

Supplementary Table S5. Deterministic Parameters

Variable	Description	Value	Dimension	Reference	Comment
x_{LCC}	Concentration of lung cancer cells	0	ml ⁻¹		Initial density
x_{CAF}	Concentration of cancer-associated fibroblasts	0	ml ⁻¹		Initial density
x_{M_1}	Concentration of M1 macrophages	1E6	ml ⁻¹	[1]	Initial density
x_{M_2}	Concentration of M2 macrophages	1E4	ml ⁻¹	[1]	Initial density
x_{MSC}	Concentration of mesenchymal stem cells	0	ml ⁻¹		Initial density
x_{Epith}	Concentration of epithelial cells	2.9E7	ml ⁻¹	Estimated ^[2]	Initial density
$y_{IL-1\beta}$	Concentration of IL-1 β	50	pM	Estimated	Initial Concentration
y_{IL-6}	Concentration of IL-6	85	pM	Estimated	Initial
y_{IL-8}	Concentration of IL-8	65	pM	Estimated	Initial
y_{IL-10}	Concentration of IL-10	5	pM	Estimated	Initial
y_{VEGF}	Concentration of VEGF	90	pM	Estimated	Initial
y_{PDGF}	Concentration of PDGF	80	pM	Estimated	Initial
y_{EGF}	Concentration of EGF	0	pM	Estimated	Initial
y_{FGF}	Concentration of FGF	0	pM	Estimated	Initial
y_{HGF}	Concentration of HGF	0	pM	Estimated	Initial
y_{IGF1}	Concentration of IGF-1	85	pM	Estimated	Initial
y_{PGE2}	Concentration of PGE2	0	pM	Estimated	Initial
$y_{TGF-\beta}$	Concentration of TGF- β	20	pM	Estimated	Initial
y_{SDF-1}	Concentration of SDF-1	0	pM	Estimated	Initial
y_{M-CSF}	Concentration of M-CSF	45	pM	Estimated	Initial
y_{GM-CSF}	Concentration of GM-CSF	30	pM	Estimated	Initial
y_{MCP-1}	Concentration of MCP-1	0	pM	Estimated	Initial
$y_{TNF-\alpha}$	Concentration of TNF	70	pM	Estimated	Initial
$y_{IFN-\gamma}$	Concentration of	10	pM	Estimated	Initial
$C_{CAF_TGF-\beta}$	Rate of supply of cancer-associated fibroblasts from resident fibroblasts by TGF- β	2500	ml ⁻¹ h ⁻¹	Estimated ^[3, 4]	
C_{CAF_PDGF}	Rate of supply of cancer-associated fibroblasts	2500	ml ⁻¹ h ⁻¹	Estimated ^[3, 4]	

	from resident fibroblasts by PDGF				
c_{CAF_FGF}	Rate of supply of cancer-associated fibroblasts from resident fibroblasts by FGF	2500	$ml^{-1} h^{-1}$	Estimated ^[3]	
c_M	Rate of recruitment of monocytes/macrophages	430	$ml^{-1} h^{-1}$	[1, 5-9]	
c_{MSC_MCP-1}	Rate of recruitment of mesenchymal stem cells from MCP-1	300	$ml^{-1} h^{-1}$	Estimated ^[10]	
c_{MSC_SDF-1}	Rate of recruitment of mesenchymal stem cells from SDF-1	300	$ml^{-1} h^{-1}$	Estimated ^[10]	
c_{MSC_HGF}	Rate of recruitment of mesenchymal stem cells from HGF	300	$ml^{-1} h^{-1}$	Estimated ^[10]	
c_{MSC_VEGF}	Rate of recruitment of mesenchymal stem cells from VEGF	300	$ml^{-1} h^{-1}$	Estimated ^[10]	
r_{LCC}	Average basal proliferation rate of lung cancer cells obtained in the absence of population limitation and cytokine stimulus	0.0347	h^{-1}	[11]	$\frac{\ln 2}{\text{cell cycle period}}$ Cell cycle~20 hours
r_{CAF}	Average basal proliferation rate of cancer-associated fibroblasts obtained in the absence of population limitation and cytokine stimulus	0.0291	h^{-1}	[11]	Cell cycle~23.8 hours
r_{MSC}	Average basal proliferation rate of mesenchymal stem cells obtained in the absence of population limitation and cytokine stimulus	0.0154	h^{-1}	[12]	Cell cycle~45 hours
r_{Epith}	Average basal proliferation rate of epithelial cells obtained in the absence of population limitation and cytokine stimulus	0.0267	h^{-1}	[13]	Cell cycle~26 hours
x_T	Concentration of T cell	3E4	ml^{-1}	[1]	Constant
x_{max}	Maximum cell population (including LCC, CAF, M1, M2, MSC, EC, Epith) level due to limited nutrition and space	3E7	ml^{-1}	[2]	Density-dependent inhibition of cell growth
u_{LCC_IL-10}	Maximum up-regulation ratio of LCC proliferation rate by IL-10	2.5		Estimated ^[14]	
u_{LCC_VEGF}	Maximum up-regulation ratio of LCC proliferation rate by VEGF	2.5		Estimated ^[15]	
u_{LCC_EGF}	Maximum up-regulation ratio of LCC proliferation rate by EGF	3		Estimated ^[14]	

u_{LCC_FGF}	Maximum up-regulation ratio of LCC proliferation rate by FGF	1.5		Estimated ^[16, 17]	
u_{LCC_HGF}	Maximum up-regulation ratio of LCC proliferation rate by HGF	1.5		Estimated ^[18]	
u_{LCC_IGF-1}	Maximum up-regulation ratio of LCC proliferation rate by IGF-1	2		Estimated ^[19]	
u_{LCC_PGE2}	Maximum up-regulation ratio of LCC proliferation rate by PGE2	2		Estimated ^[20]	
u_{LCC_SDF-1}	Maximum up-regulation ratio of LCC proliferation rate by SDF-1	1.5		Estimated ^[21]	
u_{LCC_M1}	Maximum up-regulation ratio of LCC apoptosis rate by M1	1.5		Estimated ^[10]	
u_{cell_IL-6}	Maximum up-regulation ratio of maximum cell concentration due to angiogenic effect of IL-6	0.1		[22, 23]	
u_{cell_IL-8}	Maximum up-regulation ratio of maximum cell concentration due to angiogenic effect of IL-8	0.1		[24]	
u_{cell_VEGF}	Maximum up-regulation ratio of maximum cell concentration due to angiogenic effect of VEGF	0.1		[24-27]	
u_{cell_PDGF}	Maximum up-regulation ratio of maximum cell concentration due to angiogenic effect of PDGF	0.1		[25]	
u_{cell_FGF}	Maximum up-regulation ratio of maximum cell concentration due to angiogenic effect of FGF	0.1		[27, 28]	
$u_{cell_TGF-\beta}$	Maximum up-regulation ratio of maximum cell concentration due to angiogenic effect of TGF- β	0.05		[27, 29]	
u_{cell_SDF-1}	Maximum up-regulation ratio of maximum cell concentration due to angiogenic effect of SDF-1	0.05		[30, 31]	
u_{cell_MCP-1}	Maximum up-regulation ratio of maximum cell concentration due to angiogenic effect of MCP-1	0.05		[32]	
$u_{cell_TNF-\alpha}$	Maximum up-regulation ratio of maximum cell concentration due to angiogenic effect of TNF- α	0.1		[33, 34]	
$u_{CAF_PDGF_p}$	Maximum up-regulation ratio of CAF proliferation rate by PDGF	2.821		[35]	
u_{CAF_PGE2}	Maximum up-regulation ratio of CAF proliferation rate by PGE2	1.678		[36]	
$u_{CAF_MSC_PDGF}$	Maximum up-regulation ratio of differentiation rate from MSC to CAF by PDGF	1.5		Estimated ^[37]	
$u_{CAF_MSC_TGF-\beta}$	Maximum up-regulation ratio of differentiation rate from MSC to CAF by TGF- β	1.5		Estimated ^[38]	

u_{M_VEGF}	Maximum up-regulation ratio of monocyte/macrophage recruitment rate by VEGF	2		Estimated ^[10]	
u_{M_PDGF}	Maximum up-regulation ratio of monocyte/macrophage recruitment rate by PDGF	2		Estimated ^[37]	
u_{M_M-CSF}	Maximum up-regulation ratio of monocyte/macrophage recruitment rate by M-CSF	2		Estimated ^[10]	
u_{M_MCP-1}	Maximum up-regulation ratio of monocyte/macrophage recruitment rate by MCP-1	2		Estimated ^[10, 39]	
$u_{M1_M_IFN-\gamma}$	Maximum up-regulation ratio of differentiation rate from macrophages to M1 by IFN- γ	3		Estimated ^[40]	
$u_{M1_M_TNF-\alpha}$	Maximum up-regulation ratio of differentiation rate from macrophages to M1 by TNF- α	2.5		Estimated ^[40]	
$u_{M1_M_GM-CSF}$	Maximum up-regulation ratio of differentiation rate from macrophages to M1 by GM-CSF	1		Estimated ^[40]	
$u_{M2_M_IL-10}$	Maximum up-regulation ratio of differentiation rate from macrophages to M2 by IL-10	0.8		Estimated ^[40]	
$u_{M2_M_PGE2}$	Maximum up-regulation ratio of differentiation rate from macrophages to M2 by PGE2	0.005		Estimated ^[40]	
$u_{M1_M2_TNF-\alpha}$	Maximum up-regulation ratio of activation rate from M2 to M1 by TNF- α	0.5		Estimated ^[11]	
$u_{M1_M2_IFN-\gamma}$	Maximum up-regulation ratio of activation rate from M2 to M1 by IFN- γ	1		Estimated ^[11]	
u_{M1_M2}	Maximum up-regulation ratio of activation rate from M2 to M1 by TNF- α and IFN- γ	0.994		Estimated ^[11]	
u_{Epith_IL-8}	Maximum up-regulation ratio of Epith proliferation rate by IL-8	0.2		Estimated ^[41]	
u_{Epith_EGF}	Maximum up-regulation ratio of Epith proliferation rate by EGF	0.2		Estimated ^[41]	
$u_{IL-6_IL-1\beta}$	Maximum up-regulation ratio of IL-6 production by Epith in the presence of IL-1 β	2		Estimated ^[42]	
$u_{IL-8_IL-1\beta_LCC}$	Maximum up-regulation ratio of IL-8 production by LCC in the presence of IL-1 β	2		Estimated ^[43]	
$u_{IL-8_IL-1\beta_Epith}$	Maximum up-regulation ratio of IL-8 production by Epith in the presence of IL-1 β	2		Estimated ^[43]	

u_{IL-10_EGF}	Maximum up-regulation ratio of IL-10 production by LCC in the presence of EGF	2		Estimated ^[14]	
$u_{VEGF_HGF_LCC}$	Maximum up-regulation ratio of VEGF production by LCC in the presence of HGF	2		Estimated ^[44]	
$u_{VEGF_TGF-\beta_LCC}$	Maximum up-regulation ratio of VEGF production by LCC in the presence of TGF- β	2		Estimated ^[45]	
$u_{VEGF_TGF-\beta_CAF}$	Maximum up-regulation ratio of VEGF production by CAF in the presence of TGF- β	2		Estimated ^[45]	
$u_{VEGF_TGF-\beta_Epith}$	Maximum up-regulation ratio of VEGF production by Epith in the presence of TGF- β	2		Estimated ^[46]	
u_{VEGF_LCC}	Maximum up-regulation ratio of secretion rate of VEGF from LCC due to hypoxia and hypoglycemia	3		Estimated ^[46]	
$u_{M-CSF_IL-1\beta}$	Maximum up-regulation ratio of M-CSF production by Epith in the presence of IL-1 β	2		Estimated ^[43]	
$u_{GM-CSF_IL-1\beta}$	Maximum up-regulation ratio of GM-CSF production by Epith in the presence of IL-1 β	2		Estimated ^[43]	
s_{LCC_IL-10}	Saturation concentration of IL-10 on half max regulation of LCC proliferation	49.74	pM	^[14]	
s_{LCC_VEGF}	Saturation concentration of VEGF on half max regulation of LCC proliferation	1000	pM	Estimated ^[15]	
s_{LCC_EGF}	Saturation concentration of EGF on half max regulation of LCC proliferation	6152	pM	^[14]	
s_{LCC_FGF}	Saturation concentration of FGF on half max regulation of LCC proliferation	1000	pM	Estimated ^[16, 17]	
s_{LCC_HGF}	Saturation concentration of HGF on half max regulation of LCC proliferation	800	pM	^[18]	
s_{LCC_IGF-1}	Saturation concentration of IGF-1 on half max regulation of LCC proliferation	390.1	pM	^[19]	
s_{LCC_PGE2}	Saturation concentration of PGE2 on half max regulation of LCC proliferation	59650	pM	^[20]	
s_{LCC_SDF-1}	Saturation concentration of SDF-1 on half max regulation of LCC proliferation	12500	pM	^[21]	

S_{cell_IL-6}	Saturation concentration of IL-6 on half max regulation of angiogenic effect	2000	pM	Estimated ^[22, 23]	
S_{cell_IL-8}	Saturation concentration of IL-8 on half max regulation of angiogenic effect	2000	pM	Estimated ^[24]	
S_{cell_VEGF}	Saturation concentration of VEGF on half max regulation of angiogenic effect	2000	pM	Estimated ^[24-27]	
S_{cell_PDGF}	Saturation concentration of PDGF on half max regulation of angiogenic effect	2000	pM	Estimated ^[25]	
S_{cell_FGF}	Saturation concentration of FGF on half max regulation of angiogenic effect	2000	pM	Estimated ^[27, 28]	
$S_{cell_TGF\beta}$	Saturation concentration of TGF- β on half max regulation of angiogenic effect	2000	pM	Estimated ^[27, 29]	
S_{cell_SDF-1}	Saturation concentration of SDF-1 on half max regulation of angiogenic effect	2000	pM	Estimated ^[30, 31]	
S_{cell_MCP-1}	Saturation concentration of MCP-1 on half max regulation of angiogenic effect	2000	pM	Estimated ^[32]	
$S_{cell_TNF-\alpha}$	Saturation concentration of TNF- α on half max regulation of angiogenic effect	2000	pM	Estimated ^[33, 34]	
$S_{CAF_PDGF_r}$	Saturation concentration of PDGF on half max regulation of CAF recruitment	1500	pM	Estimated	
S_{CAF_FGF}	Saturation concentration of FGF on half max regulation of CAF recruitment	1500	pM	Estimated	
$S_{CAF_TGF-\beta}$	Saturation concentration of TGF- β on half max regulation of CAF recruitment	1500	pM	Estimated	
$S_{CAF_PDGF_p}$	Saturation concentration of PDGF on half max regulation of CAF proliferation	150.7	pM	^[35]	
S_{CAF_PGE2}	Saturation concentration of PGE2 on half max regulation of CAF proliferation	20000	pM	^[36]	
$S_{CAF_MSC_PDGF}$	Saturation concentration of PDGF on half max regulation of differentiation from MSC to CAF	1500	pM	Estimated ^[37]	
$S_{CAF_MSC_TGF-\beta}$	Saturation concentration of TGF- β on half max regulation of differentiation from MSC to CAF	1500	pM	Estimated ^[38]	

S_{M_VEGF}	Saturation concentration of VEGF on half max regulation of monocyte/macrophage recruitment	1500	pM	Estimated ^[10]	
S_{M_PDGF}	Saturation concentration of PDGF on half max regulation of monocyte/macrophage recruitment	1500	pM	Estimated ^[37]	
S_{M_M-CSF}	Saturation concentration of M-CSF on half max regulation of monocyte/macrophage recruitment	1500	pM	Estimated ^[10]	
S_{M_MCP-1}	Saturation concentration of MCP-1 on half max regulation of monocyte/macrophage recruitment	1500	pM	Estimated ^[10, 39]	
$S_{M1_M2_TNF-\alpha}$	Saturation concentration of TNF- α on half max regulation of activation from M2 to M1	4.12	pM	Estimated ^[1]	
$S_{M1_M2_IFN-\gamma}$	Saturation concentration of IFN- γ on half max regulation of activation from M2 to M1	4.41	pM	Estimated ^[47]	
$S_{M1_M2_IL-10}$	Saturation concentration of IL-10 on half max regulation of activation from M2 to M1	2.69	pM	Estimated ^[48]	
S_{MSC_VEGF}	Saturation concentration of VEGF on half max regulation of MSC recruitment	1500	pM	Estimated	
S_{MSC_HGF}	Saturation concentration of HGF on half max regulation of MSC recruitment	1500	pM	Estimated	
S_{MSC_SDF-1}	Saturation concentration of SDF-1 on half max regulation of MSC recruitment	1500	pM	Estimated	
S_{MSC_MCP-1}	Saturation concentration of MCP-1 on half max regulation of MSC recruitment	1500	pM	Estimated	
S_{Epth_IL-8}	Saturation concentration of IL-8 on half max regulation of Epth proliferation	1500	pM	Estimated ^[41]	
S_{Epth_EGF}	Saturation concentration of EGF on half max regulation of Epth proliferation	1500	pM	Estimated ^[41]	
S_{M1}	Saturation concentration of M1 on half max regulation of LCC apoptosis	3e6	ml ⁻¹	Estimated	
S_{M2}	Saturation concentration of M2 on half max regulation of LCC apoptosis	5e5	ml ⁻¹	Estimated	
$S_{IFN-\gamma_M1}$	Saturation concentration of M1	1e4	pM	Estimated ^[49]	

	on half max regulation of IFN- γ production by T cells				
$S_{IFN-\gamma_M2}$	Saturation concentration of M2 on half max regulation of IFN- γ production by T cells	1e6	pM	[50]	
$S_{IL-6_IL-1\beta}$	Saturation concentration of IL-1 β on half max regulation of IL-6 production by Epith	1000	pM	Estimated ^[42]	
$S_{IL-8_IL-1\beta_LCC}$	Saturation concentration of IL-1 β on half max regulation of IL-8 production by LCC	1000	pM	Estimated ^[43]	
$S_{IL-8_IL-1\beta_Epith}$	Saturation concentration of IL-1 β on half max regulation of IL-8 production by Epith	1000	pM	Estimated ^[43]	
S_{IL-10_IL-10}	Saturation concentration of IL-10 on half max regulation of IL-10 production by M2	3	pM	Estimated ^[48]	
S_{IL-10_EGF}	Saturation concentration of EGF on half max regulation of IL-10 production by LCC	1000	pM	Estimated ^[14]	
$S_{VEGF_HGF_LCC}$	Saturation concentration of HGF on half max regulation of VEGF production by LCC	1000	pM	Estimated ^[44]	
$S_{VEGF_TGF-\beta_LCC}$	Saturation concentration of TGF- β on half max regulation of VEGF production by LCC	1000	pM	Estimated ^[45]	
$S_{VEGF_TGF-\beta_CAF}$	Saturation concentration of TGF- β on half max regulation of VEGF production by CAF	1000	pM	Estimated ^[45]	
$S_{VEGF_TGF-\beta_Epith}$	Saturation concentration of TGF- β on half max regulation of VEGF production by Epith	1000	pM	Estimated ^[46]	
S_{VEGF_LCC}	Half max concentration of LCC in hypoxia dependent VEGF production	1000	ml ⁻¹	Estimated ^[46]	
$S_{M-CSF_IL-1\beta}$	Saturation concentration of IL-1 β on half max regulation of M-CSF production by Epith	1000	pM	Estimated ^[43]	
$S_{GM-CSF_IL-1\beta}$	Saturation concentration of IL-1 β on half max regulation of GM-CSF production by Epith	1000	pM	Estimated ^[43]	
$S_{TNF-\alpha_IL-10}$	Saturation concentration of IL-10 on half max regulation of TNF- α production by M1	2.688	pM	Estimated ^[48]	
n_{LCC_IL-10}	Hill coefficient of LCC proliferation regulation by IL-10	0.3		[14]	
n_{LCC_VEGF}	Hill coefficient of LCC proliferation regulation by VEGF	2		Estimated ^[15]	

n_{LCC_EGF}	Hill coefficient of LCC proliferation regulation by EGF	0.405		[14]	
n_{LCC_FGF}	Hill coefficient of LCC proliferation regulation by FGF	2		Estimated ^[16, 17]	
n_{LCC_HGF}	Hill coefficient of LCC proliferation regulation by HGF	2		[18]	
n_{LCC_IGF-1}	Hill coefficient of LCC proliferation regulation by IGF-1	0.8918		[19]	
n_{LCC_PGE2}	Hill coefficient of LCC proliferation regulation by PGE2	1.4		[20]	
n_{LCC_SDF-1}	Hill coefficient of LCC proliferation regulation by SDF-1	2.242		[21]	
n_{cell_IL-6}	Hill coefficient of angiogenic effect regulation by IL-6	1		[22, 23]	
n_{cell_IL-8}	Hill coefficient of angiogenic effect regulation by IL-8	1		[24]	
n_{cell_VEGF}	Hill coefficient of angiogenic effect regulation by VEGF	1		[24-27]	
n_{cell_PDGF}	Hill coefficient of angiogenic effect regulation by PDGF	1		[25]	
n_{cell_FGF}	Hill coefficient of angiogenic effect regulation by FGF	1		[27, 28]	
$n_{cell_TGF\beta}$	Hill coefficient of angiogenic effect regulation by TGF- β	1		[27, 29]	
n_{cell_SDF-1}	Hill coefficient of angiogenic effect regulation by SDF-1	1		[30, 31]	
n_{cell_MCP-1}	Hill coefficient of angiogenic effect regulation by MCP-1	1		[32]	
$n_{cell_TNF-\alpha}$	Hill coefficient of angiogenic effect regulation by TNF- α	1		[33, 34]	
$n_{CAF_PDGF_r}$	Hill coefficient of CAF recruitment regulation by PDGF	2		Estimated	
n_{CAF_FGF}	Hill coefficient of CAF recruitment regulation by FGF	2		Estimated	
$n_{CAF_TGF-\beta}$	Hill coefficient of CAF recruitment regulation by TGF- β	2		Estimated	
$n_{CAF_PDGF_p}$	Hill coefficient of CAF proliferation regulation by PDGF	2.707		[35]	
n_{CAF_PGE2}	Hill coefficient of CAF proliferation regulation by PGE2	1.678		[36]	
$n_{CAF_MSC_PDGF}$	Hill coefficient of differentiation regulation from MSC to CAF by PDGF	1		Estimated ^[37]	
$n_{CAF_MSC_TGF-\beta}$	Hill coefficient of differentiation regulation from MSC to CAF by	1		Estimated ^[38]	

	TGF- β				
n_{M_VEGF}	Hill coefficient of monocyte/ macrophage recruitment regulation by VEGF	2		Estimated ^[10]	
n_{M_PDGF}	Hill coefficient of monocyte/ macrophage recruitment regulation by PDGF	2		Estimated ^[37]	
n_{M_M-CSF}	Hill coefficient of monocyte/ macrophage recruitment regulation by M-CSF	2		Estimated ^[10]	
n_{M_MCP-1}	Hill coefficient of monocyte/ macrophage recruitment regulation by MCP-1	2		Estimated ^[10, 39]	
$n_{M1_M2_TNF-\alpha}$	Hill coefficient of activation regulation from M2 to M1 by TNF- α	1		Estimated ^[11]	
$n_{M1_M2_IFN-\gamma}$	Hill coefficient of activation regulation from M2 to M1 by IFN- γ	1		Estimated ^[47]	
$n_{M1_M2_IL-10}$	Hill coefficient of activation regulation from M2 to M1 by IL-10	1		Estimated ^[48]	
n_{MSC_VEGF}	Hill coefficient of MSC recruitment regulation by VEGF	2		Estimated	
n_{MSC_HGF}	Hill coefficient of MSC recruitment regulation by HGF	2		Estimated	
n_{MSC_SDF-1}	Hill coefficient of MSC recruitment regulation by SDF-1	2		Estimated	
n_{MSC_MCP-1}	Hill coefficient of MSC recruitment regulation by MCP-1	2		Estimated	
n_{Epith_IL-8}	Hill coefficient of Epith proliferation regulation by IL-8	1		Estimated ^[41]	
n_{Epith_EGF}	Hill coefficient of Epith proliferation regulation by EGF	1		Estimated ^[41]	
$n_{IL-6_IL-1\beta}$	Hill coefficient of IL-6 production regulation from Epith by IL-1 β	1		Estimated ^[42]	
$n_{IL-8_IL-1\beta_LCC}$	Hill coefficient of IL-8 production regulation from LCC by IL-1 β	1		Estimated ^[43]	
$n_{IL-8_IL-1\beta_Epith}$	Hill coefficient of IL-8 production regulation from Epith by IL-1 β	1		Estimated ^[43]	
n_{IL-10_IL-10}	Hill coefficient of IL-10 production regulation from M2 by IL-10	1		[48]	
n_{IL-10_EGF}	Hill coefficient of IL-10 production regulation from LCC by EGF	1		Estimated ^[14]	

$n_{VEGF_HGF_LCC}$	Hill coefficient of VEGF production regulation from LCC by HGF	1		Estimated ^[44]	
$n_{VEGF_TGF-\beta_LCC}$	Hill coefficient of VEGF production regulation from LCC by TGF- β	1		Estimated ^[45]	
$n_{VEGF_TGF-\beta_CAF}$	Hill coefficient of VEGF production regulation from CAF by TGF- β	1		Estimated ^[45]	
$n_{VEGF_TGF-\beta_Epith}$	Hill coefficient of VEGF production regulation from Epith by TGF- β	1		Estimated ^[46]	
n_{VEGF_LCC}	Hill coefficient of VEGF production regulation from LCC due to hypoxia and hypoglycemia	1		Estimated ^[46]	
$n_{M-CSF_IL-1\beta}$	Hill coefficient of M-CSF production regulation from Epith by IL-1 β	1		Estimated ^[43]	
$n_{GM-CSF_IL-1\beta}$	Hill coefficient of GM-CSF production regulation from Epith by IL-1 β	1		Estimated ^[43]	
d_{LCC}	Death rate of lung cancer cell based on lifespan	0.001	h^{-1}	^[51]	$\frac{\ln 2}{\text{cell half-life}}$ Half-life ~29 days
d_{CAF}	Death rate of cancer-associated fibroblasts based on lifespan	0.001	h^{-1}	^[51]	Half-life ~29 days
d_{M1}	Death rate of M1 based on lifespan	0.0004 3	h^{-1}	^[52]	Half-life ~67 days
d_{M2}	Death rate of M2 based on lifespan	0.0004 3	h^{-1}	^[52]	Half-life ~67 days
d_{MSC}	Death rate of mesenchymal stem cells based on lifespan	0.0003 47	h^{-1}	^[51, 53]	Half-life ~83 days
d_{Epith}	Death rate of epithelial cells based on lifespan	0.0006	h^{-1}	^[51, 54]	Half-life ~48 days
$d_{IL-1\beta}$	Death rate of IL-1 β based on lifespan	0.6931	h^{-1}	^[55-60]	Half-life ~1 hour
d_{IL-6}	Death rate of IL-6 based on lifespan	0.6931	h^{-1}	^[55-60]	Half-life ~1 hour
d_{IL-8}	Death rate of IL-8 based on lifespan	0.6931	h^{-1}	^[55-60]	Half-life ~1 hour
d_{IL-10}	Death rate of IL-10 based on lifespan	0.6931	h^{-1}	^[55-60]	Half-life ~1 hour
d_{VEGF}	Death rate of VEGF based on lifespan	0.6931	h^{-1}	^[55-60]	Half-life ~1 hour
d_{PDGF}	Death rate of PDGF based on lifespan	0.6931	h^{-1}	^[55-60]	Half-life ~1 hour
d_{EGF}	Death rate of EGF based on	0.6931	h^{-1}	^[55-60]	Half-life ~1

	lifespan				hour
d_{FGF}	Death rate of FGF based on lifespan	0.6931	h^{-1}	[55-60]	Half-life ~1 hour
d_{HGF}	Death rate of HGF based on lifespan	0.6931	h^{-1}	[55-60]	Half-life ~1 hour
d_{IGF-1}	Death rate of IGF-1 based on lifespan	0.6931	h^{-1}	[55-60]	Half-life ~1 hour
d_{PGE2}	Death rate of PGE2 based on lifespan	0.6931	h^{-1}	[55-60]	Half-life ~1 hour
$d_{TGF-\beta}$	Death rate of TGF- β based on lifespan	0.6931	h^{-1}	[55-60]	Half-life ~1 hour
d_{SDF-1}	Death rate of SDF-1 based on lifespan	0.6931	h^{-1}	[55-60]	Half-life ~1 hour
d_{M-CSF}	Death rate of M-CSF based on lifespan	0.6931	h^{-1}	[55-60]	Half-life ~1 hour
d_{GM-CSF}	Death rate of GM-CSF based on lifespan	0.6931	h^{-1}	[55-60]	Half-life ~1 hour
d_{MCP-1}	Death rate of MCP-1 based on lifespan	0.6931	h^{-1}	[55-60]	Half-life ~1 hour
$d_{IFN-\gamma}$	Death rate of IFN- γ based on lifespan	0.5	h^{-1}	[61, 62]	Half-life ~1 hour
$d_{TNF-\alpha}$	Death rate of TNF- α based on lifespan	0.6931	h^{-1}	[55-60]	Half-life ~1 hour
P_{LCC_Epith}	Probability of dividing Epith mutate to LCC during each cell cycle	1e-10		[63]	
P_{M1_M2}	Probability of dividing M2 activate to M1 during each cell cycle	1e-8		Estimated ^[1, 49]	
P_{CAF_MSC}	Probability of dividing MSC differentiate to CAF during each cell cycle	0.05		Estimated	
P_{MSC_CAF}	Probability of dividing CAF dedifferentiate to MSC during each cell cycle	1e-9		Estimated	
$k_{IL-1\beta_LCC}$	Secretion rate of IL-1 β by LCC	60	$10^{-21}mol h^{-1}$	Estimated ^[19]	
$k_{IL-1\beta_M1}$	Secretion rate of IL-1 β by M1	34	$10^{-21}mol h^{-1}$	Estimated ^[10, 40]	
k_{IL-6_CAF}	Secretion rate of IL-6 by CAF	30	$10^{-21}mol h^{-1}$	Estimated ^[10]	
k_{IL-6_M1}	Secretion rate of IL-6 by M1	30	$10^{-21}mol h^{-1}$	Estimated ^[10, 40]	
k_{IL-6_MSC}	Secretion rate of IL-6 by MSC	40	$10^{-21}mol h^{-1}$	Estimated ^[10]	
k_{IL-6_Epith}	Secretion rate of IL-6 by Epith	1	$10^{-21}mol h^{-1}$	Estimated ^[42]	
k_{IL-8_LCC}	Secretion rate of IL-8 by LCC	122	$10^{-21}mol h^{-1}$	[64]	

k_{IL-8_CAF}	Secretion rate of IL-8 by CAF	60	$10^{-21} \text{mol h}^{-1}$	Estimated ^[65]	
k_{IL-8_MSC}	Secretion rate of IL-8 by MSC	60	$10^{-21} \text{mol h}^{-1}$	Estimated ^[10]	
k_{IL-8_Epith}	Secretion rate of IL-8 by Epith	2	$10^{-21} \text{mol h}^{-1}$	Estimated ^[42, 43]	
k_{IL-10_LCC}	Secretion rate of IL-10 by LCC	40	$10^{-21} \text{mol h}^{-1}$	Estimated ^[14]	
k_{IL-10_M2}	Secretion rate of IL-10 by M2	120	$10^{-21} \text{mol h}^{-1}$	Estimated ^[40]	
k_{VEGF_LCC}	Secretion rate of VEGF by LCC	30	$10^{-21} \text{mol h}^{-1}$	Estimated ^[19, 44, 45, 66]	
k_{VEGF_CAF}	Secretion rate of VEGF by CAF	90	$10^{-21} \text{mol h}^{-1}$	Estimated ^[45, 65]	
k_{VEGF_M2}	Secretion rate of VEGF by M2	90	$10^{-21} \text{mol h}^{-1}$	Estimated ^[67]	
k_{VEGF_MSC}	Secretion rate of VEGF by MSC	60	$10^{-21} \text{mol h}^{-1}$	Estimated ^[10]	
k_{VEGF_Epith}	Secretion rate of VEGF by Epith	2	$10^{-21} \text{mol h}^{-1}$	Estimated ^[46]	
k_{PDGF_LCC}	Secretion rate of PDGF by LCC	30	$10^{-21} \text{mol h}^{-1}$	Estimated ^[10]	
k_{PDGF_MSC}	Secretion rate of PDGF by MSC	60	$10^{-21} \text{mol h}^{-1}$	Estimated ^[10]	
k_{PDGF_Epith}	Secretion rate of PDGF by Epith	2	$10^{-21} \text{mol h}^{-1}$	Estimated ^[68]	
k_{EGF_LCC}	Secretion rate of EGF by LCC	150	$10^{-21} \text{mol h}^{-1}$	Estimated ^[69]	
k_{EGF_M2}	Secretion rate of EGF by M2	90	$10^{-21} \text{mol h}^{-1}$	Estimated ^[67]	
k_{FGF_LCC}	Secretion rate of FGF by LCC	60	$10^{-21} \text{mol h}^{-1}$	Estimated ^[10, 70]	
k_{FGF_CAF}	Secretion rate of FGF by CAF	104	$10^{-21} \text{mol h}^{-1}$	Estimated ^[65]	
k_{FGF_MSC}	Secretion rate of FGF by MSC	30	$10^{-21} \text{mol h}^{-1}$	Estimated ^[10]	
k_{HGF_CAF}	Secretion rate of HGF by CAF	30	$10^{-21} \text{mol h}^{-1}$	Estimated ^[10]	
k_{IGF-1_M1}	Secretion rate of IGF-1 by M1	40	$10^{-21} \text{mol h}^{-1}$	Estimated ^[19]	
k_{IGF-1_M2}	Secretion rate of IGF-1 by M2	80	$10^{-21} \text{mol h}^{-1}$	Estimated ^[19]	
k_{PGE2_LCC}	Secretion rate of PGE-2 by LCC	800	$10^{-21} \text{mol h}^{-1}$	Estimated ^[71]	
$k_{TGF-\beta_LCC}$	Secretion rate of TGF- β by LCC	60	$10^{-21} \text{mol h}^{-1}$	Estimated ^[72]	
$k_{TGF-\beta_CAF}$	Secretion rate of TGF- β by CAF	60	$10^{-21} \text{mol h}^{-1}$	Estimated ^[10]	
$k_{TGF-\beta_M2}$	Secretion rate of TGF- β by M2	10	$10^{-21} \text{mol h}^{-1}$	Estimated ^[73]	

$k_{TGF-\beta_Epith}$	Secretion rate of TGF- β by Epith	0.5	10^{-21} mol h^{-1}	Estimated ^[74]	
k_{SDF-1_LCC}	Secretion rate of SDF-1 by LCC	93.10	10^{-21} mol h^{-1}	^[21]	
k_{SDF-1_CAF}	Secretion rate of SDF-1 by CAF	23.68	10^{-21} mol h^{-1}	^[21]	
k_{M-CSF_Epith}	Secretion rate of M-CSF by Epith	1	10^{-21} mol h^{-1}	Estimated ^[43]	
k_{GM-CSF_LCC}	Secretion rate of GM-CSF by LCC	100	10^{-21} mol h^{-1}	Estimated ^[19]	
k_{GM-CSF_Epith}	Secretion rate of GM-CSF by Epith	0.5	10^{-21} mol h^{-1}	Estimated ^[42, 43]	
k_{MCP-1_CAF}	Secretion rate of MCP-1 by CAF	30	10^{-21} mol h^{-1}	Estimated ^[10]	
$k_{IFN-\gamma_T}$	Secretion rate of IFN- γ by T cell	161.76	10^{-21} mol h^{-1}	^[1]	
$k_{TNF-\alpha_M1}$	Secretion rate of TNF- α by M1	98.04	10^{-21} mol h^{-1}	^[1, 40]	
$k_{TNF-\alpha_CAF}$	Secretion rate of TNF- α by CAF	30	10^{-21} mol h^{-1}	Estimated ^[10, 75, 76]	

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