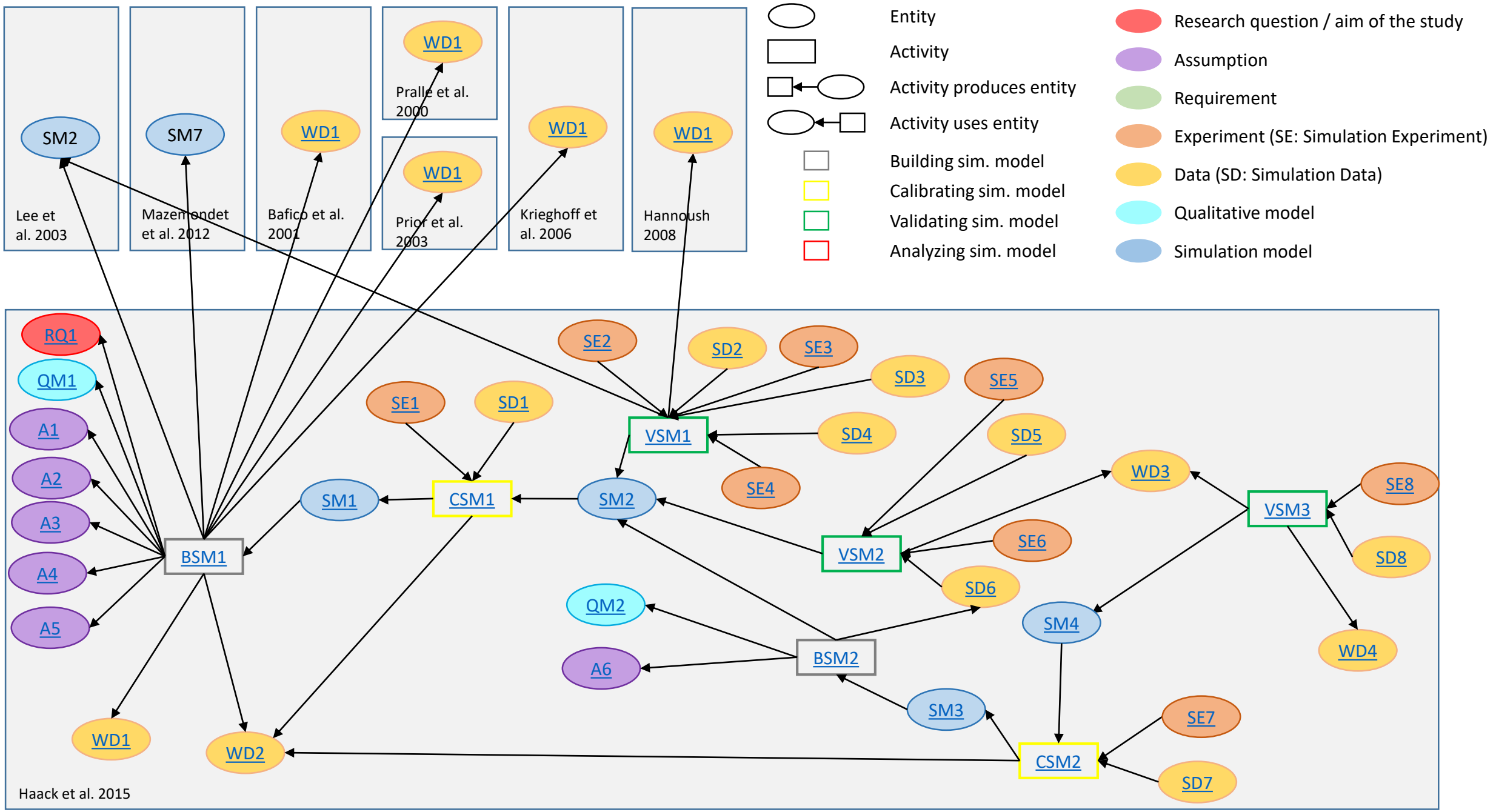
Entity
Activity
Activity produces entity
Activity uses entity
Building sim. model
Calibrating sim. model
Validating sim. model
Analyzing sim. model
Research question / aim of the study
Assumption
Requirement
Experiment (SE: Simulation Experiment)
Data (SD: Simulation Data)
Qualitative model
Simulation model
Lee et al. 2003
Mazemondet et al. 2012
Bafico et al. 2001
Pralle et al. 2000
Prior et al. 2003
Krieghoff et al. 2006
Hannoush 2008
SM2
SM7
WD1
WD1
WD1
WD1
WD1
RQ1
QM1
A1
A2
A3
A4
A5
BSM1
SE1
SD1
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SD2
SE3
SD3
SE5
SD5
SD4
SE4
VSM1
SM1
CSM1
SM2
VSM2
SE6
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WD3
VSM3
SE8
SD8
WD4
SM4
QM2
A6
BSM2
SM3
SE7
SD7
CSM2
WD1
WD2
Haack et al. 2015

WD1 Data

Type	Label
Description	A Scatchard plot of the data for [^{125}I] Dkk-1 binding to NIH3T3 cells
Reference	Figure 2f
Type of experiment	In vitro
Organism	Mouse
Cell line	Fibroblasts NIH/3T3
Study	Bafico et al. 2001

Back to the provenance graph

WD1 Data

Type	Label
Description	“Summary of the local viscous drags measured for the GPI-anchored raft-markers PLAP and YFPGLGPI and the transmembrane raft protein HA” -> “the estimated radius of the rafts is r = 26 +- 13 nm”
Reference	Figure 7
Type of experiment	In vitro
Organism	Kangaroo rat
Cell line	Epithelial kidney cells, PtK2
Study	Pralle et al. 2000

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WD1 Data

Type	Label
Description	“Visualizing lipid rafts using electron microscopy and spatial point pattern analysis.” -> “lipid raft marker displays cholesterol-dependent clustering in microdomains with a mean diameter of 44 nm that occupy 35% of the cell surface”
Reference	Figure 1
Type of experiment	In vitro
Organism	Hamster
Cell line	Baby hamster kidney cells (BHK)
Study	Prior et al. 2003

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WD1 Data

Type	Label
Description	β-catenin shuttles efficiently between nucleus and cytoplasm and is mobile in both compartments
Reference	Figure 1
Type of experiment	In vitro
Organism	Human
Cell line	Embryonic kidney cells, HEK293T
Study	Krieghoff et al. 2006

Back to the provenance graph

WD1 Data

Type	Label
Description	Kinetics of cellular β-catenin accumulation upon stimulation with Wnt3a
Reference	Figure 4C, 4D
Type of experiment	In vitro
Organism	Mouse
Cell line	Fibroblasts L cells
Study	Hannoush 2008

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RQ1 Research question

Type	Label
Description	“evaluate, whether an interplay between ROS-induced and lipid raft dependent WNT/β-catenin signaling can explain our experimental results we apply computational modeling”
Study	Haack et al. 2015

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QM1 Qualitative model

Type	Label
Description	“schematic representation of our basic WNT model”
Reference	Figure 2
Species	LRP5/6, Wnt, CK1γ, Axin, β-catenin
Compartments	Cytosol, nucleus, membrane, lipid rafts
Study	Haack et al. 2015

Back to the provenance graph

A1 Assumption

Type	Label
Description	“reduce the representation of the receptor-complex and the signalosome. Accordingly, the FZ-LRP6 receptor complex is only represented by LRP6”
Category	Equivalence (392)
Study	Haack et al. 2015

Back to the provenance graph

A2 Assumption

Type	Label
Description	“we consider solely the interaction between CK1γ and LRP6, whereas a detailed representation of DVL mediated unspecific phosphorylation of LRP6 by GSK3β is omitted”
Category	Omitted process (397)
Study	Haack et al. 2015

Back to the provenance graph

A3 Assumption

Type	Label
Description	“include lipid rafts as individual compartments within the membrane”
Category	Physical compartment (290)
Study	Haack et al. 2015

Back to the provenance graph

A4 Assumption

Type	Label
Description	“we solely consider AXIN as a condensed representation of the destruction complex disregarding its remaining components, like GSK3β, APC and CK1α”
Category	Equivalence (392)
Study	Haack et al. 2015

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A5 Assumption

Type	Label
Description	“released WNT molecules can directly induce the WNT/β-catenin signaling at the cell surface in an autocrine manner”
Category	Unknown (0)
Study	Haack et al. 2015

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WD1 Data

Type	Label
Description	Lipid rafts disruption: disruption by methyl-β cyclodextrin (MbCD) (shows no impact on lateral distribution of LRP6)
Reference	Figure 1A & Figure S1
Type of experiment	In vitro
Organism	Human
Cell line	Neural progenitor cells (ReNcell VM197)
Study	Haack et al. 2015

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WD2 Data

Type	Label
Description	“Impact of raft disruption on temporal regulation of nuclear β-catenin concentration after induction of differentiation in ReNCell”
Reference	Figure 1 B, D
Type of experiment	In vitro
Organism	Human
Cell line	Neural progenitor cells (ReNcell VM197)
Study	Haack et al. 2015

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BSM1 Building simulation model

Type	Label
Description	Creation of core model
Study	Haack et al. 2015

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SM1 Simulation model

Type	Label
Description	uncalibrated model code of QM1
Reference	Not available
Study	Haack et al. 2015

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CSM1 Calibrating simulation model

Type	Label
Description	Parameter fitting (to own results)
Study	Haack et al. 2015

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SE1 Experiment

Type	Label
Description	calibration: “fitted the remaining parameter values of the combined intracellular and membrane model against in vitro measurements we derived from human neuronal progenitor cells (ReNcell VM197)” (with SESSL)
Reference	Not available
Category	Optimization
Study	Haack et al. 2015

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SD1 Data

Type	Label
Description	Simulation results of SE1
Reference	S1 Text (optimization)
Related to	SE1
Study	Haack et al. 2015

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SM2 Simulation model

Type	Label
Description	calibrated model code of QM1
Reference	https://doi.org/10.1371/journal.pcbi.1004106.s008
Study	Haack et al. 2015

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VSM1 Validating simulation model

Type	Label
Description	Model validation (cross validation with results of Lee model)
Study	Haack et al. 2015

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SE2 Experiment

Type	Label
Description	“comparing the simulation outcome of Lee et. al. and our model”
Reference	Not available
Category	Time course analysis
Study	Haack et al. 2015

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SD2 Data

Type	Label
Description	Simulation results of SE2 (validation unsuccessful)
Reference	Figure 3A
Related to	SE2
Study	Haack et al. 2015

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SE3 Experiment

Type	Label
Description	“simulation results with the adapted model” (“adapt the temporal scale of our model by reducing all parameter values by a constant factor of 2/7”)
Reference	Not available
Category	Perturbation
Study	Haack et al. 2015

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SD3 Data

Type	Label
Description	Simulation results of SE3 (validation successful)
Reference	Figure 3B
Related to	SE3
Study	Haack et al. 2015

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SE4 Experiment

Type	Label
Description	“simulation experiments with the WNT concentrations listed in Table 2 and measured the rate of β-catenin accumulation after 2 hours of WNT stimulation”
Reference	Not available
Category	Parameter scan
Study	Haack et al. 2015

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SD4 Data

Type	Label
Description	Simulation results of SE4 (validation successful)
Reference	Figure 3C
Related to	SE4
Study	Haack et al. 2015

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WD3 Data

Type	Label
Description	“Impact of raft disruption on temporal regulation of nuclear β-catenin concentration after induction of differentiation in ReNCell” together with Lipid Raft disruption via MbCD
Reference	Figure 1 C, D
Type of experiment	In vitro
Organism	Human
Cell line	Neural progenitor cells (ReNcell VM197)
Study	Haack et al. 2015

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VSM2 Validating simulation model

Type	Label
Description	Comparison of wet-lab and simulated data of treated cells (with MbCD)
Study	Haack et al. 2015

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SE5 Experiment

Type	Label
Description	“Considering the input parameter values that are required to reproduce our experimental data, it appears that only a model parametrized with an initial amount of WNT molecules (nWNT = 90) and a constant WNT synthesis rate (kWsyn = 1.9) after a certain delay of 90 minutes yields the desired simulation result”
Reference	Not available
Category	Time course analysis
Study	Haack et al. 2015

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SD5 Data

Type	Label
Description	Simulation results of SE5 (validation successful)
Reference	Figure 4A
Related to	SE5
Study	Haack et al. 2015

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SE6 Experiment

Type	Label
Description	“in our model the MbCD treatment translates to a complete removal of lipid rafts, which in turn prevents the raft-dependent LRP6 phosphorylation by CK1γ in response to a WNT stimulus”
Reference	Not available
Category	Perturbation
Study	Haack et al. 2015

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SD6 Data

Type	Label
Description	Simulation results of SE6 (validation unsuccessful)
Reference	Figure 4B
Related to	SE6
Study	Haack et al. 2015

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BSM2 Building simulation model

Type	Label
Description	Model extension with redox-dependent/β-catenin pathway
Study	Haack et al. 2015

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QM2 Qualitative model

Type	Label
Description	QM1 + Redox Model
Reference	Figure 5
Variables / Species	LRP5/6, Wnt, CK1γ, Axin, β-catenin, Dvl, Nrx, ROS
Compartments	Cytosol, nucleus, membrane, lipid rafts
Study	Haack et al. 2015

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A6 Assumption

Type	Label
Description	“hypothesis of wnt-independent signaling stabilizing and translocating β-catenin into the nucleus”
Category	Transport (655)
Study	Haack et al. 2015

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SM3 Simulation model

Type	Label
Description	uncalibrated model code of QM2
Reference	Not available
Study	Haack et al. 2015

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CSM2 Calibrating simulation model

Type	Label
Description	Model calibration
Study	Haack et al. 2015

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SE7 Experiment

Type	Label
Description	Model calibration “simulation result of the extended WNT/ROS-β-catenin model in untreated control”
Reference	Not available
Category	Optimization
Study	Haack et al. 2015

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SD7 Data

Type	Label
Description	Simulation results of SE7
Reference	Figure 6 A, C
Related to	SE7
Study	Haack et al. 2015

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SM4 Simulation model

Type	Label
Description	calibrated model code of QM2
Reference	https://doi.org/10.1371/journal.pcbi.1004106.s009
Study	Haack et al. 2015

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VSM3 Analyzing simulation model

Type	Label
Description	Face validation: Comparison of wet-lab and simulated data
Study	Haack et al. 2015

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SE8 Experiment

Type	Label
Description	“simulation result of the extended WNT/ROS-β-catenin model in raft deficient cells”
Reference	Not available
Category	Time course analysis
Study	Haack et al. 2015

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SD8 Data

Type	Label
Description	Simulation results of SE8 (validation successful)
Reference	Figure 6 B, D
Related to	SE8
Study	Haack et al. 2015

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WD4 Data

Type	Label
Description	“test whether the proposed ROS signaling mechanism is independent of the MbCD treatment, we analyzed the mitochondrial ROS (mito-ROS) production in control and raft deficient ReNcell VM197 cells during proliferation and during the early hours of differentiation”
Reference	Figure 7
Category	In vitro
Organism	Human
Cell line	Neural progenitor cells (ReNcell VM197)
Study	Haack et al. 2015

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