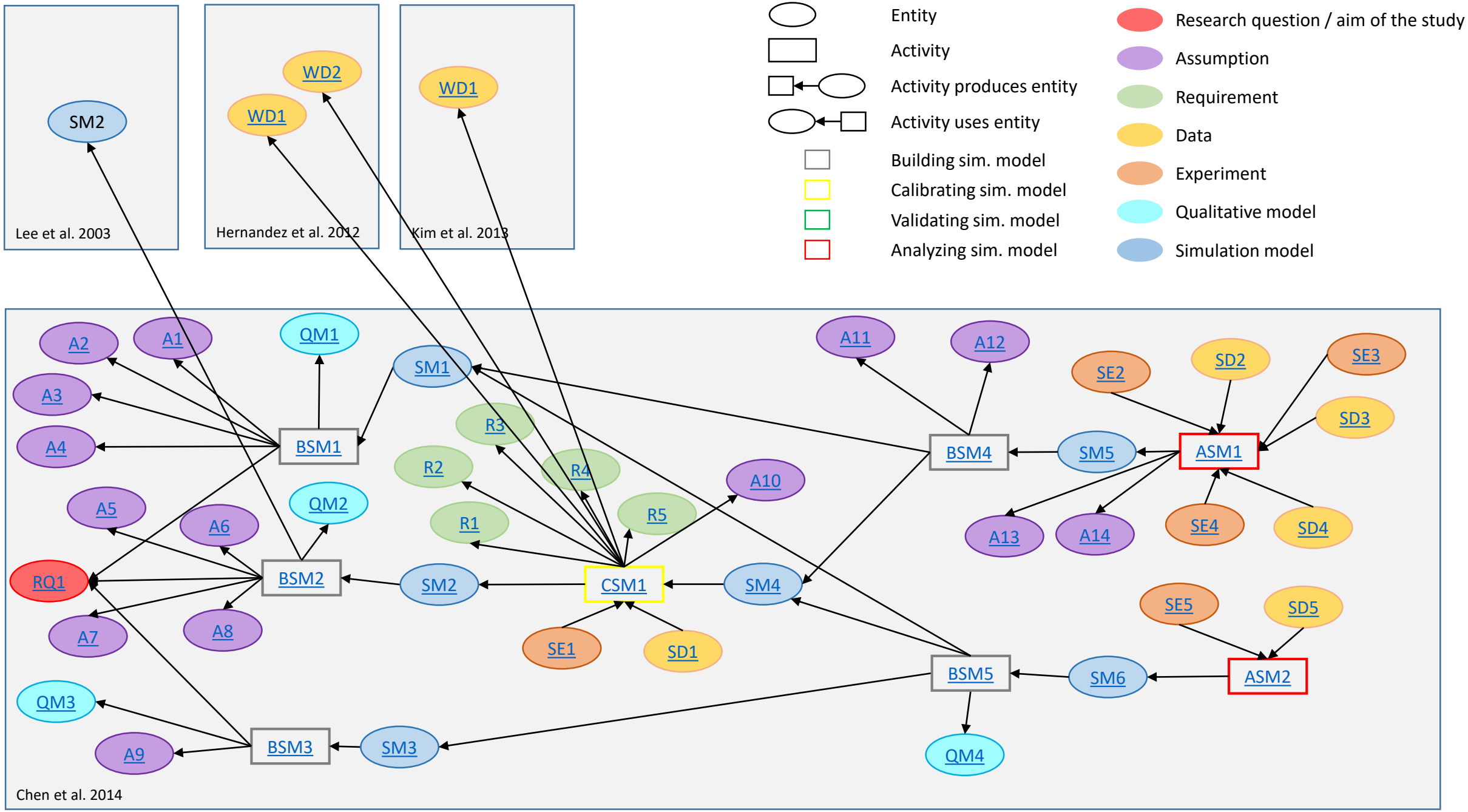
Entity
Activity
Activity produces entity
Activity uses entity
Building sim. model
Calibrating sim. model
Validating sim. model
Analyzing sim. model
Research question / aim of the study
Assumption
Requirement
Data
Experiment
Qualitative model
Simulation model
Lee et al. 2003
SM2
Hernandez et al. 2012
WD2
WD1
Kim et al. 2013
WD1
Chen et al. 2014
A2
A1
QM1
SM1
A3
A4
BSM1
R3
R2
R4
A5
QM2
A6
R1
R5
A10
RQ1
BSM2
SM2
CSM1
SM4
A7
A8
SE1
SD1
QM3
A9
BSM3
SM3
A11
A12
BSM4
SE2
SD2
SE3
SD3
SM5
ASM1
A13
A14
SE4
SD4
SE5
SD5
BSM5
SM6
ASM2
QM4

WD1 Wet-lab Data

TypeFig.	Label
Description	“Quantification of total, GSK3-, and CK1a-phosphorylated β-catenin in Wnt-stimulated RKO cells.”
Reference	Figure 2C
Type of experiment	in vitro
Organism	Human
Cell line	Colon carcinoma RKO cells
Study	Hernández et al. 2012

Back to the provenance graph

WD2 Wet-lab Data

TypeFig.	Label
Description	“size of the unphosphorylated fraction of β-catenin”
Reference	Figure 3A
Type of experiment	in vitro
Organism	Human
Cell line	Colon carcinoma RKO cells
Study	Hernández et al. 2012

Back to the provenance graph

WD1 Wet-lab Data

TypeFig.	Label
Description	“Quantifications of Wnt3a effects on ratios Axin-associated LRP6 versus total LRP6”
Reference	Figure 2B
Type of experiment	in vitro
Organism	Human
Cell line	embryonic kidney (HEK) 293T cells
Study	Kim et al. 2013

Back to the provenance graph

RQ1 Research question

Type	Label
Description	“A comprehensive model that investigates the interplay between these two processes [Wnt signaling and cadherin-mediated cell adhesion] will provide useful information to understand EMT and cancer metastasis”
Study	Chen et al. 2014

Back to the provenance graph

QM1 Qualitative model

Type	Label
Description	Cadherin-mediated cell adhesion module
Reference	Figure 2
Species	β-catenin, cadherin
Compartments	Cytosol, Golgi apparatus,
Study	Chen et al. 2014

Back to the provenance graph

A1 Assumption

Type	Label
Description	“use a single order chemical reaction to describe this process” [formation and co-localization of Cad/Cat complexes]
Category	Mass action rate law for first order reversible reactions (78)
Study	Chen et al. 2014

Back to the provenance graph

A2 Assumption

Type	Label
Description	“recycling is not considered explicitly. We use a single order chemical reaction to describe the degradation”
Category	Degradation (179)
Study	Chen et al. 2014

Back to the provenance graph

A3 Assumption

Type	Label
Description	“process of junction formation is simplified by using state transition of Cad/Cat complexes”
Category	Protein complex formation (526)
Study	Chen et al. 2014

Back to the provenance graph

A4 Assumption

Type	Label
Description	“endocytosis rate of ‘‘cis’’ complexes is lower than that of ‘‘trans’’ complexes, and ‘‘free’’ Cad/Cat complexes have the highest endocytosis rate”
Category	Transport (655)
Study	Chen et al. 2014

Back to the provenance graph

BSM1 Building simulation model

Type	Label
Description	ODE model building
Study	Chen et al. 2014

Back to the provenance graph

SM1 Simulation model

Type	Label
Description	cell adhesion module
Reference	Not available
Study	Chen et al. 2014

Back to the provenance graph

QM2 Qualitative model

Type	Label
Description	Wnt stimulation and β-catenin degradation module
Reference	Figure 3
Species	APC, Axin, β-catenin, CK1, GSK3, Wnt/receptor complex
Compartments	Cytosol
Study	Chen et al. 2014

Back to the provenance graph

A5 Assumption

Type	Label
Description	“destruction complexes undergo structural transformation that exposes β-catenins to ubiquitin/proteosome machinery after GSK3-phosphorylation”
Category	Protein complex formation (526)
Study	Chen et al. 2014

Back to the provenance graph

A6 Assumption

Type	Label
Description	“dephosphorylation of Axins trigger the transformation of destruction complex which leads to the exposure of β-catenins to ubiquitin/proteosome machinery”
Category	Protein complex formation (526)
Study	Chen et al. 2014

Back to the provenance graph

A7 Assumption

Type	Label
Description	“ABC could release from the destruct complex cycle at the stage of CK1-pBD”
Category	Reversible process (650)
Study	Chen et al. 2014

Back to the provenance graph

A8 Assumption

Type	Label
Description	“ABC release from CK1-pBD in ‘‘Wnt off’’ scene with much lower rate than that in ‘‘Wnt on’’scene”
Category	Kinetic constant (9)
Study	Chen et al. 2014

Back to the provenance graph

BSM2 Building simulation model

Type	Label
Description	Extending simulation model of Lee et al.
Study	Chen et al. 2014

Back to the provenance graph

SM2 Simulation model

Type	Label
Description	Wnt stimulation and β-catenin degradation circle module [“module of Wnt stimulation and β-catenin degradation is extended from Lee’s original mode”]
Reference	Not available
Study	Chen et al. 2014

Back to the provenance graph

QM3 Qualitative model

Type	Label
Description	Wnt target gene expressions module
Reference	Figure 4
Species	β-catenin, Bcl9, TCF, E-Cadherin, N-Cadherin, Inhibitor 2
Compartments	Cytosol, nucleus
Study	Chen et al. 2014

Back to the provenance graph

A9 Assumption

Type	Label
Description	“accumulation of ABC/Bcl9 complexes in cell nucleus and random distributions of ABC/TCF complexes on transcriptional regions of target genes”
Category	Transcription (183)
Study	Chen et al. 2014

Back to the provenance graph

BSM3 Building simulation model

Type	Label
Description	Constructing transcriptional simulation model
Study	Chen et al. 2014

Back to the provenance graph

SM3 Simulation model

Type	Label
Description	transcriptional regulation module
Reference	Not available
Study	Chen et al. 2014

Back to the provenance graph

R1 Requirement

Type	Label
Description	“Under continuous Wnt stimulation, the total β-catenins increase to six fold of its initial level”
Related to	WD1 (Hernández et al. 2012)
Main species	Wnt3a, β-catenin
Type	Quantitative
Study	Chen et al. 2014

Back to the provenance graph

R2 Requirement

Type	Label
Description	“increase of non-phosphorylated β-catenins is comparable to that of β-catenins”
Related to	WD2 (Hernández et al. 2012)
Main species	Wnt3a, β-catenin
Type	Qualitative
Study	Chen et al. 2014

Back to the provenance graph

R3 Requirement

Type	Label
Description	“the GSK3-phosphorylated β-catenins decrease in 0.5 hr then recover to its initial level in 2 hr”
Related to	WD1 (Hernández et al. 2012)
Main species	Wnt3a, β-catenin, GSK3
Type	Qualitative
Study	Chen et al. 2014

Back to the provenance graph

R4 Requirement

Type	Label
Description	“CK1-phosphorylated β-catenins decrease in 0.25 hr then increase to 3 fold of its initial level in 2 hr”
Related to	WD1 (Hernández et al. 2012)
Main species	Wnt3a, β-catenin, CK1α
Type	Qualitative
Study	Chen et al. 2014

Back to the provenance graph

R5 Requirement

Type	Label
Description	“the binding affinity between Axin and LRP6 increases in 0.5 hr then decreases in 2 hr”
Related to	WD1 (Kim et al. 2013)
Main species	LRP6, Wnt3a, Axin
Type	Qualitative
Study	Chen et al. 2014

Back to the provenance graph

A10 Assumption

Type	Label
Description	“We set up a subcellular system that occupies 2.5% volume of a whole cell. Given the measurement that the volume of a cell is around 10^{-12} L.”
Category	Physical compartment (290)
Study	Chen et al. 2014

Back to the provenance graph

CSM1 Calibrating simulation model

Type	Label
Description	Calibration of Wnt stimulation an β-catenin degradation module
Study	Chen et al. 2014

Back to the provenance graph

SE1 Experiment

Type	Label
Description	“Calibration of Wnt stimulation and β-catenin degradation module”
Reference	Not available
Category	Optimization
Study	Chen et al. 2014

Back to the provenance graph

SD1 Data

Type	Label
Description	Simulation results of SE1
Reference	Figure 5
Related to	SE1
Study	Chen et al. 2014

Back to the provenance graph

SM4 Simulation model

Type	Label
Description	calibrated Wnt stimulation and β-catenin degradation circle module
Reference	Not available
Study	Chen et al. 2014

Back to the provenance graph

A11 Assumption

Type	Label
Description	“spatial reorganization of membrane changes the binding between cadherins and β-catenins”
Category	Kinetic constant (9)
Study	Chen et al. 2014

Back to the provenance graph

A12 Assumption

Type	Label
Description	“crowding caused by cadherin clustering slows down the structural transformation in destruction complexes, which leads to more ABCs released”
Category	Kinetic constant (9)
Study	Chen et al. 2014

Back to the provenance graph

BSM4 Building simulation model

Type	Label
Description	Combining simulation models
Study	Chen et al. 2014

Back to the provenance graph

SM5 Simulation model

Type	Label
Description	combined cell adhesion and degradation model
Reference	Not available
Study	Chen et al. 2014

Back to the provenance graph

A13 Assumption

Type	Label
Description	“majority of cadherins form trans-dimers due to the diffusion trap mechanism”
Category	Protein complex formation (526)
Study	Chen et al. 2014

Back to the provenance graph

A14 Assumption

Type	Label
Description	“cell adhesion facilitates the phosphorylation of β-catenin at Y142 and the phosphorylation accelerates the association kinetics between ABC and Bcl9”
Category	Phosphorylation (216)
Study	Chen et al. 2014

Back to the provenance graph

ASM1 Analyzing simulation model

Type	Label
Description	Simulation model analysis through parameter scans
Study	Chen et al. 2014

Back to the provenance graph

SE2 Experiment

Type	Label
Description	“number of ABC in cytoplasm under different adhesion condition after 0.5 hr Wnt treatment” (neglecting the effects of membrane organization under cell adhesion)
Reference	Not available
Category	Parameter scan
Study	Chen et al. 2014

Back to the provenance graph

SD2 Data

Type	Label
Description	Simulation results of SE2
Reference	Figure 6
Related to	SE2
Study	Chen et al. 2014

Back to the provenance graph

SE3 Experiment

Type	Label
Description	Number of ABC and GSK3-phosphor-β-cat spatial under the assumption that “organizations of cadherin clusters during cell adhesion generate a crowding environment for proteins at membrane proximal regions” (“Multiple simulations were carried out by using different values of a1 and a2, so that the effects of cell adhesion can be systematically estimated.”)
Reference	Not available
Category	Parameter scan
Study	Chen et al. 2014

Back to the provenance graph

SD3 Data

Type	Label
Description	Simulation results of SE3
Reference	Figure 7
Related to	SE3
Study	Chen et al. 2014

Back to the provenance graph

SE4 Experiment

Type	Label
Description	“explored how adhesion changes β-catenin distributions under Wnt stimulations” by decomposing “the multiple factors caused by adhesion” and adding them “step by step”
Reference	Not available
Category	Parameter scan
Study	Chen et al. 2014

Back to the provenance graph

SD4 Data

Type	Label
Description	Simulation results of SE4
Reference	Figure 8
Related to	SE4
Study	Chen et al. 2014

Back to the provenance graph

QM4 Qualitative model

Type	Label
Description	Composition and interaction of three modules
Reference	Figure 1
Species	APC, Axin, β-catenin, Cadherin, CK1, GSK3, Wnt/receptor complex, Bcl9, TCF, E-Cadherin, N-Cadherin, Inhibitor 2
Compartments	Cytosol, Golgi apparatus, nucleus
Study	Chen et al. 2014

Back to the provenance graph

BSM5 Building simulation model

Type	Label
Description	Combining simulation models
Study	Chen et al. 2014

Back to the provenance graph

SM6 Simulation model

Type	Label
Description	full (combined) model → “full mathematical representation of our network model is provided in Document S1”
Reference	Not available
Study	Chen et al. 2014

Back to the provenance graph

ASM2 Analyzing simulation model

Type	Label
Description	Simulation model analysis through perturbation
Study	Chen et al. 2014

Back to the provenance graph

SE5 Experiment

Type	Label
Description	“transcription feedback caused by [constant] Wnt signaling”
Reference	Not available
Category	Perturbation
Study	Chen et al. 2014

Back to the provenance graph

SD5 Data

Type	Label
Description	Simulation results of SE5
Reference	Figure 9
Related to	SE5
Study	Chen et al. 2014

Back to the provenance graph