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

Daniel R. Bergman 1, Matthew Karikomi 1, Qing Nie 1,2,* and Adam L. MacLean 3,*

 $^1{\rm Department}$ of Mathematics, University of California, Irvine, Irvine, CA 92697, USA $^2{\rm Department}$ of Cell and Developmental Biology, University of

California, Irvine, CA 92697, USA ³Department of Biological Sciences, University of Southern California,

Los Angeles, CA 90089, USA *Correspondence: qnie@uci.edu (Q.N.); macleana@usc.edu (A.L.M.)

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1 Definition of parameters specifying the model

Name	Name Description	
p	proliferation rate of tissue cells	
d_C	death rate of tissue cells	
$\Delta_{ m MIE}$	mesenchymal immune evasion	
$\Delta_{ m MGA}$	mesenchymal growth arrest	
Δ_A	mutant cells decreased apoptosis	
$\Delta_{ m IE}$	mutant cells increased immune evasion	
Δ_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		
K_2	EC50 term for Treg inhibition of cytotoxic functions	
K_3	EC50 term for how much TGF- β each cell has	
K_4	EC50 term for TGF- β activation of Tregs	
$E_{ m NK}$	rate of NKs clearing mutants	
$E_{\rm CTL}$	rate of CTLs clearing mutants	
$\sigma_{ m NK}$	NK source rate	
$\sigma_{ m CTL}$	CTL source rate per cleared mutant cell	
$\sigma_{ m Treg}$	Treg source rate per cleared mutant cell	
$d_{ m NK}$	NK death rate	
d_{CTL}	CTL death rate	
d_{Treg}	Treg death rate	
$k_{ m EMT}$	EMT/MET rate	
σ	standard deviation of noise in TGF- β each cell receives	
$ au_{ m max}$	max amount of TGF- β any cell can receive	
$ au_{ ext{MUT}}$ rate of TGF- eta production by mutant cells		
$ au_{\mathrm{Treg}}$	rate of TGF- β production by Treg	

Table S1: 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

P weight of proliferation for tissue cells 0.28 d_C weight of apoptosis for tissue cells 0.14 $\Delta_{\rm MRCA}$ $\Delta_{\rm MGA}$ 0.2 $\Delta_{\rm AGA}$ $\Delta_{\rm MGA}$ 0.2 $\Delta_{\rm AGA}$ $\Delta_{\rm AGA}$ 0.3 $\Delta_{\rm AGA}$ $\Delta_{\rm AGA}$ 0.4 $\Delta_{\rm AGA}$ $\Delta_{\rm AGA}$ 0.4 $\Delta_{\rm AGA}$ $\Delta_{\rm AGA}$ 0.5 $\Delta_{\rm AGA}$ $\Delta_$	Nama	Degenintien	INDI Law Value	
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	Name	Description	INFL Low Value	
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sis for cells with mutated apoptosis pathway $\Delta_{\rm IE}$ proportional increase to weight of immune evasion for cells with mutated immune evasion pathway Δ_P proportional increase to weight of proliferation for cells with mutated proliferation pathway K_0 proportional increase to weight of proliferation pathway	$\Delta_{ m MGA}$	MGA	0.2	
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	Δ_A		0.3	
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$		sis for cells with mutated apoptosis path-		
$\begin{array}{c} \text{evasion for cells with mutated immune} \\ \text{evasion pathway} \\ \Delta_P \\ \text{proportional increase to weight of proliferation pathway} \\ K_0 \\ \text{EC50 term for negative feedback of tissue} \\ \text{cells on own proliferation} \\ K_1 \\ \text{EC50 term for probability of NK cell finding mutant cell} \\ K_2 \\ \text{EC50 term for Treg inhibition of cytotoxic functions} \\ K_3 \\ \text{EC50 term for Treg inhibition of cytotoxic functions} \\ K_4 \\ \text{EC50 term for TGF-β activation of Tregs} \\ \text{EC50 term for TGF-β activation of Tregs} \\ \text{E00 weight of NKs clearing mutants} \\ \text{E01 correct of CTLs clearing mutants} \\ \text{E01 correct of CTLs clearing mutants} \\ \text{E01 correct of TGF-β activation of Tregs} \\ \text{E01 correct of CTL cource rate per cleared mutant cell} \\ \text{E01 correct of CTL cource rate per cleared mutant cell} \\ \text{E02 correct of CTL cource rate per cleared mutant cell} \\ \text{E03 correct of CTL death rate} \\ \text{E04 correct of CTL death rate} \\ \text{E020 cells / (cleared mutants \times concentration)} \\ \text{E03 correct of Treg death rate} \\ \text{E04 correct of CTL death rate} \\ \text{E04 correct of Treg death rate} \\ \text{E04 correct of Treg} \\ \text{E04 correct of TGF-β and cell receives} \\ \text{E05 term for TGF-β and cell can receive} \\ E06 concentration of TGF-β concentration of TGF-$		· ·		
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ation for cells with mutated proliferation pathway 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 cumulative absorption of TGF- β K_4 EC50 term for TGF- β activation of Tregs E_{NK} weight of NKs clearing mutants E_{CTL} weight of CTLs clearing mutants E_{CTL} work source rate E_{CTL} CTL source rate per cleared mutant cell E_{CTL} CTL cath rate E_{CTL} CTL death rate E_{CTL} CTL death rate E_{CTL} CTL death rate E_{CTL} CTL death rate E_{CTL} Treg death rate E_{CTL} Treg death rate E_{CTL} CTL deat				
	Δ_P		0.36	
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$ \begin{array}{c} \text{cells on own proliferation} \\ K_1 \\ EC50 \text{ term for probability of NK cell finding mutant cell} \\ K_2 \\ EC50 \text{ term for Treg inhibition of cytotoxic functions} \\ K_3 \\ EC50 \text{ term for cumulative absorption of TGF-β} \\ EC50 \text{ term for TGF-β activation of Tregs} \\ EC50 \text{ term for TGF-β activation of Tregs} \\ ENK \\ \text{weight of NKs clearing mutants} \\ ENK \\ \text{weight of CTLs clearing mutants} \\ \text{O}_{\text{TNK}} \\ \text{NK source rate} \\ \text{O}_{\text{CTL}} \\ \text{CTL source rate per cleared mutant cell} \\ \text{O}_{\text{Treg}} \\ \text{Treg source rate per cleared mutant cell} \\ \text{O}_{\text{Treg}} \\ \text{Treg death rate} \\ \text{O}_{\text{CTL}} \\ \text{CTL death rate} \\ \text{O}_{\text{CD200}} \\ \text{Cycle} \\ \text{d}_{\text{CTL}} \\ \text{Treg death rate} \\ \text{O}_{\text{O}} \\ \text{200 colls} \\ \text{k}_{\text{EMT}} \\ \text{EMT} \\ \text{EMT/MET rate} \\ \text{O}_{\text{O}} \\ \text{cell receives} \\ \text{T}_{\text{max}} \\ \text{max amount of TGF-β any cell can receive} \\ \text{T}_{\text{Treg}} \\ \text{Tate of TGF-β production by mutant cells} \\ \text{O.5 concentration of TGF-β cell rate of TGF-β production by Treg} \\ \text{RP Cancer Line} \\ \text{O.5} \\ \text{INFL High Duration} \\ \text{Mes Threshold} \\ \text{maximum initial mutation damage after warmup} \\ \text{increase in probability to mutate for non-} \\ \text{Increase in probability in mutate in probability in mutation} \\ Increase in probability in mutate in p$				
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	K_0	9	80 cells	
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$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	T.	=		
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	K_2		5 cells / volume	
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$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	K_3	_	200 amount / volume	
$E_{\rm NK}$ weight of NKs clearing mutants10 $E_{\rm CTL}$ weight of CTLs clearing mutants200 $\sigma_{\rm NK}$ NK source rate1.3 cells / cycle $\sigma_{\rm CTL}$ CTL source rate per cleared mutant cell100 cells / (cleared mutants × concentration $\sigma_{\rm Treg}$ Treg source rate per cleared mutant cell200 cells / (cleared mutants × concentration $d_{\rm NK}$ NK death rate0.13 / cycle $d_{\rm CTL}$ CTL death rate0.0260 / cycle $d_{\rm Treg}$ Treg death rate0.0260 / cycle $E_{\rm MT}$ EMT/MET rate0.01 / concentration of TGF σ standard deviation of noise in TGF- β each cell receives6 concentration of TGF- β $\tau_{\rm max}$ max amount of TGF- β any cell can receive500 concentration of TGF- β $\tau_{\rm max}$ max amount of TGF- β production by mutant cells0.05 concentration of TGF- β / cell $\tau_{\rm Treg}$ rate of TGF- β production by Treg0.5 concentration of TGF- β / cellRP Cancer Line0.5INFL High Duration30 cyclesINFL Low Duration30 cyclesMes Threshold0.7maximum initial mutation damage after warmup0.01increase in probability to mutate for non-0.0001	7.7	,	F0 / 1	
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$k_{\rm EMT}$ EMT/MET rate 0.01 / concentration of TGF σ standard deviation of noise in TGF- β each cell receives6 concentration of TGF- β $\tau_{\rm max}$ max amount of TGF- β any cell can receive 500 concentration of TGF- β $\tau_{\rm MUT}$ rate of TGF- β production by mutant cells 0.05 concentration of TGF- β / cell $\tau_{\rm Treg}$ rate of TGF- β production by Treg 0.5 concentration of TGF- β / cellRP Cancer Line 0.5 INFL High Duration30 cyclesINFL Low Duration30 cyclesMes Threshold 0.7 maximum initial mutation damage after warmup 0.01 increase in probability to mutate for non- 0.0001				
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$\tau_{\rm Treg}$ rate of TGF-β production by Treg 0.5 concentration of TGF-β / cell RP Cancer Line 0.5 INFL High Duration 30 cycles INFL Low Duration 30 cycles Mes Threshold 0.7 maximum initial mutation damage after warmup 0.01 increase in probability to mutate for non- 0.0001		· -	,	
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maximum initial mutation damage after warmup 0.01 increase in probability to mutate for non- 0.0001			v v	
increase in probability to mutate for non- 0.0001				
increase in probability to mutate for non- 0.0001		maximum initial mutation damage after	0.01	
		warmup	0.0004	
mutating proliferating cells			0.0001	
		mutating proliferating cells		

Table S2: 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	
$\Delta_{ m MIE}$	MIE	0.6	
$\Delta_{ m MGA}$	MGA	0.2	
Δ_A	mutant cells decreased apoptosis	0.3	
$\Delta_{ m IE}$	mutant cells increased immune evasion	0.48	
Δ_P	mutant cells increased proliferation	0.36	
K_0	EC50 term for negative feedback of tissue	80	
	cells on own proliferation		
K_1	EC50 term for probability of NK cell find-	8	
	ing mutant cell		
K_2	EC50 term for Treg inhibition of cytotoxic	5	0.025
	functions		
K_3	EC50 term for how much TGF- β each cell	200	
	has		
K_4	EC50 term for TGF- β activation of Tregs	50	
$E_{ m NK}$	rate of NKs clearing mutants	10	30
E_{CTL}	rate of CTLs clearing mutants	200	600
$\sigma_{ m NK}$	NK source rate	1.3	
$\sigma_{ m CTL}$	CTL source rate per cleared mutant cell	100	
$\sigma_{ m Treg}$	Treg source rate per cleared mutant cell	200	
$d_{ m NK}$	NK death rate	0.13	
d_{CTL}	CTL death rate	0.0260	
d_{Treg}	Treg death rate	0.0260	
$k_{\rm EMT}$	EMT/MET rate	0.01	
σ	standard deviation of noise in TGF- β each	6	
	cell receives		
$ au_{ m max}$	max amount of TGF- β any cell can receive	500	
$ au_{ ext{MUT}}$	rate of TGF- β production by mutant cells	0.05	
$ au_{ m Treg}$	rate of TGF- β 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	0.01	
	warmup		
	increase in probability to mutate for non-	0.0001	
	mutating proliferating cells		

Table S3: 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.

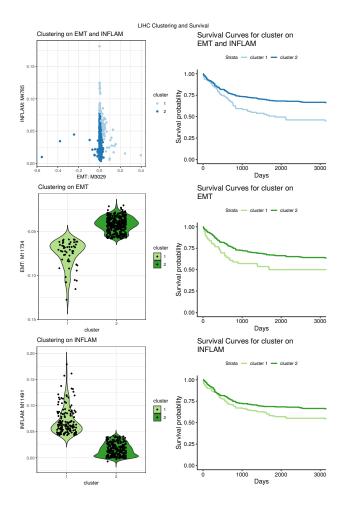


Figure S1: A. K-means clustering of LIHC using gene ontology terms indicative of EMT and inflammation signatures (k=2). B. Survival plots corresponding to the clustering on EMT and inflammation. C. K-means clustering of LIHC using gene ontology terms indicative of an EMT signature (k=2). D. Survival plots corresponding to the clustering on EMT. E. K-means clustering of LIHC using gene ontology terms indicative of inflammation (k=2). F. Survival plots corresponding to the clustering on inflammation.