

# Supplementary Materials for Modeling the competing effects of the immune system and EMT on epithelial cancers

Daniel R. Bergman<sup>1</sup>, Matthew Karikomi<sup>1</sup>, Qing Nie<sup>1,2,\*</sup> and  
Adam L. MacLean<sup>3,\*</sup>

<sup>1</sup>Department of Mathematics, University of California, Irvine, Irvine,  
CA 92697, USA

<sup>2</sup>Department of Cell and Developmental Biology, University of  
California, Irvine, Irvine, CA 92697, USA

<sup>3</sup>Department of Biological Sciences, University of Southern California,  
Los Angeles, CA 90089, USA

\*Correspondence: qnie@uci.edu (Q.N.); macleana@usc.edu (A.L.M.)

## Contents

<b>1</b>	<b>Definition of parameters specifying the model</b>	<b>2</b>
<b>2</b>	<b>Parameter values used for simulation</b>	<b>3</b>

## 1 Definition of parameters specifying the model

Name	Description
$p$	proliferation rate of tissue cells
$d_C$	death rate of tissue cells
$\Delta_{\text{MIE}}$	mesenchymal immune evasion
$\Delta_{\text{MGA}}$	mesenchymal growth arrest
$\Delta_A$	mutant cells decreased apoptosis
$\Delta_{\text{IE}}$	mutant cells increased immune evasion
$\Delta_P$	mutant cells increased proliferation
$K_0$	EC50 term for negative feedback of tissue cells on own proliferation
$K_1$	EC50 term for probability of NK cell finding mutant cell
$K_2$	EC50 term for Treg inhibition of cytotoxic functions
$K_3$	EC50 term for how much TGF- $\beta$ each cell has
$K_4$	EC50 term for TGF- $\beta$ activation of Tregs
$E_{\text{NK}}$	rate of NKs clearing mutants
$E_{\text{CTL}}$	rate of CTLs clearing mutants
$\sigma_{\text{NK}}$	NK source rate
$\sigma_{\text{CTL}}$	CTL source rate per cleared mutant cell
$\sigma_{\text{Treg}}$	Treg source rate per cleared mutant cell
$d_{\text{NK}}$	NK death rate
$d_{\text{CTL}}$	CTL death rate
$d_{\text{Treg}}$	Treg death rate
$k_{\text{EMT}}$	EMT/MET rate
$\sigma$	standard deviation of noise in TGF- $\beta$ each cell receives
$\tau_{\text{max}}$	max amount of TGF- $\beta$ any cell can receive
$\tau_{\text{MUT}}$	rate of TGF- $\beta$ production by mutant cells
$\tau_{\text{Treg}}$	rate of TGF- $\beta$ production by Treg

Table 1: The model parameter names and descriptions. Note that many of these values are affected by the inflammation state of the system.

## 2 Parameter values used for simulation

Name	Description	INFL Low Value
$p$	weight of proliferation for tissue cells	0.28
$d_C$	weight of apoptosis for tissue cells	0.14
$\Delta_{\text{MIE}}$	MIE	0.6
$\Delta_{\text{MGA}}$	MGA	0.2
$\Delta_A$	proportional decrease to weight of apoptosis for cells with mutated apoptosis pathway	0.3
$\Delta_{\text{IE}}$	proportional increase to weight of immune evasion for cells with mutated immune evasion pathway	0.48
$\Delta_P$	proportional increase to weight of proliferation for cells with mutated proliferation pathway	0.36
$K_0$	EC50 term for negative feedback of tissue cells on own proliferation	80 cells
$K_1$	EC50 term for probability of NK cell finding mutant cell	8 cells
$K_2$	EC50 term for Treg inhibition of cytotoxic functions	5 cells / volume
$K_3$	EC50 term for cumulative absorption of TGF- $\beta$	200 amount / volume
$K_4$	EC50 term for TGF- $\beta$ activation of Tregs	50 amount / volume
$E_{\text{NK}}$	weight of NKs clearing mutants	10
$E_{\text{CTL}}$	weight of CTLs clearing mutants	200
$\sigma_{\text{NK}}$	NK source rate	1.3 cells / cycle
$\sigma_{\text{CTL}}$	CTL source rate per cleared mutant cell	100 cells / (cleared mutants $\times$ c
$\sigma_{\text{Treg}}$	Treg source rate per cleared mutant cell	200 cells / (cleared mutants $\times$ concentration o
$d_{\text{NK}}$	NK death rate	0.13 / cycle
$d_{\text{CTL}}$	CTL death rate	0.0260 / cycle
$d_{\text{Treg}}$	Treg death rate	0.0260 / cycle
$k_{\text{EMT}}$	EMT/MET rate	0.01 / concentration of TGF
$\sigma$	standard deviation of noise in TGF- $\beta$ each cell receives	6 concentration of TGF- $\beta$
$\tau_{\text{max}}$	max amount of TGF- $\beta$ any cell can receive	500 concentration of TGF- $\beta$
$\tau_{\text{MUT}}$	rate of TGF- $\beta$ production by mutant cells	0.05 concentration of TGF- $\beta$ / cel
$\tau_{\text{Treg}}$	rate of TGF- $\beta$ production by Treg	0.5 concentration of TGF- $\beta$ / cell
	RP Cancer Line	0.5
	INFL High Duration	30 cycles
	INFL Low Duration	30 cycles
	Mes Threshold	0.7
	maximum initial mutation <sub>3</sub> damage after warmup	0.01
	increase in probability to mutate for non-mutating proliferating cells	0.0001

Table 2: The model parameter names, descriptions, and values during both low and high inflammation. Parameters with only one value do not change with the inflammatory state.

Name	Description	INFL Low Value	INFL High Value
$p$	proliferation rate of tissue cells	0.28	
$d_C$	death rate of tissue cells	0.14	
$\Delta_{\text{MIE}}$	MIE	0.6	
$\Delta_{\text{MGA}}$	MGA	0.2	
$\Delta_A$	mutant cells decreased apoptosis	0.3	
$\Delta_{\text{IE}}$	mutant cells increased immune evasion	0.48	
$\Delta_P$	mutant cells increased proliferation	0.36	
$K_0$	EC50 term for negative feedback of tissue cells on own proliferation	80	
$K_1$	EC50 term for probability of NK cell finding mutant cell	8	
$K_2$	EC50 term for Treg inhibition of cytotoxic functions	5	0.025
$K_3$	EC50 term for how much TGF- $\beta$ each cell has	200	
$K_4$	EC50 term for TGF- $\beta$ activation of Tregs	50	
$E_{\text{NK}}$	rate of NKs clearing mutants	10	30
$E_{\text{CTL}}$	rate of CTLs clearing mutants	200	600
$\sigma_{\text{NK}}$	NK source rate	1.3	
$\sigma_{\text{CTL}}$	CTL source rate per cleared mutant cell	100	
$\sigma_{\text{Treg}}$	Treg source rate per cleared mutant cell	200	
$d_{\text{NK}}$	NK death rate	0.13	
$d_{\text{CTL}}$	CTL death rate	0.0260	
$d_{\text{Treg}}$	Treg death rate	0.0260	
$k_{\text{EMT}}$	EMT/MET rate	0.01	
$\sigma$	standard deviation of noise in TGF- $\beta$ each cell receives	6	
$\tau_{\text{max}}$	max amount of TGF- $\beta$ any cell can receive	500	
$\tau_{\text{MUT}}$	rate of TGF- $\beta$ production by mutant cells	0.05	
$\tau_{\text{Treg}}$	rate of TGF- $\beta$ production by Treg	0.5	
	RP Cancer Line	0.5	
	INFL High Duration	30	
	INFL Low Duration	30	
	Mes Threshold	0.7	
	maximum initial mutation damage after warmup	0.01	
	increase in probability to mutate for non-mutating proliferating cells	0.0001	

Table 3: The model parameter names, descriptions, and values during both low and high inflammation. Parameters with only one value do not change with the inflammatory state.