Appendix to *A mathematical model for DC vaccine treatment of type I diabetes.*

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Model Equations

$$\frac{d}{dt}M = J + (k+b)M_a - cM - f_M M B_a - f_M M B_n - e_1 M(M + M_a), \tag{1}$$

$$\frac{d}{dt}M_a = f_M M B_a + f_M M B_n - k M_a - e_2 M_a(M + M_a). \tag{2}$$

$$\frac{d}{dt}B = \alpha_B K_1(G) B - \delta_B B - \eta_e(t) K_2(E,R) B - W(B,t). \tag{3}$$

$$K_1(G, G_{hb}) = \frac{G^2}{G^2 + G_{hb}^2}. \tag{4}$$

$$K_2(E,R) = \frac{(s_E E)^2}{1 + (s_E E)^2 + (s_R R)^2}, \tag{5}$$

$$\eta_e(t) = \eta + 2\eta(1 + \tanh(\alpha_e(t - \beta_e))). \tag{6}$$

$$W(B,t) = .1 w B e^{-\left(\frac{t-9}{9}\right)^2} \tag{7}$$

$$\begin{aligned}\frac{d}{dt}B_a =& \tilde{\delta}_B B + \tilde{\eta}_e(t) K_2(E,R) B + \tilde{W}(B,t) - d B_a - f_M M B_a \\ &- f_{M_a} M_a B_a - f_{tD}(D_{ss} - D) B_a - f_D D B_a\end{aligned} \tag{8}$$

$$\frac{d}{dt}B_n = d B_a - f_M M B_n - f_{M_a} M_a B_n - f_{tD}(D_{ss} - D) B_n - f_D D B_n. \tag{9}$$

$$\frac{d}{dt}G = R_0 - (G_0 + S_I I) G, \tag{10}$$

$$\frac{d}{dt}I = \sigma_I K_1(G, G_I) B - \delta_I I. \tag{11}$$

$$\frac{d}{dt}D = f_{tD} B_n (D_{ss} - D - tD) + f_{tD} B_n tD - b_{DE} E D - \mu_D D \tag{12}$$

$$\frac{d}{dt}tD = f_{tD} B_a (D_{ss} - D - tD) - f_{tD} B_n tD - b_{IR} R tD - \mu_D tD. \tag{13}$$

$$\frac{dE}{dt} = a_E (T_{naive} - E) + b_P \frac{DE}{\theta_D + D} - r_{am} E + b_E D E m - \mu_E E R, \tag{14}$$

$$\frac{dR}{dt} = a_R (T_{naive} - R) + b_P \frac{tDR}{\theta_D + tD} - r_{am} R + b_R tD E m - \mu_R E R, \tag{15}$$

$$\frac{dEm}{dt} = r_{am}(E + R) - (a_{Em} + b_E D + b_R tD) Em. \tag{16}$$

Model Parameters

Parameter name	Balb/c Mice	NOD Mice	Units	Description;Eq. number	Citation
J	5×10^4	5×10^4	cells ml^{-1} day^{-1}	Resting macrophage influx; Eq. (1)	[1]
k	0.4	0.4	day^{-1}	Macrophage deactivation rate; Eq. (1)-(2)	[1]
b	0.09	0.09	day^{-1}	Recruitment rate of macrophages by activated macrophages; Eq. (1)	[1]
c	0.1	0.1	day^{-1}	Macrophage egress rate; Eq. (1)	[1]
e_1	1×10^{-8}	1×10^{-8}	cells^{-1} day^{-1}	Effect of crowding on macrophages; Eq. (1)	[1]
e_2	1×10^{-8}	1×10^{-8}	cells^{-1} day^{-1}	Effect of crowding on active macrophages; Eq. (2)	[1]
f_M	$0.0623 \times 2 \times 10^{-5}$	$0.0623 \times 1 \times 10^{-5}$	ml cells^{-1} day^{-1}	Rate macrophages engulf necrotic and apoptotic β-cells; Eq. (1)-(2) and Eq. (8)-(9)	Modified from [1]
f_{M_a}	$0.0623 \times 5 \times 10^{-5}$	$0.0623 \times 1 \times 10^{-5}$	ml cells^{-1} day^{-1}	Rate activated macrophages engulf necrotic and apoptotic β-cells; Eq. (8)-(9)	Modified from [1]
α_B	0.0334	0.0334	day^{-1}	Rate β-cells are produced from glucose; Eq. (3)	[2]
G_{hb}	90	90	mg dl^{-1}	Glucose level of half-max β-cell production; Eq. (3)-(4)	[2]
δ_B	0.0167	0.0167	day^{-1}	β-cell death rate; Eq. (3) and Eq. (8)	[2]
Q_{panc}	0.194	0.194	ml	Volume of mouse pancreas	[3]
B_{conv}	2.59×10^5	2.59×10^5	cell mg^{-1}	β-cells per milligram	Uses β-cell count from [4]
η	0.02	0.02	day^{-1}	Rate at which T cells eliminate β-cells; Eq. (3) and Eq. (8)	Estimated here
s_E	1	1	ml cells^{-1}	Relative impact of effector T cells on β-cell death; Eq. (5)	Estimated here
s_R	36	36	ml cells^{-1}	Relative impact of regulatory T cells on β-cell death; Eq. (5)	Estimated here
α_e	.11	.11	day^{-1}	Rate of effector T cell avidity for β-cells; Eq. (6)	Estimated from [5]
β_e	21	21	day	Half-max value for T cell killing of β-cells; Eq. (6)	Estimated from [5]
d	0.50	0.50	day^{-1}	β-cell rate of necrosis; Eq. (8)-(9)	[1]
f_D	1.71×10^{-7}	1.71×10^{-7}	ml cells^{-1} day^{-1}	Rate DCs engulf β-cells; Eq. (8)-(9)	Computed, see Sect. 2.5
f_{tD}	1.19×10^{-6}	1.19×10^{-6}	ml cells^{-1} day^{-1}	Rate naive or tolerogenic DCs engulf β-cells; Eq. (8)-(9); Eq. (12-13)	Computed, see Sect. 2.5
D_{ss}	1×10^5	1×10^5	cells ml^{-1}	Steady-state DC population; Eq. (8)-(9), Eq. (12)-(13)	Estimated here
R_0	864	864	mg dl^{-1}	Basal rate of glucose production; Eq. (10)	[6]
G_0	1.44	1.44	day^{-1}	Rate of glucose decay; Eq. (10)	[6]
S_I	0.72	0.72	ml μU^{-1} day^{-1}	Rate of glucose elimination via insulin; Eq. (10)	[6]
G_I	$\sqrt{20000}$	$\sqrt{20000}$	mg dl^{-1}	Glucose level of half-max insulin production; Eq. (11)	[6]
σ_I	43.2	43.2	μU ml^{-1} day^{-1} mg^{-1}	Maximum rate of insulin production by β-cells; Eq. (11)	[6]
δ_I	432	432	day^{-1}	Rate of insulin decay; Eq. (11)	[6]
b_{DE}	0.487×10^{-5}	0.487×10^{-5}	ml cells^{-1} day^{-1}	Rate of elimination of DCs by effector T cells; Eq. (12)	[7]
b_{IR}	0.487×10^{-5}	0.487×10^{-5}	ml cells^{-1} day^{-1}	Rate of elimination of tDCs by regulatory T cells; Eq. (13)	Estimated same as b_{DE}
μ_D	0.51	0.51	day^{-1}	Rate of removal from pancreas for DC and tDC; Eq. (12)-(13)	Estimated from [7]

a_E	.1199	.1199	day^{-1}	Rate of initial expansion of naive T cells into effector T cells; Eq. (14)	[7]
a_R	.1199	.1199	day^{-1}	Rate of initial expression of naive T cells into regulatory T cells; Eq. (15)	Estimated same as a_E
T_{naive}	370	370	cells ml^{-1}	Density of naive T cells contributing to initial production of effector and regulatory T cells in the spleen; Eq. (14)-(15)	[7]
b_P	12	12	day^{-1}	Maximal expansion rate of effector and regulatory T cells due to DCs; Eq. (14)-(15)	[7]
r_{am}	0.01	0.01	day^{-1}	Reversion rate of effector and regulatory T cells to memory T cells; Eq. (14)-(16)	[7]
b_E	1×10^{-3}	1×10^{-3}	ml day cells^{-1}	Activation rate for effector T cells from memory T cells; Eq. (16)	Estimated from [7]
μ_E	2×10^{-6}	2×10^{-6}	day^{-1}	Rate of effector T cell removal due to regulatory T; Eq. (14)	Estimated here
θ_D	2.12×10^5	2.12×10^5	day^{-1}	DC value for half-maximal effector T cell expansion; Eq. (14)-(15)	Estimated from [7]
b_R	1×10^{-3}	1×10^{-3}	ml day cells^{-1}	Activation rate for regulatory T cells from memory T cells; Eq. (15)-(16)	Estimated same as b_E
μ_R	2×10^{-6}	2×10^{-6}	day^{-1}	Rate of regulatory T cell removal due to effector T; Eq. (15)	Estimated same as μ_E
a_{Em}	0.01	0.01	day^{-1}	Death rate of memory T cells; Eq. (16)	[7]

Table 1: Model parameters.

References

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