Supporting Information

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Numerical Methods

To illustrate our numerical method we consider the following diffusion equation:

$$\frac{\partial X}{\partial t} - D_X \nabla^2 X = F_X \text{ in } \Omega, \qquad \text{[S1]}$$

where the right-hand side accounts for all of the "active" terms. Let X_{ij}^n denote a numerical approximation of $X(ih_x, jh_y, n\tau)$, where h_x and h_y are the step size in the x and y directions, respectively, and τ is the time step size. Then, a discretization is derived by the explicit Euler five-point finite difference scheme, that is,

$$\frac{X_{ij}^{n+1} - X_{ij}^n}{\tau} - D_X \left(\frac{X_{i+1,j}^n + X_{i-1,j}^n - 2X_{i,j}^n}{h_x^2} + \frac{X_{i,j+1}^n + X_{i,j-1}^n - 2X_{i,j}^n}{h_y^2} \right) = F_X\left(X_{i,j}^n\right) \text{ in } \Omega. \qquad \text{[S2]}$$

To make the scheme stable, we take $\tau \le h^2/4D_X$, namely $\tau = 0.1(h^2/D_X)$, where $h = h_x = h_y$. To test the convergence, we take $h = 1/N$, where $n = 10$, 20, 40, 80, 160, and 320. The "exact" solution is taken to be the solution with $h = 640$. The solution is computed up to $t = 60$ d and the L_2 error of the velocity and numerical order of accuracy are listed in Table S1. We can clearly observe the second-order accuracy in this table.

Parameter Estimation

A summary of all of the model parameters is given in Tables S2 and S3.

Eq. 4.

- d_E: Corneal epithelial half life is at least 4–5 wk (1). We take the tubular epithelial half-life to be 6 wk. Then, $d_E = ln(2)/42 = 1.65 \times 10^{-2}$ d^{-1}.
- E^*: We assume that the tubular radius is 10 μm and that the tubules occupy up to 90% of the renal cortex. Accordingly, the density of the tubular epithelial cell (TEC) in healthy tissue is taken to be $E^* = 0.8$ g/mL.
- A_E: The steady state of Eq. **4** in healthy tissue is $A_E - d_E E^* = 0$. Hence, $A_E = 8.27 \times 10^{-3}$ g·cm^{-3}·d^{-1}.
- d_{EM}: The TECs are decreased by the activated macrophages. Assuming that if M is large, after a long period the TEC density will decrease by 10% even if TGF-β is not activated. Accordingly, $d_{EM} = 1/10 d_E = 1.65 \times 10^{-3}$ d^{-1}.
- K_{T_β}: Based on ref. 2, the concentration of TGF-β in tumor microenvironment was estimated to be about 10 ng/mL. Because tumors secrete a large amount of TGF-β, K_{T_β} in our model should be significantly smaller; we take $K_{T_\beta} = 10^{-10}$ g/cm^3.
- λ_{ET_β}: We assume that the increase of TEC apoptosis by macrophages is double the natural apoptosis rate when TGF-β is approximately at its saturation value; hence, $\lambda_{ET_\beta} = 2$.

Eq. 5.

- A_f: Fibroblasts make up 7% of healthy renal tissue (3), so that

$$f^* = 7 \times 10^{-2} \text{ g/cm}^3.$$

The steady state of Eq. **5** in healthy tissue is $A_f - d_f f = 0$. Because $d_f = 1.66 \times 10^{-2}$ d^{-1} (4), we get

$$A_f = d_f f^* \approx 1.66 \times 10^{-2} \times 7 \times 10^{-2} = 1.16 \times 10^{-3} \text{ g/cm}^3 \text{ d}^{-1}.$$

- λ_{mfT}: In the cancer microenviroment, the transformation from fibroblast to myofibroblast by TGF-β was represented in ref. 5 by the term $a_{21} T_\beta f$, where $a_{21} = 6 \times 10^2$ cm^3·g^{-1}·s^{-1}. We assume that in our model myofibroblast production rate is smaller than in ref. 5; this rate in our model has the form $\lambda_{mfT}(T_\beta/K_{T_\beta} + T_\beta)f$ and, to compare this with $a_{21} T_\beta f$, we take the inhibition $K_{T_\beta} + T_\beta$ to be $3/2 K_{T_\beta}$. We then choose λ_{mfT} such that

$$\lambda_{mfT} \frac{T_\beta}{\frac{3}{2}K_{T_\beta}} f = \frac{1}{10} a_{21} T_\beta f.$$

Hence, $\lambda_{mfT} = 0.12$ d^{-1}.

- λ_{mfG}: We assume that PDGF and TGF-β affect the transformation from f to m to approximately the same extent (6–8) and take $\lambda_{mfG} = \lambda_{mfT}$.
- λ_{fE}: We assume that in the absence of PDGF the production of fibroblasts by TEC is approximately twice the transformation of fibroblasts into myofibroblasts, that is, $\lambda_{fE} E = 2\lambda_{mfT} f$, and take λ_{fE} by setting $E = E^*$, $f = f^*$; then $\lambda_{fE} = 1.05 \times 10^{-2}$ d^{-1}.

Eq. 7.

- $\lambda_{\rho T_\beta}$: We assume that TGF-β doubles the production of ECM by myofibroblast when TGF-β is approximately at its saturation value. Hence, $\lambda_{\rho T_\beta} = 2$.
- $\lambda_{\rho f}$: In the cancer microenvironment, the remodeling rate of ECM is 0.432 d^{-1} (9). We assume that in renal fibrosis the remodeling rate is much smaller and take $\lambda_{\rho f} = 3 \times 10^{-3}$ d^{-1}. We also assume that the production rate of ECM by myofibroblasts is twice the production rate by fibroblasts (in the absence of TGF-β), namely, $\lambda_{\rho m} = 2\lambda_{\rho f} = 6 \times 10^{-3}$.
- ρ^*: The steady state of ρ, ρ^* is determined by solving the following steady-state equation in a healthy renal tissue:

$$\lambda_{\rho f} f \left(1 - \frac{\rho}{\rho_0}\right) - d_\rho \rho = 0.$$

Taking $f = f^*$, $\rho_0 = 10^{-3}$ g/cm^3 (9), and $d_\rho = 0.37$ d^{-1} (10), we get $\rho^* = 3.62 \times 10^{-4}$ g/cm^3.

Eq. 8.

- K_P: In ref. 11 it was demonstrated that renal epithelial cells, in response to inflammation by crystals of calcium oxalate monohydrate and excess oxalate ions, secreted monocyte chemotactic protein-1 (MCP-1) at levels of at least 267 pg/mL, which is ∼0.3 ng/mL. We assume that in patients with renal fibrosis the MCP-1 saturation can reach up to 5 ng/mL and take $K_P = 5 \times 10^{-9}$ g/mL.
- λ_{PM}: The degradation rate of MCP-1 is $d_P = 1.73$ d^{-1} (12). We assume that, when M and P are large, the production of MCP-1 by macrophages is three times larger than the degradation of MCP-1, that is, $\lambda_{PM} M_0 = 3 d_P K_P$. Because $M_0 = 5 \times 10^{-5}$ g/cm^3 (13), we get $\lambda_{PM} = 3 d_P K_P / M_0 = 3 \times 10^{-3}$ d^{-1}.
- d_{PM}: MCP-1 internalized by macrophages. We assume that the rate of internalization is smaller by a factor of 1/10 than

the rate of production by macrophages when M are P are large, so that

$$d_{PM} = 1/10\lambda_{PM};$$

hence, $d_{PM} = 2.08 \times 10^{-4}$ d^{-1}.

Eq. 12.

- $\lambda_{T_\beta M}$**:** In the cancer microenvironment, the production rate of TGF-β by TECs is 1.7×10^{-4} d^{-1} (5). We assume that in our model the production rate by macrophages is much larger and take $\lambda_{T_\beta M} = 1.5 \times 10^{-2}$ d^{-1}.

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Table S1. Accuracy of numerical method

N	L_2 error	Order
20	1.09e-1	
40	3.39e-2	1.69
80	1.01e-2	1.75
160	2.75e-3	1.87
320	7.11e-4	1.95

Table S2. Parameter descriptions and values

Parameter	Description	Value and refs.
D_M	Dispersion coefficient of macrophages	8.64×10^{-7} cm^2·d^{-1} (1, 2)
D_P	Diffusion coefficient of MCP-1	1.728×10^{-1} cm^2·d^{-1} (3)
D_G	Diffusion coefficient of PDGF	8.64×10^{-2} cm^2·d^{-1} (4)
D_Q	Diffusion coefficient of MMP	4.32×10^{-2} cm^2·d^{-1} (5, 6)
D_{Q_r}	Diffusion coefficient for TIMP	4.32×10^{-2} cm^2·d^{-1} (5, 6)
D_{T_β}	Diffusion coefficient for TGF-β	4.32×10^{-2} cm^2·d^{-1} (5)
D_f	Dispersion coefficient of fibroblasts	1.47×10^{-6} cm^2·d^{-1} (7)
D_m	Dispersion coefficient of myofibroblasts	1.47×10^{-5} cm^2·d^{-1} (7)
λ_{ET_β}	Rate of TEC apoptosis enhanced by TGF-β	(5) estimated
$\lambda_{T_\beta M}$	Production rate of TGF-β by macrophages	1.5×10^{-2} d^{-1} (7) and estimated
λ_{GM}	Production rate of PDGF by macrophages	2.4×10^{-5} d^{-1} (4)
λ_{QM}	Production rate of MMP by macrophages	3×10^{-4} d^{-1} (2)
λ_{Q_rM}	Production rate of TIMP by macrophages	6×10^{-5} d^{-1} (2, 6)
λ_{PE}	Activation rate of MCP-1 due to TECs	$1 \times 10^{-8} \sim 1 \times 10^{-7}$ d^{-1} (6) and estimated
λ_{PM}	Activation rate of MCP-1 due to macrophages	3×10^{-3} d^{-1} estimated
$\lambda_{\rho f}$	Activation rate of ECM due to fibroblasts	3×10^{-3} d^{-1} (2) and estimated
$\lambda_{\rho m}$	Activation rate of ECM due to myofibroblasts	6×10^{-3} d^{-1} (2) and estimated
$\lambda_{\rho T_\beta}$	Activation rate of ECM due to TGF-β	(5) estimated
λ_{fE}	Activation rate of fibroblasts due to TECs	1.2×10^{-2} d^{-1} (7) and estimated
λ_{mfT}	Activation rate of myofibroblasts due to TGF-β	0.12 d^{-1} (7) and estimated
λ_{mfG}	Activation rate of myofibroblasts due to PDGF	0.12 d^{-1} (7) and estimated
d_M	Death rate of macrophages	0.015 d^{-1} (8)
d_E	Death rate of TECs	1.65×10^{-2} d^{-1} estimated
d_{EM}	Increased death rate of TECs by macrophages	1.65×10^{-3} d^{-1} (9) and estimated
d_ρ	Degradation rate of ECM	0.37 d^{-1} (4)
d_P	Degradation rate of MCP-1	1.73 d^{-1} (3)
d_{PM}	Internalization rate of MCP-1 by macrophages	2.08×10^{-4} d^{-1} (3)
d_G	Degradation rate of PDGF	3.84 d^{-1} (4)
d_{QQ_r}	Binding rate of MMP to TIMP	4.98×10^{8} cm^3·g^{-1}·d^{-1} (3, 6, 10)
d_{Q_rQ}	Binding rate of TIMP to MMP	1.04×10^{9} cm^3·g^{-1}·d^{-1} (3, 6, 10)
d_Q	Degradation rate of MMP	4.32 d^{-1} (11)
d_{Q_r}	Degradation rate of TIMP	21.6 d^{-1} (6, 12)
$d_{\rho Q}$	Degradation rate of ECM due to MMP	2.59×10^{7} cm^3·g^{-1}·d^{-1} (1)
d_{T_β}	Degradation rate of TGF-β	3.33×10^{2} d^{-1} (13)
d_f	Death rate of fibroblasts	1.66×10^{-2} d^{-1} (14)
d_m	Death rate of myofibroblasts	1.66×10^{-2} d^{-1} (14)

MMP, matrix metalloproteinase; TIMP, tissue inhibitor of metalloproteinase.

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Table S3. Parameter descriptions and values

Parameter	Description	Value and refs.
χ_P	Chemotactic sensitivity parameter by MCP-1	10 $cm^5 \cdot g^{-1} \cdot d^{-1}$ (1, 2)
A_E	Intrinsic TEC proliferation	8.27×10^{-3} $g \cdot cm^{-3} \cdot d^{-1}$ estimated
A_f	Intrinsic fibroblast proliferation	1.16×10^{-3} $g \cdot cm^{-3} \cdot d^{-1}$ (3, 4) and estimated
K_Q	MMP saturation for activation of scar	3×10^{-8} $g \cdot cm^{-3}$ (5, 6)
K_G	PDGF saturation for activation of myofibroblasts	1.5×10^{-1} $g \cdot cm^{-3}$ (6, 7)
K_M	Macrophage saturation for apoptosis of TECs	5×10^{-5} $g \cdot cm^{-3}$ (8)
K_{T_β}	TGF-β saturation for inhibition of TECs	1×10^{-10} $g \cdot cm^{-3}$ (9)
K_P	MCP-1 saturation for influx of macrophages	5×10^{-9} $g \cdot cm^{-3}$ (10)
ρ_0	ECM saturation	10^{-3} $g \cdot cm^{-3}$ (11)
ρ^*	ECM density in health	3.62×10^{-4} $g \cdot cm^{-3}$ estimated
E^*	TEC density in health	0.8 $g \cdot cm^{-3}$ estimated
f^*	Fibroblast density in health	0.07 $g \cdot cm^{-3}$ (12) and estimated
M_0	Source/influx of macrophages from blood	5×10^{-5} $g \cdot cm^{-3}$ (8)
α	Influx rate of macrophages into interstitium	0.2 cm^{-1} (6)

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Table S4. Patient data for different levels of interstitial fibrosis based on kidney biopsy

Damage	Patient index	uTGFb*	uMCP1*	% fibrosis	INF†	Patient index	uTGFb*	uMCP1*	% fibrosis	INF†
Low	1	0.018	0.78	0	1	2	0.056	1.14	0	1
	3	0.089	1.4	0	1	4	0.223	2.27	0	2
	5	0.005	1.1	0	1	6	0.003	0.33	0	1
	7	0.101	1.94	0	1	8	0.053	0.82	0	1
	9	0.0016	0.7	0	1	10	0.034	0.51	2	1
	11	0.029	1.33	2	1	12	0.268	4.12	2	2
	13	0.056	0.95	2	1	14	0.014	0.75	5	1
	15	0.002	2.23	5	2	16	0.072	1.756	5	1
	17	0.033	1.5	5	1	18	0.0007	0.81	5	1
	19	0.0055	1.24	5	1					
Intermediate	20	0.084	3.94	10	2	21	0.038	6.26	10	1
	22	0.502	3.5	10	1	23	0.0046	0.2	10	1
	24	0.0009	0.78	10	1	25	0.00097	0.5	10	1
	26	0.0058	1.24	10	1	27	0.021	0.58	10	1
	28	0.126	4.41	10	2	29	0.004	2.2	10	2
	30	1.42	2	15	1	31	0.021	0.73	15	1
	32	0.035	2.18	17.5	1	33	0.788	21.4	20	1
	34	0.0009	0.53	20	1	35	0.001	0.36	20	1
	36	0.0019	2.1	25	1	37	0.0035	0.33	25	1
	38	0.002	2.6	25	2					
High	39	0.052	1.51	30	1	40	0.293	19.8	33	2
	41	0.177	10.8	35	2	42	0.0039	1.34	40	2
	43	0.0014	0.85	50	2	44	0.0032	0.48	50	1
	45	0.005	0.6	50	1	46	0.003	2.05	70	1
	47	0.0055	0.99	80	2					

*The units for urine MCP-1 and urine TGF-β are nanograms per milligram urine creatinine.
†INF is the degree of interstitial inflammation; 1 and 2 indicate that the degree of interstitial inflammation is <25% and ≥25%, respectively.