S2_Table: Differential equations and species initial conditions

Species	Differential Equations ($\frac{d[Species]}{dt}$)	Species Initial Condition (μM)
	Oxygen Sensing Module	
HIF1α	v1-v2-v3-v7	0.173
HIF1α-FIH complex	v3-v12	0.0183
HIF1α-PHD complex	v7-v13	0.0131
FIH-O_2-Fe-DG	v4+v12-v3	1.09
O_2	-v4-v8	Nx(21% O_2):209, Hx (2% O_2):19.9
FIH-DG-Fe	v5-v4	0.257
DG	-v5-v9	999
FIH-Fe	v6-v5	8.28e-3
Fe	-v6-v10	49.6
FIH	-v6	4.17e-4
$CoCl_2$	Constant	0
HIF1α/OH	v11+v12-v13	5.39e-4
VHL	v14-v13	1.22
HIF1α/OH-VHL	v13-v14	0.0120
PHD2-O_2-Fe-DG	v12+v8-v7	0.788
PHD2-Fe-DG	v9-v8	0.947
PHD2-Fe	v10-v9	0.0568
PHD2	-v10	2.29e-3
$HIF1\alpha_N$	v2-v15	0.0480
$HIF1\beta_N$	-v15	0.883
TTP	v17-v16	0.0509
	HIF-dependent Transcription Module	
mTTP	v19-v18	9.35e-4
HIF1-$dimer_N$	v15	8.48e-3
mVEGFA	v20-v24-v31+v34	4.49e-6
VEGFA	v22-v23	2.09e-3
Pri-let-7_N	v21-v36	6.16e-5
	VEGF Repression by MiR-15a Module	
Pri-miR-$15a_N$	v25-v26	3.40e-3
Pre-miR-15a	v26-v27-v28	3.33e-3
Dicer	v53-v54	1.04
miR-15a	v28-v29-v30	0.0171
AGO1	v41-v55-v42-v30	0.581
miR-15a RISC	v30-v31+v32	3.97e-3
miR-15a RISC-mVEGFA	v31-v32	1.06e-7
mVEGFA/p-body	v32-v33-v34	1.25e-4
	Let-7 Biogenesis and Targeting Module	
Pre-let-7	v36-v35-v37	1.11e-5
Let-7	v37-v38-v42	4.79e-4
Let-7 RISC	v42-v49-v43+v44+v50	3.98e-3
mAGO1/p-body	v44-v45-v46	0.0192

Species	Differential Equations ($\frac{d[Species]}{dt}$)	Species Initial Condition (μM)
mAGO1	v40-v39-v43+v46	9.52e-4
Let-7 RISC-mAGO1	v43-v44	6.74e-5
mDicer	v47-v48-v49+v52	2.91e-3
Let-7 RISC-mDicer	v49-v50	4.22e-5
mDicer/p-body	v50-v51-v52	0.0376
LNA, miR RISC	-v56	0
miR RISC-LNA	v56	0
siRNA, mRNA	-v57	0
mRNA-siRNA	v57	0

S2_Table. Model differential equations and species initial conditions. Initial conditions here also refer to the steady-state (normoxia) concentration of each species. The different O_2 initial condition in the simulation corresponds to different O_2 abundance. PHD2, FIH, Fe, O_2, DG, HIF1α initial conditions are estimated based on the measurements made by Tuckerman et al [1]. $CoCl_2$ initial condition is changed to 200 μM to mimic hypoxia in a normoxic O_2 environment, and in all other simulations the level of $CoCl_2$ is zero [2]. To maintain a moderate complexity, the model assumes that transcription factors or enzymes in Hill-type (Michaelis-Menten) reactions are unconsumed, and mRNAs are unconsumed in translation.

References

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2. Liu Q, Xu Z, Mao S, Chen W, Zeng R, Zhou S, et al. Effect of hypoxia on hypoxia inducible factor-1alpha, insulin-like growth factor I and vascular endothelial growth factor expression in hepatocellular carcinoma HepG2 cells. Oncology letters. 2015;9(3):1142-8. doi: 10.3892/ol.2015.2879. PubMed PMID: 25663870; PubMed Central PMCID: PMC4315007.