

Supplementary Material

Daniel R. Bergman¹, Matthew Karikomi¹, Qing Nie^{1,2,*} and Adam L. MacLean^{3,*}

¹Department of Mathematics, University of California, Irvine, Irvine, CA 92697, USA

²Department of Cell and Developmental Biology, University of California, Irvine, Irvine, CA 92697, USA

³Department of Biological Sciences, University of Southern California, Los Angeles, CA 90089, USA

*Correspondence: qnie@uci.edu (QN); macleana@usc.edu (ALM).

Name	Description
	RP Cancer Line
Δ_{MIE}	
Δ_{MGA}	MGA
	INFL High Duration
	INFL Low Duration
	Mes Threshold
p	proliferation rate of tissue cells
d_C	death rate of tissue cells
K_1	EC50 term for probability of NK cell finding mutant cell
K_0	EC50 term for negative feedback of tissue cells on own proliferation
E_{NK}	rate of NKs clearing mutants
K_2	EC50 term for Treg inhibition of cytotoxic functions
E_{CTL}	rate of CTLs clearing mutants
	increased NK efficacy during high inflammation
	increased CTL efficacy during high inflammation
	increased Treg efficacy during high inflammation
σ_{NK}	NK source rate
σ_{CTL}	CTL source rate per cleared mutant cell
σ_{Treg}	Treg source rate per cleared mutant cell
	increased NK source rate during high inflammation
	increased CTL source rate during high inflammation
	increased Treg source rate during high inflammation

	maximum initial mutation damage after warmup
	increase in probability to mutate for non-mutating proliferating cells
Δ_A	mutant cells decreased apoptosis
Δ_{IE}	mutant cells increased immune evasion
Δ_P	mutant cells increased proliferation
k_{EMT}	EMT/MET rate
σ	standard deviation of noise in TGF- β each cell receives
K_3	EC50 term for how much TGF- β each cell has
τ_{\max}	max amount of TGF- β any cell can receive
τ_{MUT}	rate of TGF- β production by mutant cells
τ_{Treg}	rate of TGF- β production by Treg

Name	Description	Value
RP Cancer Line	When proportion of mutant cells reaches this number, then cancer is declared	0.5
MIE	(mesenchymal immune evasion) proportional decrease of probability immune cells clear mutated mesenchymal cells	0.6
MGA	(mesenchymal growth arrest) proportional decrease of probability mesenchymal cells proliferate; this decreased probability is accompanied and an equal and opposite increase in probability of rest	0.2
INFL High Duration	Number of consecutive cell cycles a patient will experience high inflammation before returning to a low inflammatory state	30
INFL Low Duration	Number of consecutive cell cycles a patient will experience low inflammation before returning to a high inflammatory state	30
Mes Threshold	the threshold EMT score above which a cell is labeled mesenchymal and below which it is labeled epithelial	0.7
p	weight of a cell proliferating during a cell cycle	0.28
d	weight of a cell dying during a cell cycle	0.14
N_{00}	EC50 term for Hill functions describing likelihood of cytotoxic immune cells locating mutated cells	8
N_0	EC50 term for Hill function describing negative feedback of total cell population on cell proliferation rates	80
NK Efficacy Low	weight of NK cell clearing mutated cells during low inflammation	0.2
Treg EC50 Low	EC50 term for Hill functions describing Treg-mediated inhibition of efficacy of cytotoxic immune cells during low inflammation	5
CTL Efficacy Low	weight of CTL cell clearing mutated cells during low inflammation	4
NK Efficacy Up	proportional increase of NK Efficacy Low during high inflammation	2
CTL Efficacy Up	proportional increase of CTL Efficacy Low during high inflammation	3
Treg Efficacy Up	during high inflammation, Treg EC50 is Treg EC50 Low / Treg Efficacy Up	200
NK Source Low	rate at which NK cells enter TME during low inflammation	1.3
CTL Recruitment Low	rate at which CTL cells are recruited after mutated cells are lysed during low inflammation	100
Treg Recruitment Low	rate at which Treg cells are recruited after mutated cells are lysed during low inflammation	200

NK Recruitment Up	proportional increase of NK source rate during high inflammation	1
CTL Recruitment Up	proportional increase of CTL recruitment rate during high inflammation	1
Treg Recruitment Up	proportional increase of Treg recruitment rate during high inflammation	1
$p_{mutation}$ Start	maximum probability of mutating after the warmup period ends	1e-2
$p_{mutation}$	increase in probability of a cell mutating after it proliferates but does not mutate	1e-4
Apoptosis Down	proportional decrease in apoptosis weight for cells with apoptosis pathway mutated	0.3
Immune Evasion	proportional decrease in immune clearance weight for cells with immune pathway mutated	0.48
Proliferation Up	proportional increase in proliferation weight for cells with proliferation pathway mutation	0.36
k_{EMT}	rate parameter controlling speed of EMT and MET	.01
c	standard deviation of noise on TGF- β received by each cell	6
TGFB Received EC50	EC50 term for Hill function determining how much TGF- β in TME enters a cell	200
TGFB Max	maximum amount of TGF- β that can enter a cell from the TME during a cell cycle	500
Mutant TGFB	amount of TGF- β produced by each mutated cell each cycle	5e-2
Treg TGFB	amount of TGF- β produced by each Treg cell each cycle	5e-1

Name	Base Value	Single Patient	Survival Curve	Vary MIE	Vary MGA	
RP Cancer Line	0.5					
MIE	0.6	0.9	0.4-0.9	0.7	0.5	
MGA	0.2		0.1-0.4	0	0.2	
INFL High Duration	30				60	
INFL Low Duration	30					
Mes Threshold	0.7					
p	0.28					
d	0.14					
N_{00}	8					
N_0	80					
NK Efficacy Low	0.2	10		10	10	
Treg EC50 Low	5					
CTL Efficacy Low	4	200		200	200	
NK Efficacy Up	2				1.2	
CTL Efficacy Up	3				3	
Treg Efficacy Up	200				10	
NK Source Low	1.3					
CTL Recruitment Low	100					
Treg Recruitment Low	200					
NK Recruitment Up	1					
CTL Recruitment Up	1					
Treg Recruitment Up	1					
$p_{mutation}$ Start	1e-2					
$p_{mutation}$	1e-4					
Apoptosis Down	0.3					
Immune Evasion	0.48					
Proliferation Up	0.36					
k_{EMT}	.01					
c	6					
TGFB Received EC50	200					
TGFB Max	500	700				
Mutant TGFB	5e-2					
Treg TGFB	5e-1					