

# Supporting Information

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## S2: Nondimensionalization of the mathematical model

The governing equations for the variables in the main text in the presence of TGF- $\beta$  antibody ( $A$ ) are as follows:

$$\begin{aligned}
\frac{\partial n}{\partial t} &= \nabla \cdot \left( D_n \nabla n - \chi_E n \frac{\nabla E}{\delta_E + \sigma_E |\nabla E|} - \chi_\rho I_S n \frac{\nabla \rho}{\delta_\rho + \sigma_\rho |\nabla \rho|} \right) \\
&\quad + r \left( 1 + r_E \frac{E^m}{k_E^m + E^m} \right) n \left( 1 - \frac{n}{n_0} \right) - \mu_n N_1 n \quad \text{in } \Omega_*, t > 0, \\
\frac{\partial N_1}{\partial t} &= \nabla \cdot \left( D_1 \nabla N_1 - \chi_1 N_1 \frac{\nabla C}{\delta_1 + \sigma_C |\nabla C|} \right) + \lambda_1 N_1 - \lambda_{12} G N_1 \quad \text{in } \Omega_*, t > 0, \\
\frac{\partial N_2}{\partial t} &= \nabla \cdot \left( D_2 \nabla N_2 - \chi_2 N_2 \frac{\nabla C}{\delta_2 + \sigma_C |\nabla C|} \right) + \lambda_{12} G N_1 + \lambda_2 (G) N_2 \quad \text{in } \Omega_*, t > 0, \\
\frac{d\rho}{dt} &= -(\mu_{\rho 1} E + \mu_{\rho 2} P) n \quad \text{in } S, t > 0, \\
\frac{\partial C}{\partial t} &= D_C \Delta C + \lambda_C n - \mu_C C \quad \text{in } \Omega_*, t > 0, \\
\frac{\partial G}{\partial t} &= D_G \Delta G + \lambda_G n - \mu_G G - \mu_{AG} A G \quad \text{in } \Omega_*, t > 0, \\
\frac{\partial E}{\partial t} &= D_E \Delta E + \lambda_E N_2 - \mu_E E - \mu_{ED} \frac{ED^l}{K_D^l + D^l} \quad \text{in } \Omega_*, t > 0, \\
\frac{\partial P}{\partial t} &= D_P \Delta P + \lambda_P N_2 - \mu_{PM} \frac{PM^m}{K_M^m + M^m} - \mu_P P \quad \text{in } \Omega_*, t > 0, \\
\frac{\partial D}{\partial t} &= D_D \Delta D + \lambda_D I_{\Omega_I} - \mu_D D \quad \text{in } \Omega_*, t > 0, \\
\frac{\partial M}{\partial t} &= D_M \Delta M + \lambda_M - \mu_M M \quad \text{in } \Omega_*, t > 0, \\
\frac{\partial A}{\partial t} &= D_A \Delta A + \lambda_A - \mu_A A \quad \text{in } \Omega_*, t > 0.
\end{aligned}$$

We non-dimensionalize the variables and the parameters in the governing equations above as follows

$$\begin{aligned}
\bar{t} &= \frac{t}{T}, \quad \bar{x} = \frac{x}{L}, \quad \bar{n} = \frac{n}{n^*}, \quad \bar{N}_1 = \frac{N_1}{N_1^*}, \quad \bar{N}_2 = \frac{N_2}{N_2^*}, \quad \bar{\rho} = \frac{\rho}{\rho^*}, \quad \bar{C} = \frac{C}{C^*}, \quad \bar{G} = \frac{G}{G^*}, \quad \bar{E} = \frac{E}{E^*}, \quad \bar{P} = \frac{P}{P^*}, \\
\bar{D} &= \frac{D}{D^*}, \quad \bar{M} = \frac{M}{M^*}, \quad \bar{A} = \frac{A}{A^*}, \quad \bar{D}_n = \frac{D_n}{D_\dagger}, \quad \bar{D}_1 = \frac{D_1}{D_\dagger}, \quad \bar{D}_2 = \frac{D_2}{D_\dagger}, \quad \bar{D}_C = \frac{D_C}{D_\dagger}, \quad \bar{D}_G = \frac{D_G}{D_\dagger}, \\
\bar{D}_E &= \frac{D_E}{D_\dagger}, \quad \bar{D}_P = \frac{D_P}{D_\dagger}, \quad \bar{D}_D = \frac{D_D}{D_\dagger}, \quad \bar{D}_M = \frac{D_M}{D_\dagger}, \quad \bar{D}_A = \frac{D_A}{D_\dagger}, \quad \bar{r} = rT, \quad \bar{r}_E = r_E, \quad \bar{k}_E = \frac{k_E}{E^*}, \\
\bar{n}_0 &= \frac{n_0}{n^*}, \quad \bar{\lambda}_1 = \lambda_1 T, \quad \bar{\lambda}_{12} = \lambda_{12} T G^*, \quad \bar{\lambda}_{12}^\dagger = \frac{\lambda_{12} T G^* N_1^*}{N_2^*}, \quad \bar{\lambda}_2 = \lambda_2 T, \quad \bar{\lambda}_C = \frac{\lambda_C T n^*}{C^*}, \quad \bar{\lambda}_G = \frac{\lambda_G T n^*}{G^*}, \\
\bar{\lambda}_E &= \frac{\lambda_E T N_2^*}{E^*}, \quad \bar{\lambda}_P = \frac{\lambda_P T N_2^*}{P^*}, \quad \bar{\lambda}_D = \frac{\lambda_D T}{D^*}, \quad \bar{\lambda}_M = \frac{\lambda_M T}{M^*}, \quad \bar{\lambda}_A = \frac{\lambda_A T}{A^*}, \quad \bar{\mu}_n = \mu_n T N_1^*,
\end{aligned}$$

Table S1. Reference variables used in the model.

	Description	Dimensional Value	Refs.
$T$	Time	1 h	
$L$	Length	1.0 mm	
$D_{\dagger}$	Diffusion coefficients ( $= L^2/T$ )	$2.78 \times 10^{-6} \text{ cm}^2 \text{ s}^{-1}$	
$n^*$	Tumor density	$2.5 \times 10^4 \text{ cells/cm}^3$	[1, 2]
$N_1^*$	N1 neutrophil density	$1.0 \times 10^5 \text{ cells/cm}^3$	[1, 3, 4]
$N_2^*$	N2 neutrophil density	$= N_1^*$	[1, 3]
$\rho^*$	ECM density	$5.0 \times 10^{-4} \text{ g/cm}^3$	[5–10]
$C^*$	CXCL8 (IL-8) concentration	$1 \times 10^{-12} \text{ g/cm}^3$	[11]
$G^*$	TGF- $\beta$ concentration	$1.1 \times 10^{-8} \text{ g/cm}^3$	[2, 12, 13]
$E^*$	Neutrophil elastase concentration	$6.46 \times 10^{-9} \text{ g/cm}^3$	[14, 15]
$P^*$	MMP concentration	$1.6 \times 10^{-9} \text{ g/cm}^3$	[16]
$D^*$	NE inhibitor (DNase I) concentration	$3.2 \times 10^{-9} \text{ g/cm}^3$	[17–19]
$M^*$	TIMP concentration	$4.6385 \times 10^{-8} \text{ g/cm}^3$	[20]
$A^*$	Concentration of anti-body of TGF- $\beta$	$0.172 \text{ } \mu\text{M}$	[21]

$$\begin{aligned}
\bar{\mu}_{\rho 1} &= \frac{\mu_{\rho 1} T E^* n^*}{\rho^*}, \quad \bar{\mu}_{\rho 2} = \frac{\mu_{\rho 2} T P^* n^*}{\rho^*}, \quad \bar{\mu}_C = \mu_C T, \quad \bar{\mu}_G = \mu_G T, \quad \bar{\mu}_E = \mu_E T, \quad \bar{\mu}_{ED} = \mu_{ED} T, \\
\bar{K}_D &= \frac{K_D}{D^*}, \quad \bar{\mu}_P = \mu_P T, \quad \bar{\mu}_D = \mu_D T, \quad \bar{K}_M = \frac{K_M}{M^*}, \quad \bar{\mu}_M = \mu_M T, \quad \bar{\mu}_{PM} = \mu_{PM} T, \quad \bar{\mu}_A = \mu_A T, \\
\bar{\mu}_{AG} &= \mu_{AG} T A^*, \quad \bar{\chi}_E = \frac{\chi_E T}{L}, \quad \bar{\delta}_E = \frac{\delta_E L}{E^*}, \quad \bar{\sigma}_E = \sigma_E, \quad \bar{\chi}_\rho = \frac{\chi_\rho T}{L}, \quad \bar{\delta}_\rho = \frac{\delta_\rho L}{\rho^*}, \quad \bar{\sigma}_\rho = \sigma_\rho, \\
\bar{\chi}_1 &= \frac{\chi_1 T}{L}, \quad \bar{\delta}_1 = \frac{\delta_1 L}{C^*}, \quad \bar{\sigma}_C = \sigma_C, \quad \bar{\chi}_2 = \frac{\chi_2 T}{L}, \quad \bar{\delta}_2 = \frac{\delta_2 L}{C^*}.
\end{aligned}$$

where reference values  $T, L, D, n^*, N_1^*, N_2^*, \rho^*, C^*, G^*, E^*, P^*, D^*, M^*, A^*$  are given in Table S1. Here,  $D_{\dagger} = L^2/T$  is the characteristic diffusion coefficient for characteristic length  $L$  and time  $T$  in Table S1.

Then, the governing equations in a dimensionless form are

$$\begin{aligned}
\frac{\partial \bar{n}}{\partial \bar{t}} &= \bar{\nabla} \cdot (\bar{D}_n \bar{\nabla} \bar{n}) - \bar{\nabla} \cdot \left( \bar{\chi}_E \bar{n} \frac{\bar{\nabla} \bar{E}}{\bar{\delta}_E + \bar{\sigma}_E |\bar{\nabla} \bar{E}|} \right) - \bar{\nabla} \cdot \left( \bar{\chi}_\rho I_{\bar{S}} \bar{n} \frac{\bar{\nabla} \bar{\rho}}{\bar{\delta}_\rho + \bar{\sigma}_\rho |\bar{\nabla} \bar{\rho}|} \right) \\
&\quad + \bar{r} \left( 1 + \bar{r}_E \frac{\bar{E}^m}{\bar{k}_E + \bar{E}^m} \right) \bar{n} \left( 1 - \frac{\bar{n}}{\bar{n}_0} \right) - \bar{\mu}_n \bar{N}_1 \bar{n} \quad \text{in } \bar{\Omega}_*, \bar{t} > 0, \\
\frac{\partial \bar{N}_1}{\partial \bar{t}} &= \bar{\nabla} \cdot \left( \bar{D}_1 \bar{\nabla} \bar{N}_1 - \bar{\chi}_1 \bar{N}_1 \frac{\bar{\nabla} \bar{C}}{\bar{\delta}_1 + \bar{\sigma}_C |\bar{\nabla} \bar{C}|} \right) + \bar{\lambda}_1 \bar{N}_1 - \bar{\lambda}_{12} \bar{G} \bar{N}_1 \quad \text{in } \bar{\Omega}_*, \bar{t} > 0, \\
\frac{\partial \bar{N}_2}{\partial \bar{t}} &= \bar{\nabla} \cdot \left( \bar{D}_2 \bar{\nabla} \bar{N}_2 - \bar{\chi}_2 \bar{N}_2 \frac{\bar{\nabla} \bar{C}}{\bar{\delta}_2 + \bar{\sigma}_C |\bar{\nabla} \bar{C}|} \right) + \bar{\lambda}_{12} \bar{G} \bar{N}_1 + \bar{\lambda}_2 (\bar{G}) \bar{N}_2 \quad \text{in } \bar{\Omega}_*, \bar{t} > 0, \\
\frac{d \bar{\rho}}{d \bar{t}} &= -(\bar{\mu}_{\rho 1} \bar{E} + \bar{\mu}_{\rho 2} \bar{P}) \bar{n} \quad \text{in } \bar{S}, t > 0, \\
\frac{\partial \bar{C}}{\partial \bar{t}} &= \bar{D}_C \bar{\Delta} \bar{C} + \bar{\lambda}_C \bar{n} - \bar{\mu}_C \bar{C} \quad \text{in } \bar{\Omega}_*, \bar{t} > 0, \\
\frac{\partial \bar{G}}{\partial \bar{t}} &= \bar{D}_G \bar{\Delta} \bar{G} + \bar{\lambda}_G \bar{n} - \bar{\mu}_G \bar{G} - \bar{\mu}_{AG} \bar{A} \bar{G} \quad \text{in } \bar{\Omega}_*, \bar{t} > 0, \\
\frac{\partial \bar{E}}{\partial \bar{t}} &= \bar{D}_E \bar{\Delta} \bar{E} + \bar{\lambda}_E \bar{N}_2 - \bar{\mu}_E \bar{E} - \bar{\mu}_{ED} \frac{\bar{E} \bar{D}^l}{\bar{K}_D^l + \bar{D}^l} \quad \text{in } \bar{\Omega}_*, \bar{t} > 0, \\
\frac{\partial \bar{P}}{\partial \bar{t}} &= \bar{D}_P \bar{\Delta} \bar{P} + \bar{\lambda}_P \bar{N}_2 - \bar{\mu}_{PM} \frac{\bar{P} \bar{M}^m}{\bar{K}_M^m + \bar{M}^m} - \bar{\mu}_P \bar{P} \quad \text{in } \bar{\Omega}_*, \bar{t} > 0, \\
\frac{\partial \bar{D}}{\partial \bar{t}} &= \bar{D}_D \bar{\Delta} \bar{D} + \bar{\lambda}_D I_{\Omega_l} - \bar{\mu}_D \bar{D} \quad \text{in } \bar{\Omega}_*, \bar{t} > 0, \\
\frac{\partial \bar{M}}{\partial \bar{t}} &= \bar{D}_M \bar{\Delta} \bar{M} + \bar{\lambda}_M - \bar{\mu}_M \bar{M} \quad \text{in } \bar{\Omega}_*, \bar{t} > 0, \\
\frac{\partial \bar{A}}{\partial \bar{t}} &= \bar{D}_A \bar{\Delta} \bar{A} + \bar{\lambda}_A - \bar{\mu}_A \bar{A} \quad \text{in } \bar{\Omega}_*, \bar{t} > 0.
\end{aligned}$$

Note that  $\bar{\lambda}_{12}^\dagger = \bar{\lambda}_{12}$  under the assumption of  $N_1^* = N_2^*$ ; otherwise  $\bar{\lambda}_{12}^\dagger$  is different from  $\bar{\lambda}_{12}$ .

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