Supplementary Materials: Derivation of a Dynamic Model for Palmitate-induced NFκB Signaling Pathway through Systems Biology Approach

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TABLE I: Nominal parameter values of the AMPK-SIRT1 model

Parameter	value	Parameter	value
k_{gn}	15.5 s^{-1}	k_{gne}	6.22×10^3 s^{-1}
K_{gne}	4.50×10^3	k_{bo}	0.0021 s^{-1}
K_{bo}	195.6	k_{c1}	0.047 s^{-1}
k_{c2}	0.18 s^{-1}	v_{dad}	2.8 s^{-1}
K_{dnad}	3.3×10^5	k_{dn}	5.66×10^{-5} s^{-1}
k_{tran}	$3.4 \times 10^{-6} \mu M^{-1} s^{-1}$	k_{dc}	0.0298 s^{-1}
K_{dc}	73.4	k_{ps}	5.73×10^{-6} s^{-1}
k_{sc}	5.5106−5 s^{-1}	k_{cs}	0.0501 s^{-1}
k_{aa}	6.55×10^{-4} s^{-1}	K_{1max}	0.036
K_1	1.0310^3	k_{a2c}	22.6 s^{-1}
K_M	9.3×10^6 s^{-1}	k_p	0.0083s^{-1}
k_{spmax}	0.124 s^{-1}	K_{sp}	0.015
k_{syn}	0.013 s^{-1}	k_{synmax}	8.18 s^{-1}
K_2	7.24	k_{d1}	4.77 ×10^{-5} s^{-1}
k_{da}	0.066 s^{-1}	k_{damax}	6.41 s^{-1}
K_{da}	3.91×10^{-4}	PP2A	1.3×10^7

TABLE II: Model Equations for the AMPK-SIRT1 regulation model

$$\frac{d\,NAD^+}{dt} = k_{gn} + k_{gne}\frac{pAMPK}{pAMPK+K_{gne}} - 7k_{bo}\cdot pAMPK\frac{Pal}{Pal+K_{bo}} - k_{c1}\cdot NAD^+ + k_{c2}\cdot NADH - NAD^+\frac{v_{dnad}}{NAD^+ + K_{dnad}} - k_{dn}\cdot NAD^+$$

$$\frac{d\,NADH}{dt} = 7k_{bo}\cdot pAMPK\frac{Pal}{Pal+K_{bo}} + k_{c1}\cdot NAD^+ - k_{c2}\cdot NADH$$

$$\frac{d\,Pal_o}{dt} = -k_{tran}\cdot Pal_o$$

$$\frac{d\,Pal}{dt} = -k_{tran}\cdot Pal_o - k_{bo}\cdot pAMPK\frac{pAMPK}{pAMPK+K_{bo}} - k_{dc}\cdot\frac{Pal}{Pal+K_{dc}} + k_{ps}$$

$$\frac{d\,Cer}{dt} = k_{dc}\frac{Pal}{Pal+K_{dc}} - k_{sc}\cdot Cer + k_{cs}$$

$$\frac{d\,pAMPK}{dt} = -(k_{aa} + K_{1max}\frac{Cer}{Cer+K_1})\cdot PP2A\frac{pAMPK}{pAMPK+K_M} - k_{a2c}\cdot PP2C\frac{pAMPK}{pAMPK+K_M} + (k_p + k_{spmax}\frac{SIRT1}{SIRT1+K_{sp}})\cdot(AMPK_t - pAMPK)$$

$$\frac{d\,PP2C}{dt} = k_{syn} + k_{synmax}\frac{TNFRa}{TNFRa+K_2} - k_{d1}\cdot PP2C$$

$$\frac{d\,NF\kappa Ba}{dt} = -a_1\cdot k_v\cdot I\kappa Bn\cdot NF\kappa Ba + k_{ac}\cdot NF\kappa Bn - (k_{da} + k_{damax}\frac{SIRT1}{SIRT1+K_{da}})NF\kappa Ba$$

$$\frac{d\,NF\kappa Bn}{dt} = i_1 NF\kappa B - a_1\cdot k_v\cdot I\kappa Bn - k_{ac}\cdot NF\kappa Bn + (k_{da} + k_{damax}\frac{SIRT1}{SIRT1+K_{da}})NF\kappa Ba$$

$$\frac{d\,NF\kappa Bn - I\kappa Bn}{dt} = a_1\cdot k_v\cdot I\kappa Bn(NF\kappa Bn + NF\kappa Ba) - e_{2a} * NF\kappa Bn - I\kappa Ban$$

TABLE III: Model parameters in the AMPK-SIRT1 regulation model

k_{gn}	constitutive NAD^+ generation rate constant	k_{gne}	rate constant of NAD^+ generation due to pAMPK
K_{gne}	Michaelis constant of pAMPK-induced NAD^+ generation	k_{bo}	palmitate oxidation rate constant
K_{bo}	Michaelis constant of palmitate oxidation	k_{c1}	rate constant for conversion from NAD^+ to NADH
k_{c2}	rate constant for conversion from NADH to NAD^+	v_{dad}	maximum degradation rate for NAD^+
K_{dnad}	Michaelis constant for NAD^+ degradation	k_{dn}	nonspecific degradation rate constant
k_{tran}	rate constant of palmitate translocation to cytoplasm	k_{dc}	ceramide generation rate constant from palmitate
K_{dc}	Michaelis constant for ceramide degradation	k_{ps}	constitutive palmitate synthesis rate constant
k_{sc}	ceramide degradation rate constant	k_{cs}	constitutive ceramide synthesis rate constant
k_{aa}	PP2A-induced AMPK dephosphorylation rate constant	K_{1max}	maximum AMPK dephosphorylation rate due to ceramide
K_1	Michaelis constant for Cer-induced AMPK dephosphorylation	k_{a2c}	PP2C-induced AMPK dephosphorylation rate constant
K_M	Michaelis constant for PP2C-induced AMPK dephosphorylation	k_p	constitutive AMPK phosphorylation rate constant
k_{spmax}	SIRT1-induced AMPK phosphorylation rate constant	K_{sp}	Michaelis constant for SIRT1-induced AMPK phosphorylation
k_{syn}	constitutive PP2C synthesis rate constant	k_{synmax}	maximum PP2C synthesis rate enhanced by TNFRa
K_2	Michaelis constant for TNFRa-induced PP2C synthesis	k_{d1}	PP2C degradation rate constant
k_{da}	constitutive NFκB deacetylation rate	k_{damax}	maximum SIRT1-induced NFκB deactylation rate
K_{da}	Michaelis constant for SIRT1-induced NFκB deactylation	PP2A	the number of PP2A molecules