



COSBI



UNIVERSITÀ DEGLI STUDI
DI TRENTO

Dipartimento di Matematica

Modellazione matematica del sistema insulina-glucosio

Federico Reali

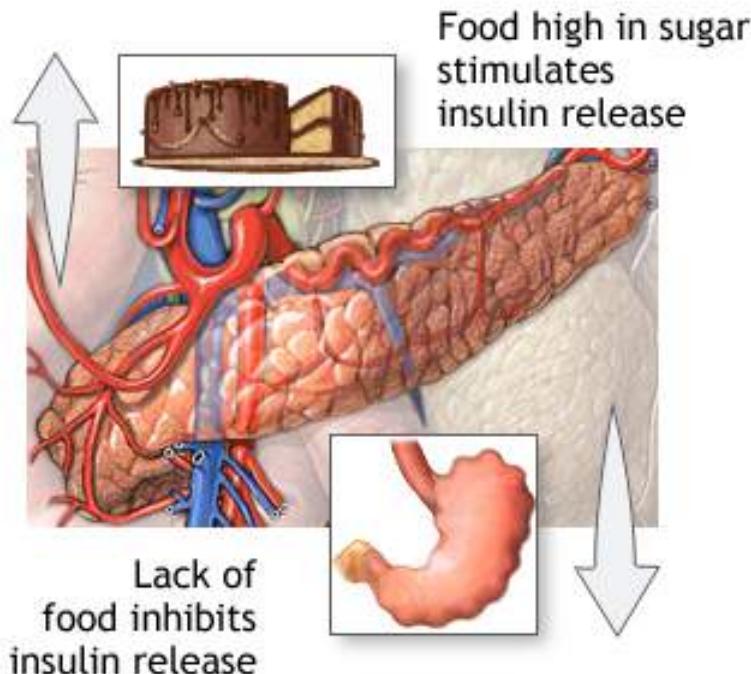
Perugia
Maggio 2017



DIABETES

“Diabetes is a chronic disease in which the body cannot regulate the amount of sugar in the blood”

Medical Encyclopaedia - U.S. National Library of Medicine



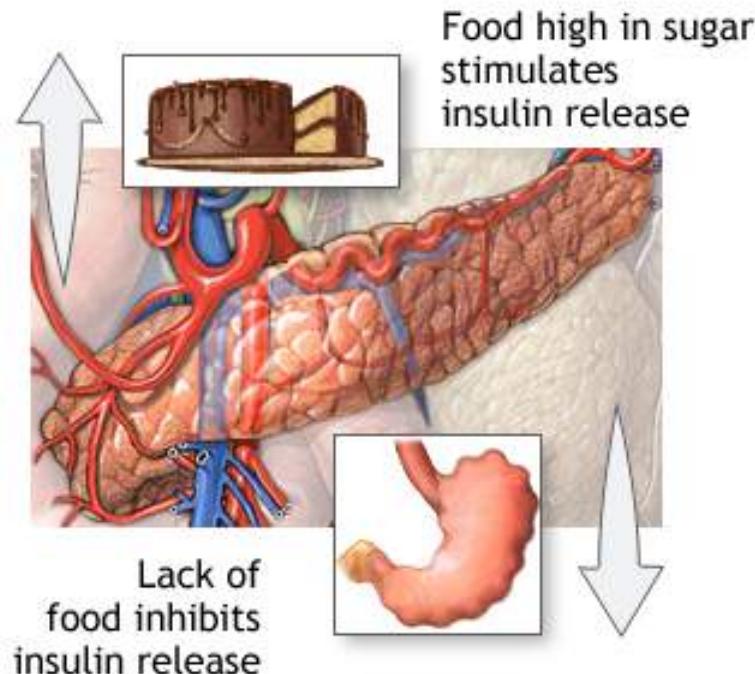
ADAM.

DIABETES

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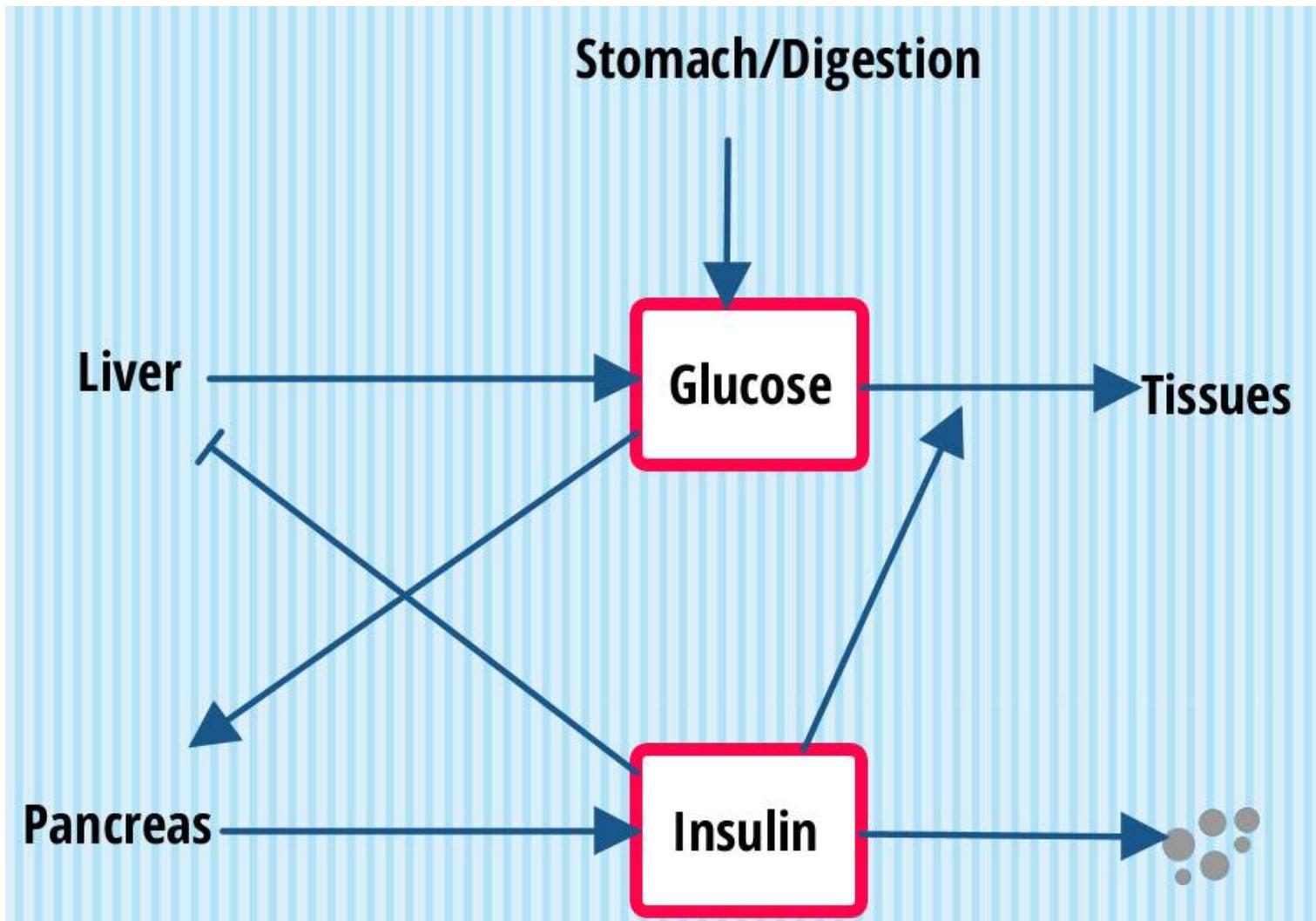
Medical Encyclopaedia - U.S. National Library of Medicine

Diabetes type 1:
the body
produces little or
no insulin.



Diabetes type 2:
tissues do not
respond correctly
to insulin.

INSULIN-GLUCOSE HOMEOSTASIS



INSULIN-GLUCOSE MODEL - T1DM PATIENTS



Corrado Priami



Luca Marchetti



AZIENDA OSPEDALIERA UNIVERSITARIA INTEGRATA
VERONA



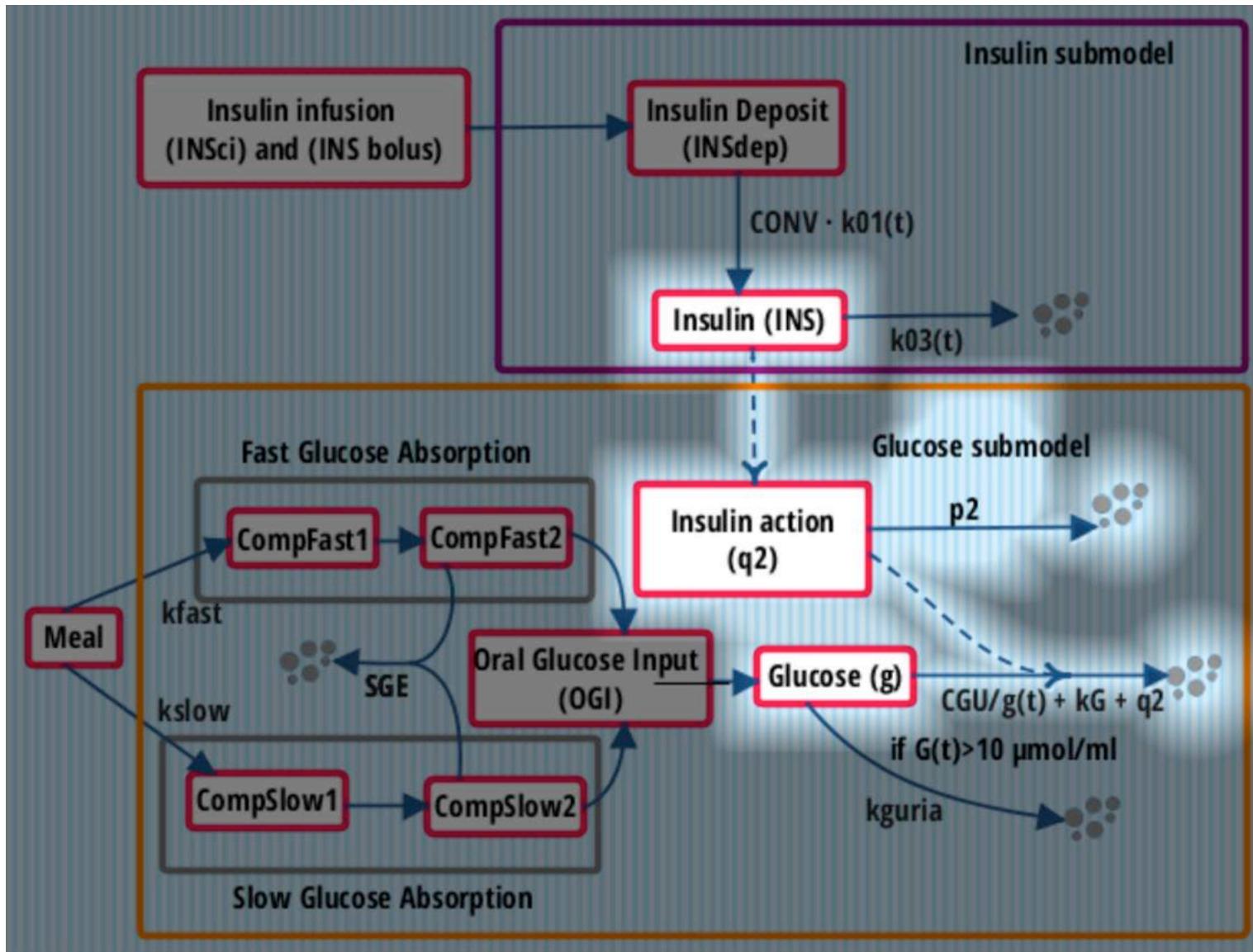
SCIENTIFIC REPORTS

OPEN

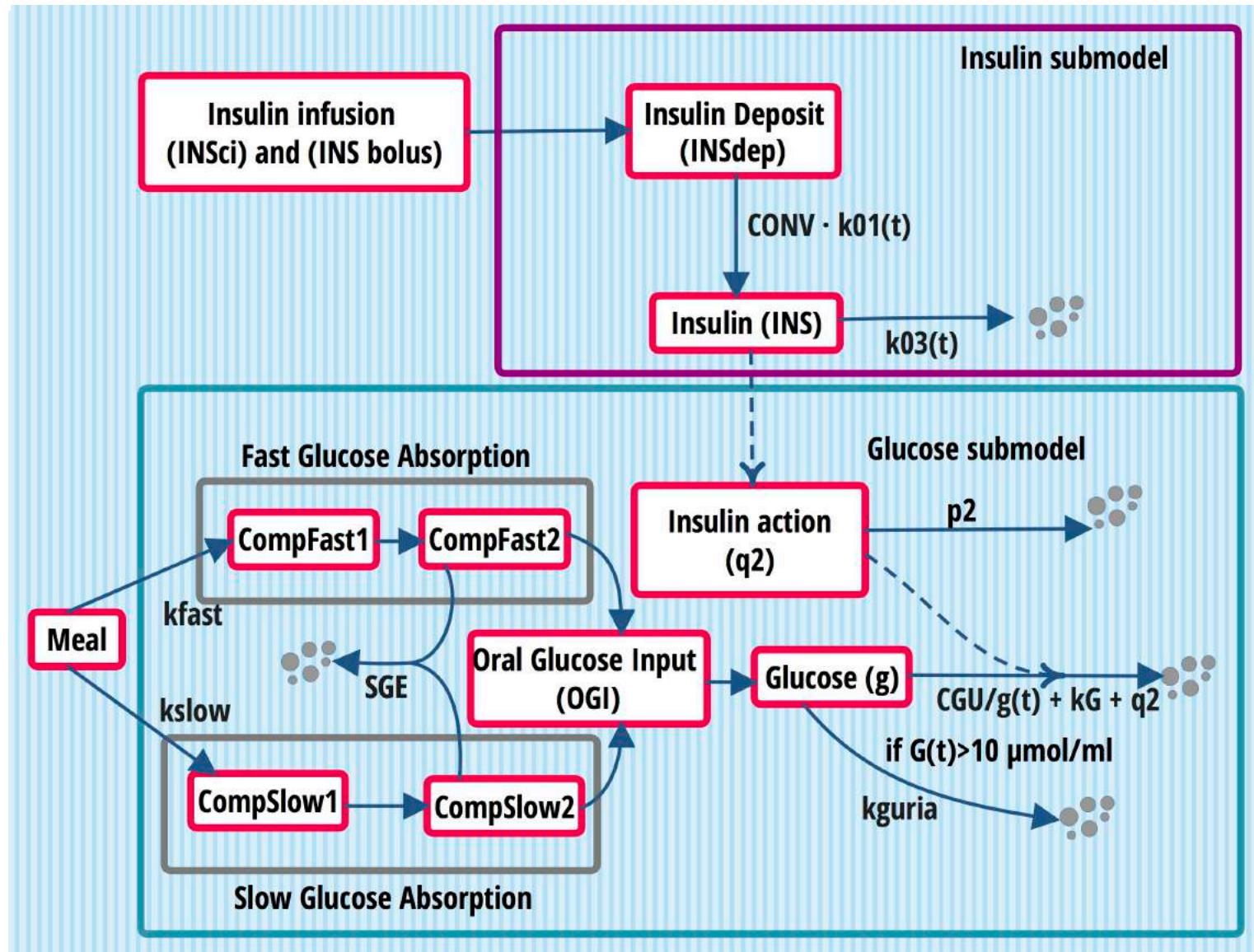
A Novel Insulin/Glucose Model after a Mixed-Meal Test in Patients with Type 1 Diabetes on Insulin Pump Therapy

Luca Marchetti^{1,*}, Federico Reali^{1,2,*}, Marco Dauriz³, Corinna Brangani³, Linda Boselli³, Giulia Ceradini³, Enzo Bonora^{3,4}, Riccardo C. Bonadonna^{5,6} & Corrado Priami^{1,2}

GLUKINSLOOP 2.0 - CLAMP



GLUKINSLOOP 2.0



GLUKINSLOOP 2.0

$$\frac{d}{dt} INS(t) = CONV \cdot INS_{dep}(t) \cdot k_{01}(t) - k_{03}(t) \cdot INS(t)$$
$$\frac{d}{dt} INS_{dep}(t) = \begin{cases} INS_{ci} + INS_{bolus} - INS_{dep}(t) \cdot k_{01}(t), & \text{if } 0 < t \leq \text{Timebolus} \\ INS_{ci} - INS_{dep}(t) \cdot k_{01}(t), & \text{otherwise.} \end{cases}$$

$$\frac{d}{dt} g(t) = \begin{cases} CGU + S_G \cdot G_{ss} - k(0, G) \cdot g(t), & \text{if } CGU + S_G \cdot G_{ss} - (1 - SGE) \cdot OGI(t) \geq 0 \\ (1 - SGE) \cdot OGI(t) - k(0, G) \cdot g(t), & \text{otherwise.} \end{cases}$$

$$\frac{d}{dt} q2(t) = [INS(t) - INS_{Action}^{Threshold}]^+ \cdot p_2 \cdot S_I/V_G - p_2 \cdot q2(t)$$

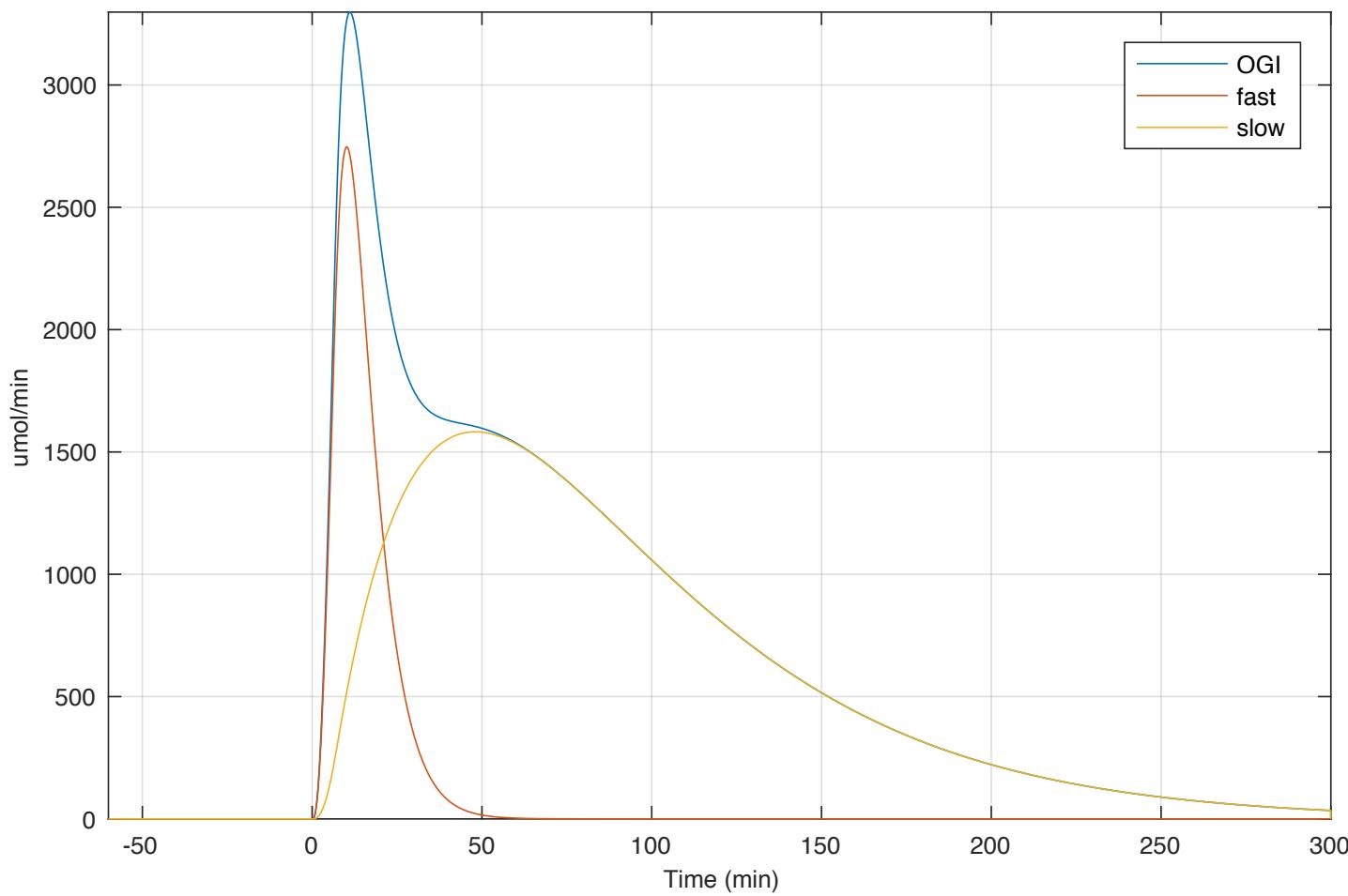
Where:

$$k_{01}(t) = \frac{1}{SCAR \cdot \sqrt[3]{\frac{3}{4\pi}} \cdot INS_{dep}(t)}$$

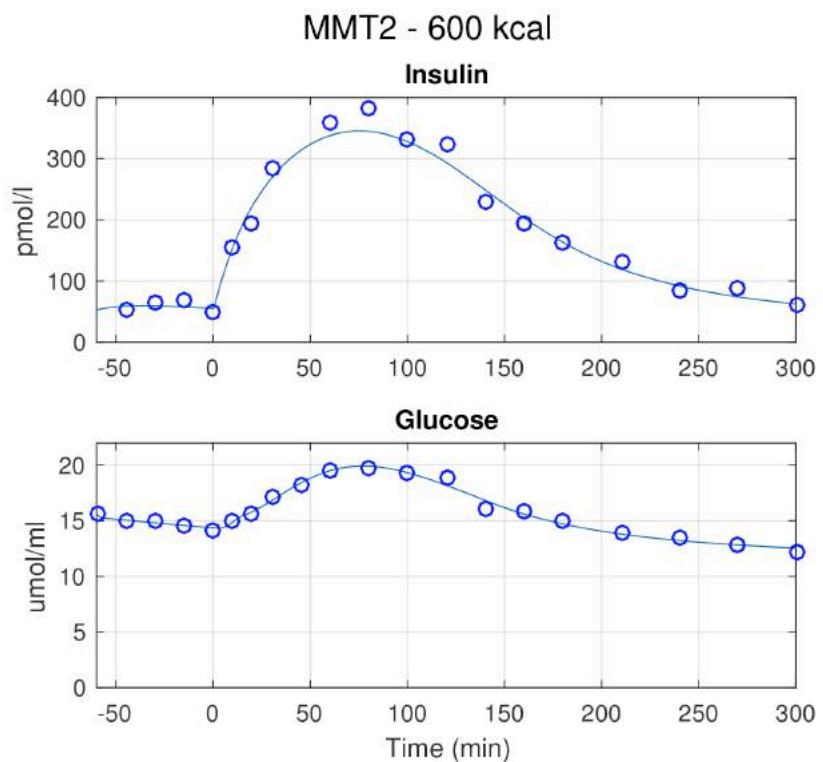
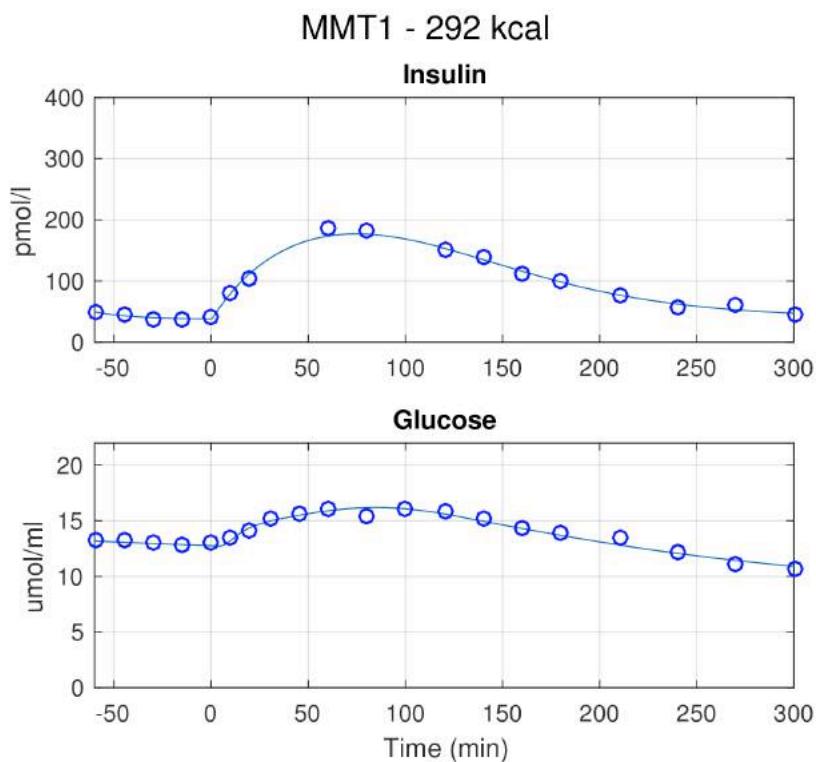
$$k_{03}(t) = INSCAT + INSCAT2 \cdot [1 - \tanh(FEPER \cdot INS(t))]$$

$$k(0, G) = \begin{cases} [CGU/g(t)] + k_G + q2(t), & \text{if } G(t) < 10 \text{ mmol} \cdot l^{-1} \\ [CGU/g(t)] + k_G + kguria(t) + q2(t), & \text{otherwise.} \end{cases}$$

GLUKINSLOOP 2.0



GLUKINSLOOP 2.0



GLUKINSLOOP 2.0

	S_I (ml/min)/(pmol/l)	S_G (ml/min)	Glucose MTT (min)	Insulin MTT (min)
MMT1	0.78±0.31	20.8±18.4	117±35	112±36
MMT2	0.76±0.38	24.2±14.7	109±35	131±66

Model estimates (mean ± SD) of the key physiological parameters.

SPHINGOLIPIDS AND INSULIN RESISTANCE



Corrado Priami



Ozan
Kahramanogullari



Melissa Morine



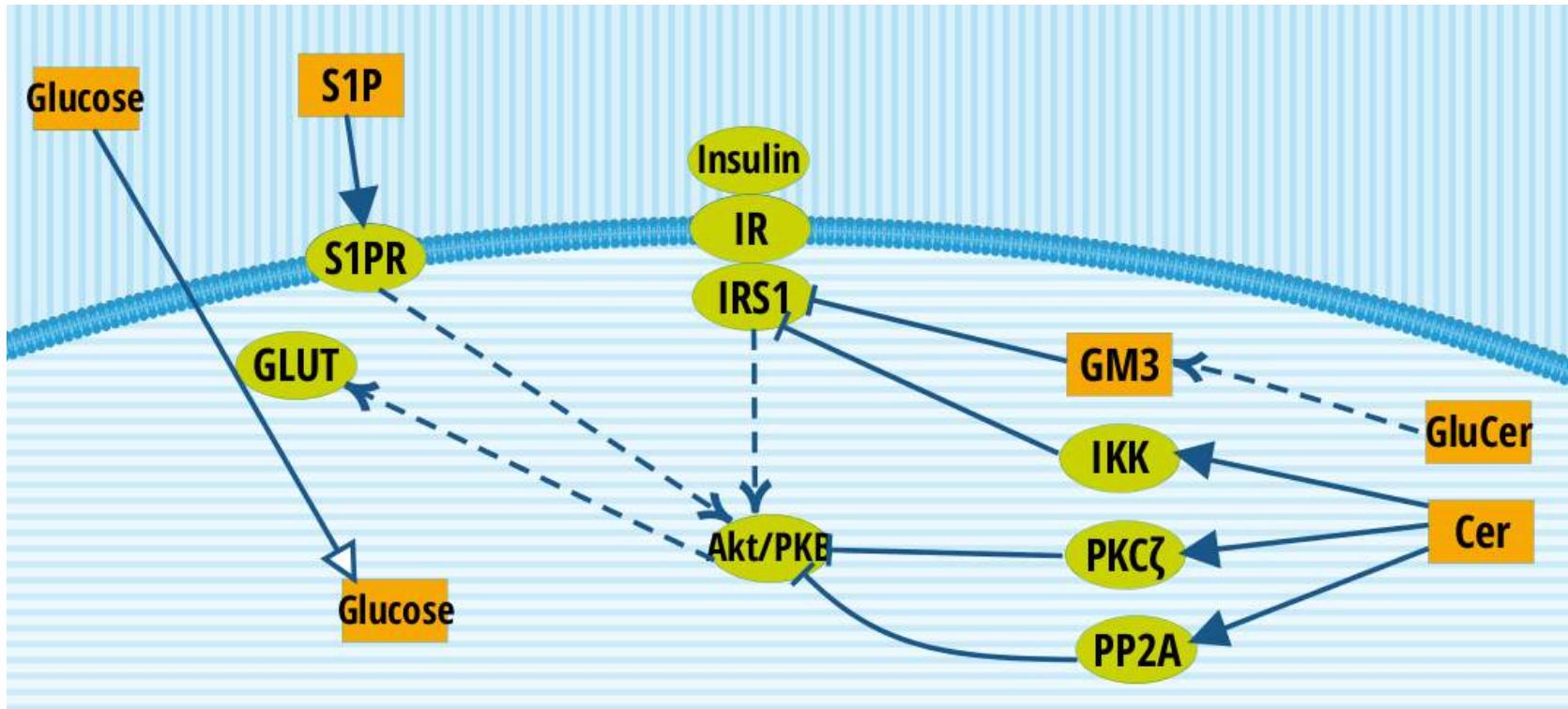
SCIENTIFIC REPORTS

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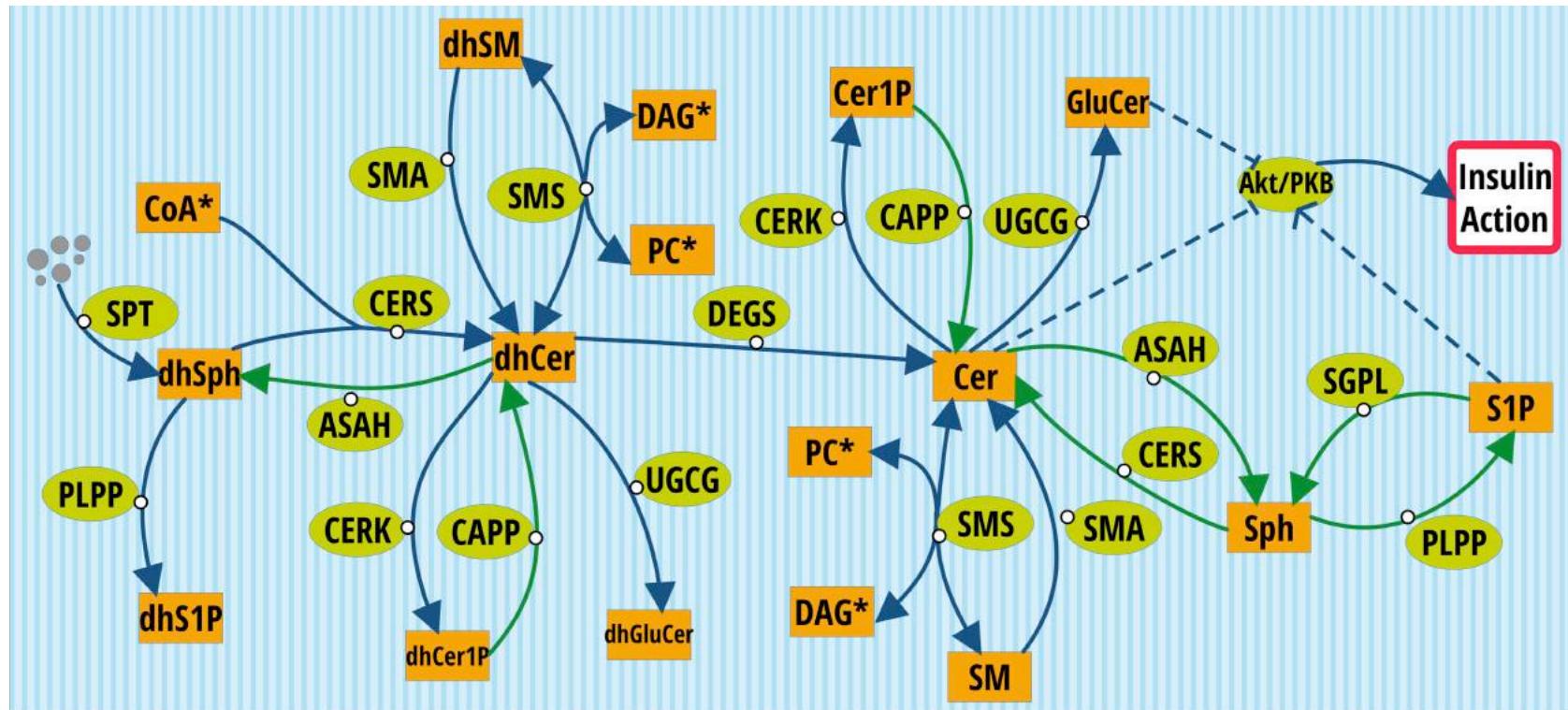
Mechanistic interplay between ceramide and insulin resistance

Federico Reali^{1,2,*}, Melissa J. Morine^{1,*}, Ozan Kahramanoğulları^{1,2,*}, Suryaprakash Raichur³, Hans-Christoph Schneider⁴, Daniel Crowther⁴ & Corrado Priami^{1,2}

CERAMIDE AND INSULIN RESISTANCE

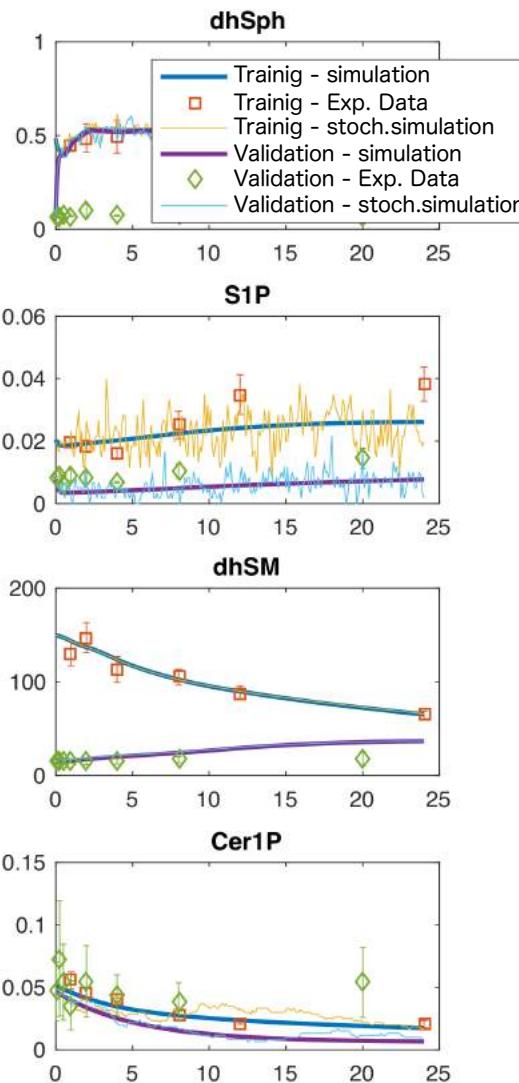
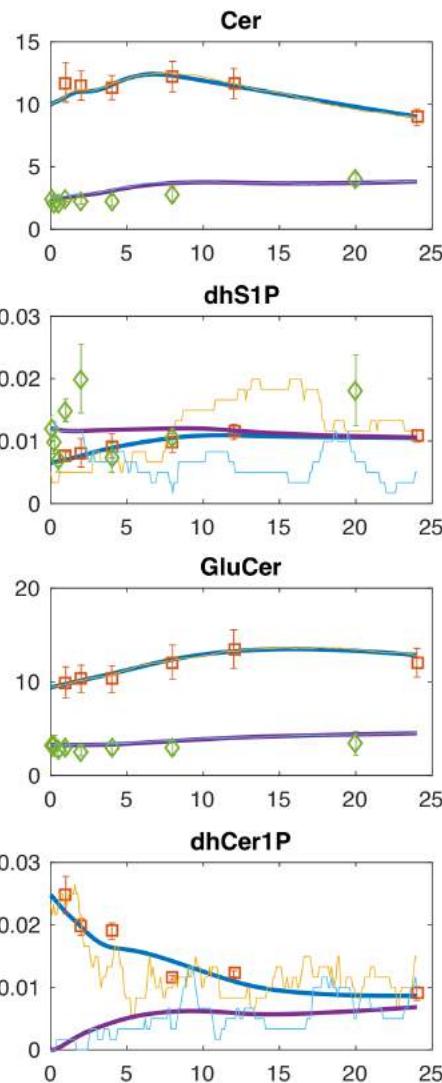
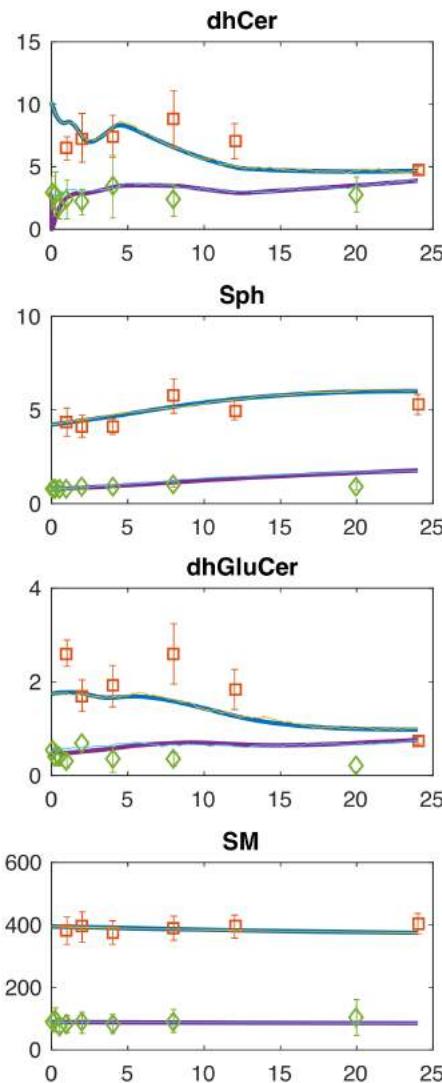


SPHINGOLIPID MODEL



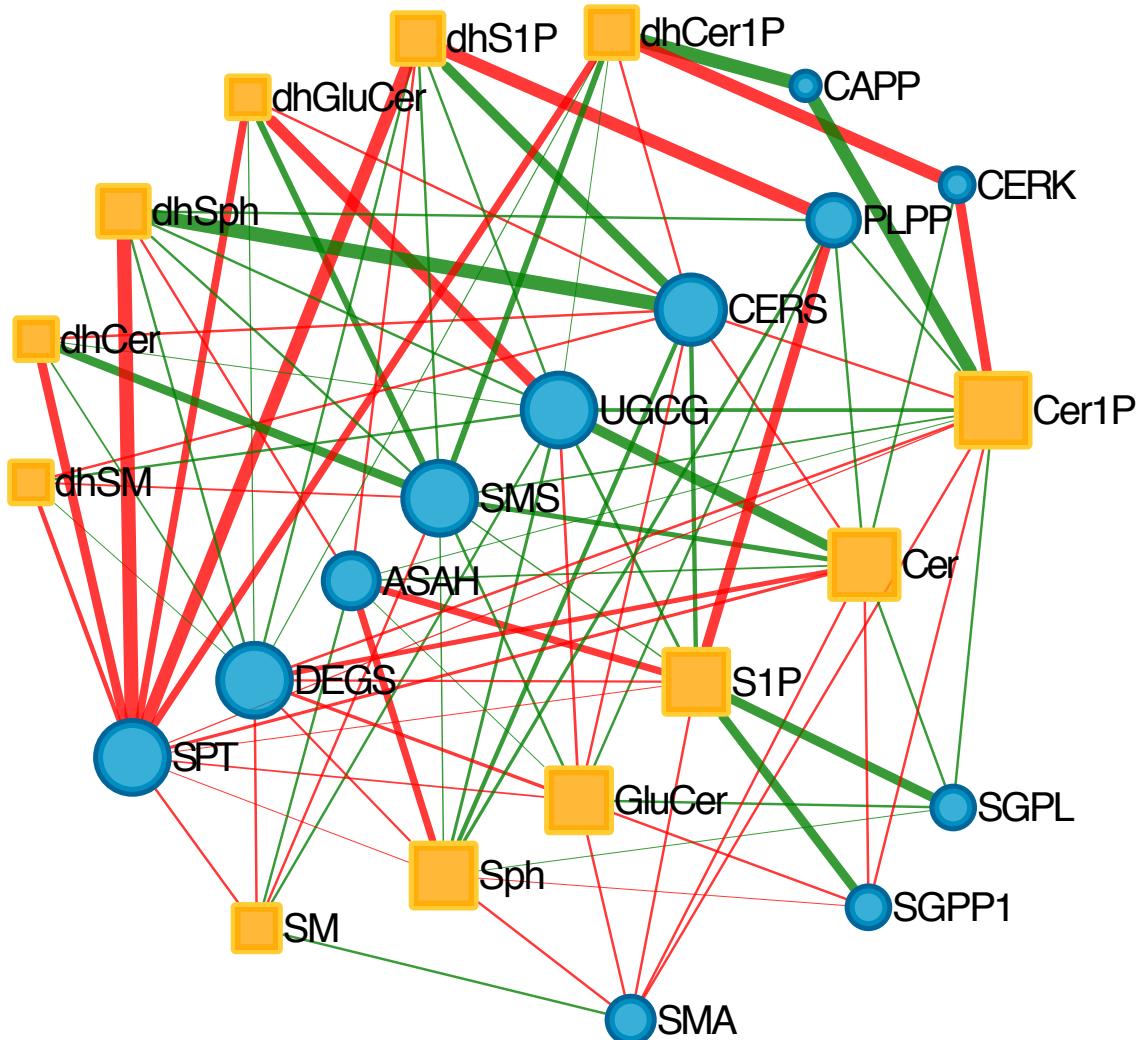
SPHINGOLIPID MODEL

Concentrations (pmol/ μ g DNA)



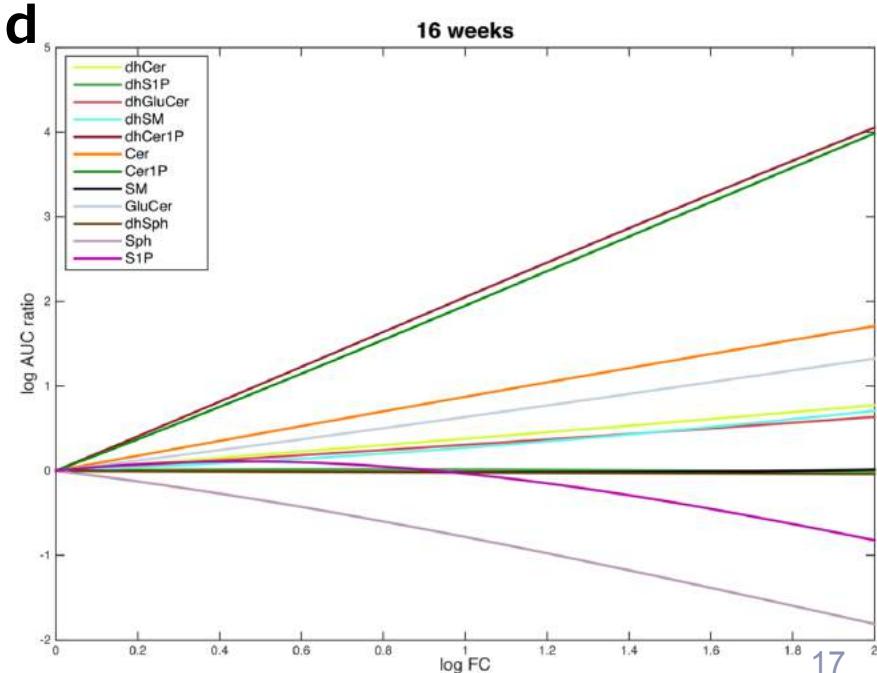
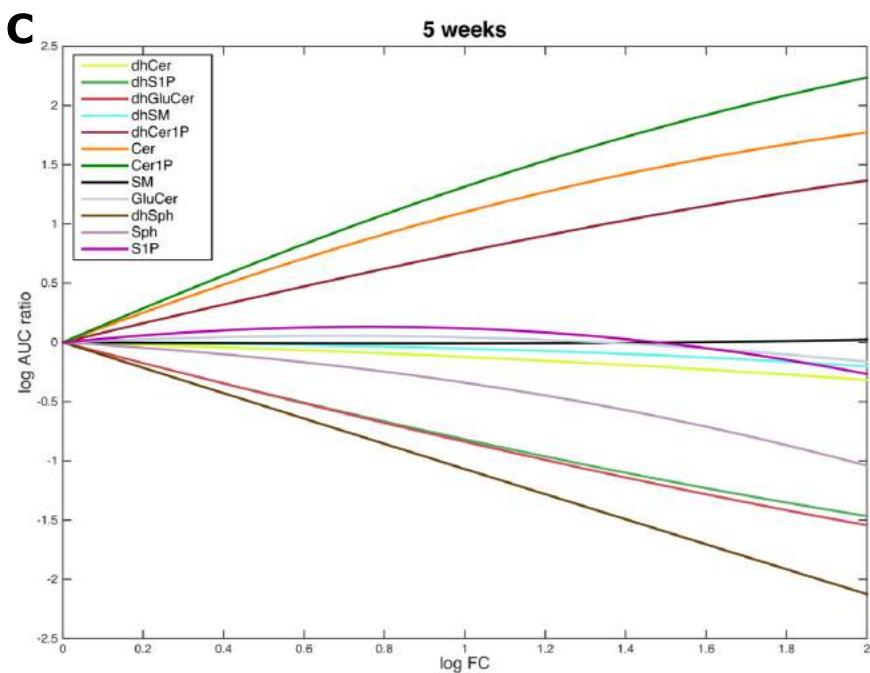
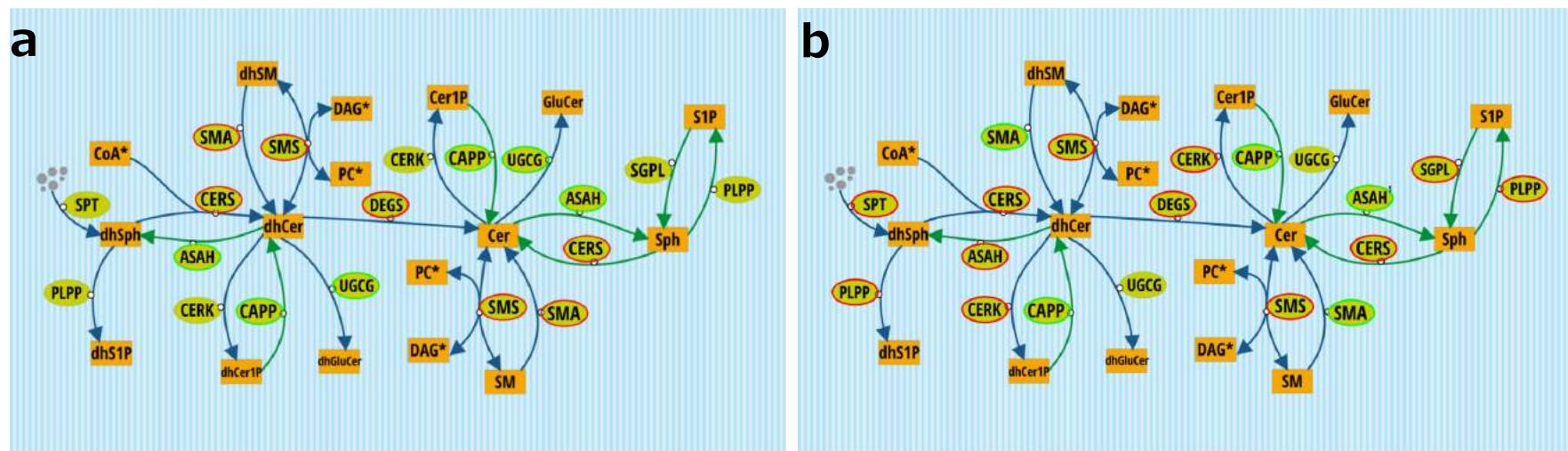
Time (hr)

SPHINGOLIPID MODEL – SENSITIVITY ANALYSIS

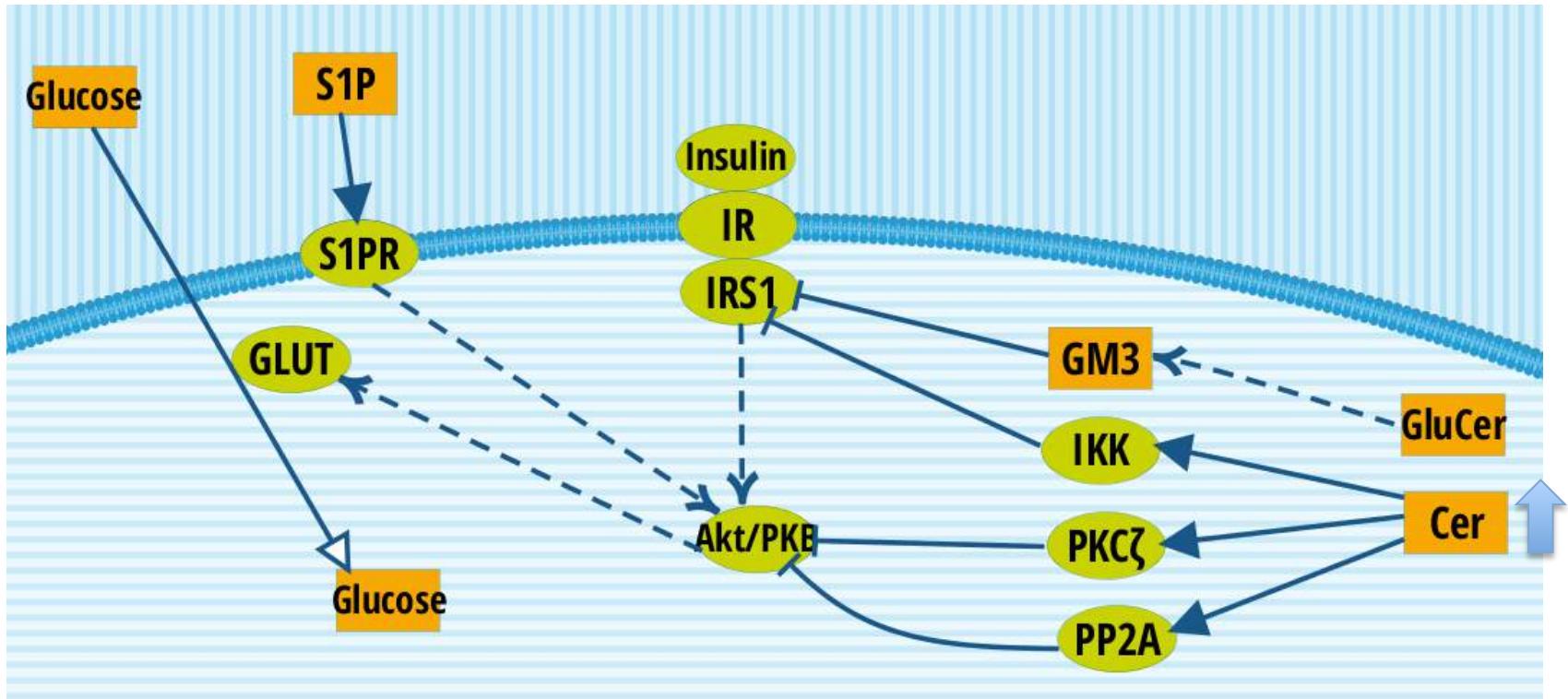


- Orange rectangles: sphingolipids
- blue circles: enzymes;
- edges are colored in red if as the enzyme increases, the concentration of the sphingolipid increases as well;
- in green if the concentration decreases;
- the thickness of the edges is proportional to the effect.

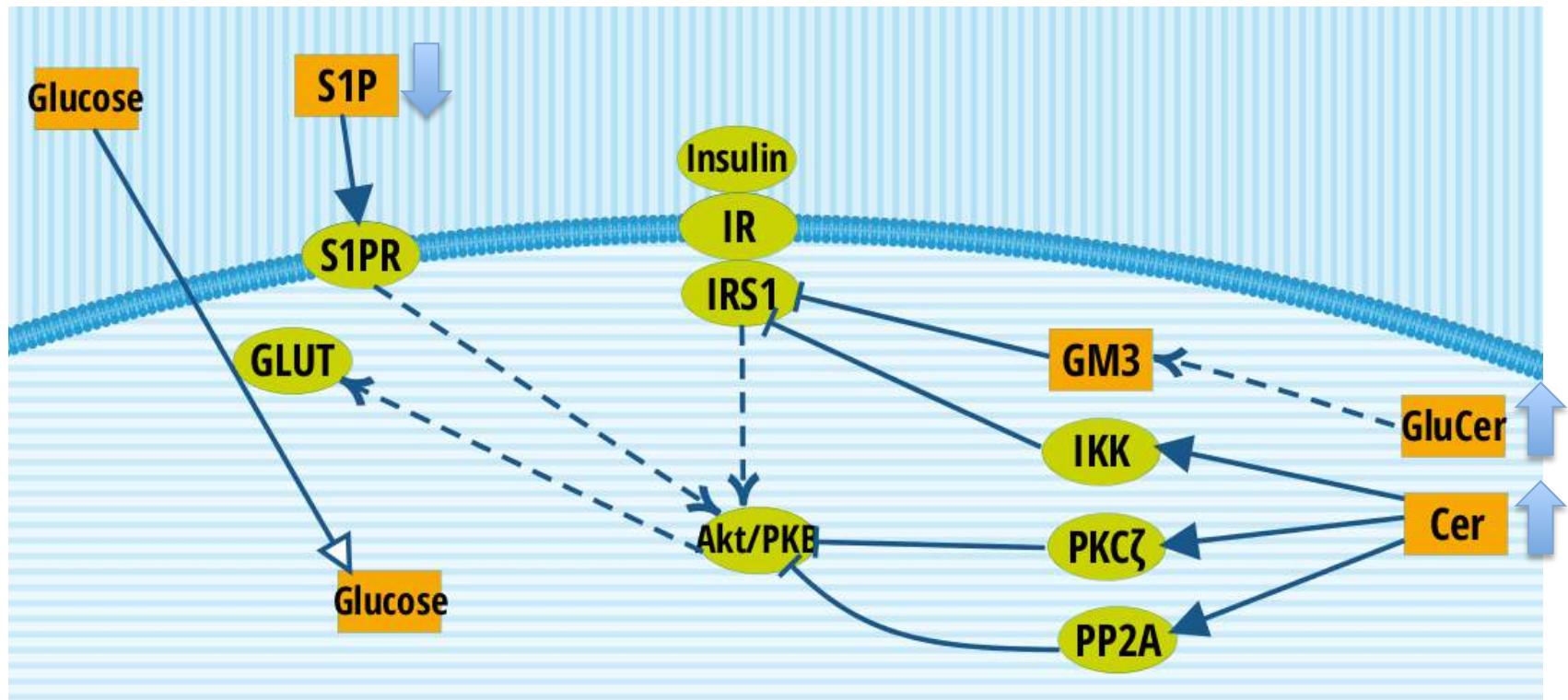
SPHINGOLIPID MODEL – TESTING HYPOTHESIS



SPHINGOLIPID MODEL – 5 WEEKS



SPHINGOLIPID MODEL – 16 WEEKS





Thanks
