SBML Model Report

Model name: "Tham2008 - PDmodel, Tumour shrinkage by gemcitabine and carboplatin"

May 5, 2016

1 General Overview

This is a document in SBML Level 2 Version 4 format. This model was created by the following three authors: Vijayalakshmi Chelliah[1], Lai-San Tham[2] and Geoffrey Nunns[3] at November 16th 2009 at 12:37 a. m. and last time modified at March 17th 2015 at 11:24 a. m. Table 1 gives an overview of the quantities of all components of this model.

Table 1: Number of components in this model, which are described in the following sections.

Element	Quantity	Element	Quantity
compartment types	0	compartments	1
species types	0	species	1
events	0	constraints	0
reactions	0	function definitions	0
global parameters	18	unit definitions	9
rules	8	initial assignments	0

Model Notes

Tham2008 - PDmodel, Tumour shrinkage by gemcitabine and carboplatin

This model is described in the article:A pharmacodynamic model for the time course of tumor shrinkage by gemcitabine + carboplatin in non-small cell lung cancer patients.Tham LS, Wang

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L, Soo RA, Lee SC, Lee HS, Yong WP, Goh BC, Holford NH.Clin. Cancer Res. 2008 Jul; 14(13): 4213-4218

Abstract:

PURPOSE: This tumor response pharmacodynamic model aims to describe primary lesion shrinkage in non-small cell lung cancer over time and determine if concentration-based exposure metrics for gemcitabine or that of its metabolites, 2',2'-difluorodeoxyuridine or gemcitabine triphosphate, are better than gemcitabine dose for prediction of individual response. EXPERIMENTAL DESIGN: Gemcitabine was given thrice weekly on days 1 and 8 in combination with carboplatin, which was given only on day 1 of every cycle. Gemcitabine amount in the body and area under the concentration-time curves of plasma gemcitabine, 2',2'-difluorodeoxyuridine, and intracellular gemcitabine triphosphate in white cells were compared to determine which best describes tumor shrinkage over time. Tumor growth kinetics were described using a Gompertz-like model. RESULTS: The apparent half-life for the effect of gemcitabine was 7.67 weeks. The tumor turnover time constant was 21.8 week.cm. Baseline tumor size and gemcitabine amount in the body to attain 50% of tumor shrinkage were estimated to be 6.66 cm and 10,600 mg. There was no evidence of relapse during treatment. CONCLUSIONS: Concentration-based exposure metrics for gemcitabine and its metabolites were no better than gemcitabine amount in predicting tumor shrinkage in primary lung cancer lesions. Gemcitabine dose-based models did marginally better than treatment-based models that ignored doses of drug administered to patients. Modeling tumor shrinkage in primary lesions can be used to quantify individual sensitivity and response to antitumor effects of anticancer drugs.

2 Unit Definitions

This is an overview of 14 unit definitions of which five are predefined by SBML and not mentioned in the model.

2.1 Unit `effect_unit`

Name normalised

Definition dimensionless

2.2 Unit `week`

Name week

Definition 604800 s

2.3 Unit sec_per_week

Name sec_per_week

Definition $\mathrm{s} \cdot (604800\ \mathrm{s})^{-1}$

2.4 Unit cm

Name cm

Definition cm

2.5 Unit mg

Name mg

Definition mg

2.6 Unit cm_week

Name cm_week

Definition $\mathrm{cm} \cdot 604800\ \mathrm{s}$

2.7 Unit per_week

Name per_week

Definition $(604800\ \mathrm{s})^{-1}$

2.8 Unit per_cm_per_week

Name per_cm_per_week

Definition $\mathrm{cm}^{-1} \cdot (604800\ \mathrm{s})^{-1}$

2.9 Unit m2

Name m2

Definition m^2

2.10 Unit substance

Notes Mole is the predefined SBML unit for `substance`.

Definition mol

2.11 Unit volume

Notes Litre is the predefined SBML unit for volume.

Definition l

2.12 Unit area

Notes Square metre is the predefined SBML unit for area since SBML Level 2 Version 1.

Definition m^2

2.13 Unit length

Notes Metre is the predefined SBML unit for length since SBML Level 2 Version 1.

Definition m

2.14 Unit time

Notes Second is the predefined SBML unit for time.

Definition s

3 Compartment

This model contains one compartment.

Table 2: Properties of all compartments.

Id	Name	SBO	Spatial Dimensions	Size	Unit	Constant	Outside
COMpartment			3	1	litre	☑	

3.1 Compartment COMpartment

This is a three dimensional compartment with a constant size of one litre.

4 Species

This model contains one species. Section 7 provides further details and the derived rates of change of each species.

Table 3: Properties of each species.

Id	Name	Compartment	Derived Unit	Constant	Boundary Condition
`Ce`	Ce	`COMpartment`	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟

5 Parameters

This model contains 18 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
rem_time	rem_time		0.000	604800 s	☐
Exposure	Exposure		0.000	mg	☐
Size	Size		6.660	cm	☐
Effect	Effect		0.000	dimensionless	☐
Dose	Dose		5203.840	mg	☑
Dose_Int1	Dose_Int1		0.000	604800 s	☑
Dose_Int2	Dose_Int2		1.000	604800 s	☑
Dose_Length	Dose_Length		0.444	604800 s	☑
Cycle_Int	Cycle_Int		3.000	604800 s	☑
N_Cycle	N_Cycle		6.000	dimensionless	☑
conversion_factor	conversion_factor		604800.000	$\mathrm{s} \cdot (604800\ \mathrm{s})^{-1}$	☑
AE50	AE50		10600.000	mg	☑
Keq	Keq		0.000	$(604800\ \mathrm{s})^{-1}$	☐
Teq	Teq		7.670	604800 s	☑
Size_0	Size_0		6.660	cm	☑
RateIn	RateIn		0.000	$(604800\ \mathrm{s})^{-1}$	☐
T_Turnover	T_Turnover		21.800	$\mathrm{cm} \cdot 604800\ \mathrm{s}$	☑
Kover	Kover		0.000	$\mathrm{cm}^{-1} \cdot (604800\ \mathrm{s})^{-1}$	☐

6 Rules

This is an overview of eight rules.

6.1 Rule Ce

Rule Ce is a rate rule for species Ce:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Ce} = \frac{\mathrm{Exposure}}{1} - [\mathrm{Ce}] \cdot \mathrm{Keq} \tag{1}$$

6.2 Rule Size

Rule Size is a rate rule for parameter Size:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Size} = (\mathrm{RateIn} \cdot \mathrm{Effect} - \mathrm{Kover} \cdot \mathrm{Size}) \cdot \mathrm{Size} \tag{2}$$

Derived unit $(604800\ \mathrm{s})^{-1} \cdot \mathrm{cm}$

6.3 Rule `Exposure`

Rule `Exposure` is an assignment rule for parameter `Exposure`:

$$\begin{aligned}&\mathrm{Exposure}\\ &= \begin{cases} \mathrm{Dose} & \text{if } (\mathrm{time} < \mathrm{Cycle\_Int} \cdot \mathrm{N\_Cycle}) \wedge (\mathrm{rem\_time} < \mathrm{Dose\_Length}) \\ \mathrm{Dose} & \text{if } (\mathrm{time} < \mathrm{Cycle\_Int} \cdot \mathrm{N\_Cycle}) \wedge (\mathrm{rem\_time} < \mathrm{Dose\_Int2} + \mathrm{Dose\_Length}) \\ 0 & \text{otherwise} \end{cases}\end{aligned} \tag{3}$$

6.4 Rule `rem_time`

Rule `rem_time` is an assignment rule for parameter `rem_time`:

$$\mathrm{rem\_time} = \frac{\mathrm{time} \cdot \mathrm{conversion\_factor} - \left\lfloor \frac{\mathrm{time} \cdot \mathrm{conversion\_factor}}{\mathrm{Cycle\_Int} \cdot \mathrm{conversion\_factor}} \right\rfloor \cdot \mathrm{Cycle\_Int} \cdot \mathrm{conversion\_factor}}{\mathrm{conversion\_factor}} \tag{4}$$

Derived unit s

6.5 Rule `Keq`

Rule `Keq` is an assignment rule for parameter `Keq`:

$$\mathrm{Keq} = \frac{\ln 2}{\mathrm{Teq}} \tag{5}$$

Derived unit $(604800\ \mathrm{s})^{-1}$

6.6 Rule `Effect`

Rule `Effect` is an assignment rule for parameter `Effect`:

$$\mathrm{Effect} = 1 - \frac{[\mathrm{Ce}]}{\mathrm{AE50} + [\mathrm{Ce}]} \tag{6}$$

6.7 Rule `RateIn`

Rule `RateIn` is an assignment rule for parameter `RateIn`:

$$\mathrm{RateIn} = \mathrm{Size\_0} \cdot \mathrm{Kover} \tag{7}$$

Derived unit $(604800\ \mathrm{s})^{-1}$

6.8 Rule Kover

Rule Kover is an assignment rule for parameter Kover:

$$\text{Kover} = \frac{1}{\text{T\_Turnover}} \tag{8}$$

7 Derived Rate Equation

When interpreted as an ordinary differential equation framework, this model implies the following set of equations for the rate of change of the following species.

7.1 Species Ce

Name Ce

SBO:0000247 simple chemical

Initial concentration $0\ \text{mol} \cdot \text{l}^{-1}$

Involved in rule Ce

One rule which determines this species' quantity.

A Glossary of Systems Biology Ontology Terms

SBO:0000247 simple chemical: Simple, non-repetitive chemical entity

SBML2LaTeX was developed by Andreas Dräger[a], Hannes Planatscher[a], Dieudonné M Wouamba[a], Adrian Schröder[a], Michael Hucka[b], Lukas Endler[c], Martin Golebiewski[d] and Andreas Zell[a]. Please see http://www.ra.cs.uni-tuebingen.de/software/SBML2LaTeX for more information.

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