

Supplementary Material

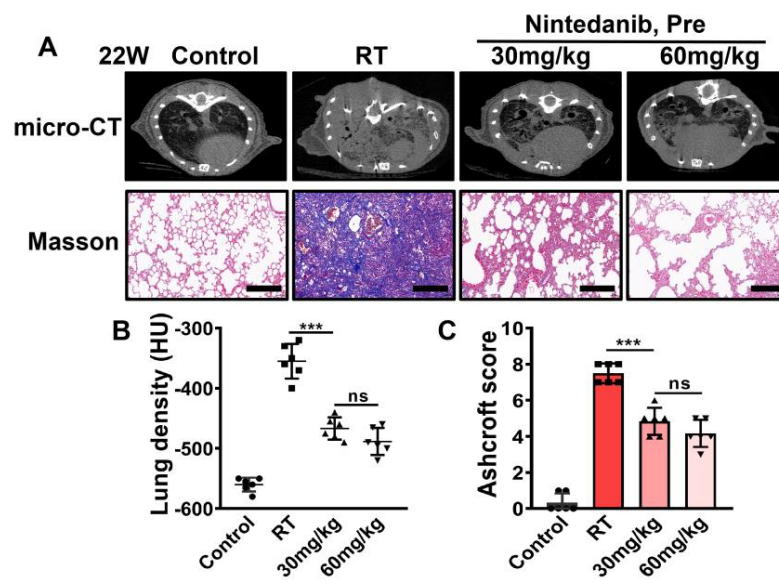


Figure S1. (A) Representative micro-CT images Masson's trichrome staining of lung samples from different treatment groups at week 22 post-radiation. (B) Assessment of lung density in micro-CT images. (C) Ashcroft score was used to determine the pulmonary fibrosis degree. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$, ns: not significant.

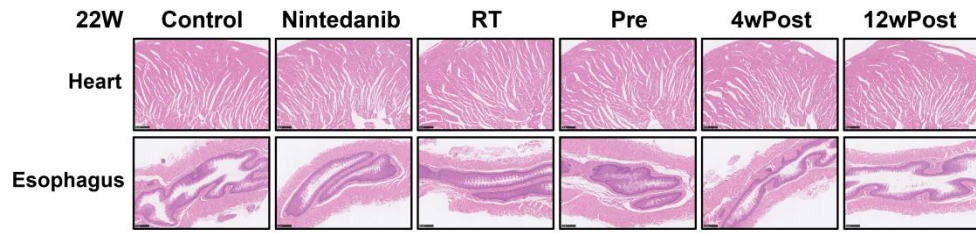


Figure S2. The results of hematoxylin and eosin (H&E) staining of heart and esophagus samples obtained at week 22 post-radiation (scale bar = 250 μ m).

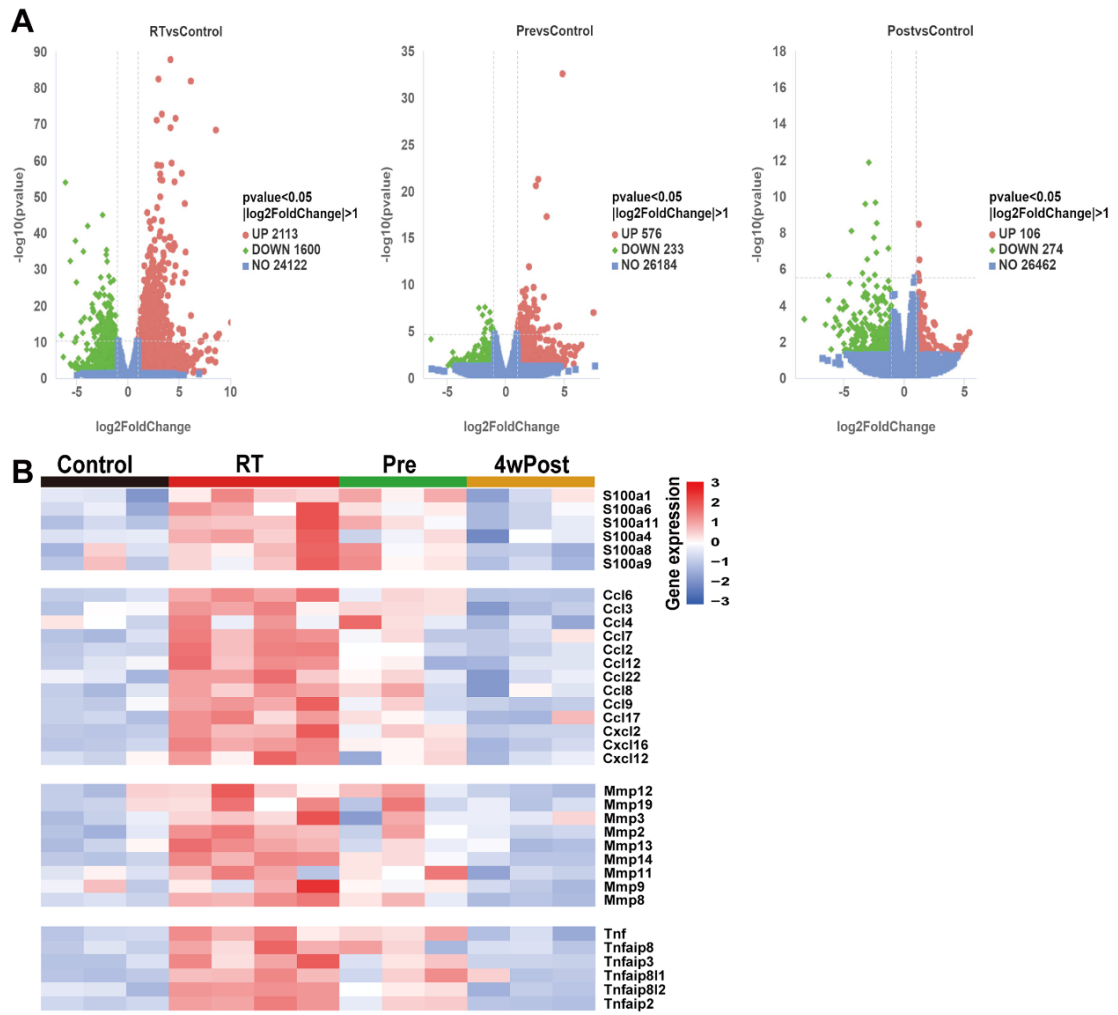


Figure S3. (A) Volcano plot of selected DEGs in the RT, Pre and 4wPost groups relative to control. (B) The expression levels of representative inflammation-related genes and ECM remodeling-related genes.

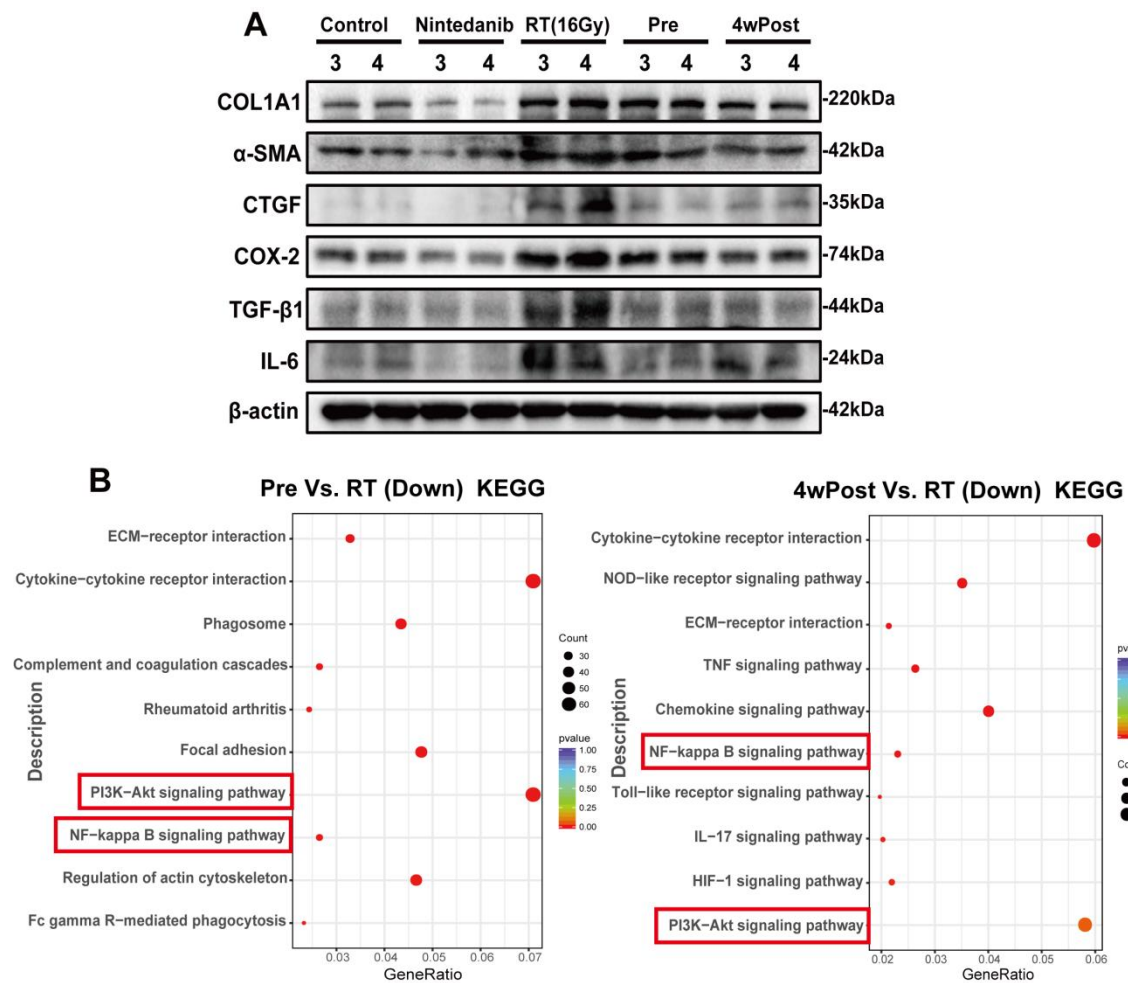


Figure S4. (A) Representative western blot images of COL1A1, α -SMA, CTGF, COX-2, TGF- β and IL-6 in lung tissue of mice. (B) Enriched KEGG dot plot from Pre vs. RT (down) groups and 4wPost vs. RT (down) groups. Noteworthy signaling pathways were marked with red rectangles.

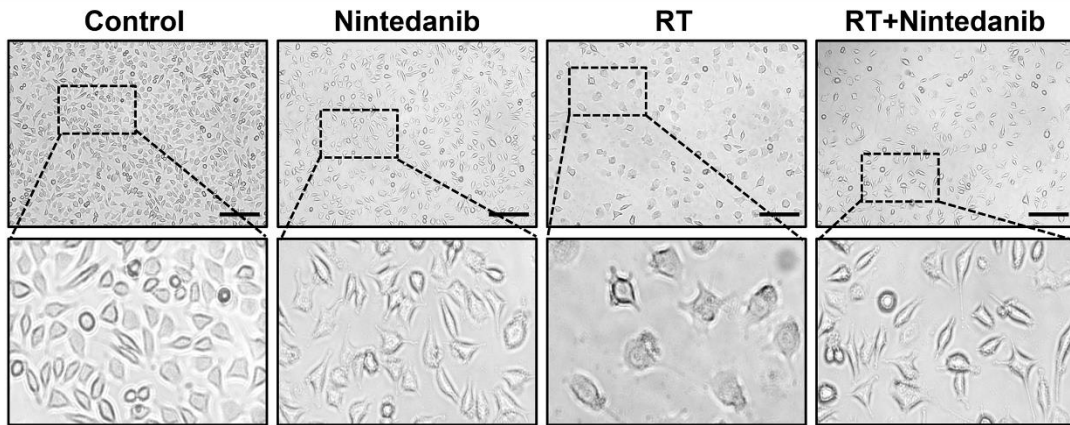


Figure S5. The morphological changes in L929 fibroblasts after different treatments. Scale bar = 200 μ m.

Table S1. Union list of the top 100 inflammation-related GO terms for the DEGs from the RT vs. control groups, Pre vs. control groups, and 4wPost vs. control groups.

GOID	Description	GeneRatio	pvalue
GO:0035456	response to interferon-beta	12/427	1.29E-09
GO:0035458	cellular response to interferon-beta	11/427	1.46E-09
GO:0071346	cellular response to interferon-gamma	12/427	9.57E-06
GO:0034341	response to interferon-gamma	12/427	6.34E-05
GO:0060330	regulation of response to interferon-gamma	4/427	3.23E-04
GO:0060334	regulation of interferon-gamma-mediated signaling pathway	4/427	3.23E-04
GO:0072593	reactive oxygen species metabolic process	16/427	4.93E-04
GO:0060333	interferon-gamma-mediated signaling pathway	4/427	1.39E-03
GO:0010634	positive regulation of epithelial cell migration	10/427	1.47E-03
GO:0001961	positive regulation of cytokine-mediated signaling pathway	5/427	3.49E-03
GO:0000305	response to oxygen radical	4/427	5.00E-03
GO:0060760	positive regulation of response to cytokine stimulus	5/427	5.76E-03
GO:0014909	smooth muscle cell migration	7/427	5.90E-03
GO:0010595	positive regulation of endothelial cell migration	7/427	6.29E-03
GO:0070665	positive regulation of leukocyte proliferation	9/427	7.82E-03
GO:0034599	cellular response to oxidative stress	13/427	7.90E-03
GO:0060326	cell chemotaxis	13/427	1.09E-02
GO:0002443	leukocyte mediated immunity	63/999	5.46E-19
GO:0030595	leukocyte chemotaxis	48/999	8.64E-19
GO:0002250	adaptive immune response	67/999	1.48E-18
GO:0060326	cell chemotaxis	56/999	1.86E-18
GO:0050900	leukocyte migration	61/999	2.27E-18
GO:0097529	myeloid leukocyte migration	45/999	3.75E-18
GO:0002694	regulation of leukocyte activation	76/999	1.66E-16
GO:0002274	myeloid leukocyte activation	44/999	3.50E-16
GO:0002697	regulation of immune effector process	61/999	1.28E-15
GO:0030593	neutrophil chemotaxis	29/999	1.38E-15
GO:0097530	granulocyte migration	35/999	1.49E-15
GO:0071621	granulocyte chemotaxis	32/999	2.81E-15
GO:1990266	neutrophil migration	31/999	6.13E-15
GO:0001819	positive regulation of cytokine production	63/999	1.23E-13
GO:0002253	activation of immune response	57/999	2.00E-13
GO:0019221	cytokine-mediated signaling pathway	56/999	2.48E-13
GO:0006909	phagocytosis	39/999	2.89E-13
GO:0002703	regulation of leukocyte mediated immunity	40/999	6.98E-13
GO:0031349	positive regulation of defense response	52/999	9.71E-13
GO:0002444	myeloid leukocyte mediated immunity	26/999	1.03E-12

GO:0046651	lymphocyte proliferation	48/999	3.72E-12
GO:0006959	humoral immune response	32/999	3.79E-12
GO:0032943	mononuclear cell proliferation	48/999	4.90E-12
GO:0050663	cytokine secretion	40/999	9.05E-12
GO:0042110	T cell activation	64/999	1.07E-11
GO:0050670	regulation of lymphocyte proliferation	41/999	1.08E-11
GO:0032944	regulation of mononuclear cell proliferation	41/999	1.47E-11
GO:0002696	positive regulation of leukocyte activation	49/999	1.49E-11
GO:0050727	regulation of inflammatory response	49/999	1.69E-11
GO:0070661	leukocyte proliferation	48/999	2.11E-11
GO:0002449	lymphocyte mediated immunity	42/999	2.28E-11
GO:0002526	acute inflammatory response	28/999	2.51E-11
GO:0002764	immune response-regulating signaling pathway	48/999	3.50E-11
GO:0070663	regulation of leukocyte proliferation	41/999	3.64E-11
GO:0002275	myeloid cell activation involved in immune response	23/999	4.86E-11
GO:0002886	regulation of myeloid leukocyte mediated immunity	19/999	5.18E-11
GO:0051249	regulation of lymphocyte activation	57/999	6.03E-11
GO:0002685	regulation of leukocyte migration	36/999	6.51E-11
GO:0002690	positive regulation of leukocyte chemotaxis	24/999	6.70E-11
GO:0002688	regulation of leukocyte chemotaxis	27/999	7.10E-11
GO:0002819	regulation of adaptive immune response	32/999	7.79E-11
GO:0045088	regulation of innate immune response	42/999	8.23E-11
GO:0034612	response to tumor necrosis factor	34/999	1.14E-10
GO:0002366	leukocyte activation involved in immune response	40/999	1.20E-10
GO:0019724	B cell mediated immunity	27/999	1.40E-10
GO:0002687	positive regulation of leukocyte migration	30/999	1.81E-10
GO:0002263	cell activation involved in immune response	40/999	2.10E-10
GO:0050764	regulation of phagocytosis	23/999	2.54E-10
GO:0002521	leukocyte differentiation	66/999	3.03E-10
GO:0034341	response to interferon-gamma	28/999	3.36E-10
GO:0016064	immunoglobulin mediated immune response	26/999	4.85E-10
GO:0045807	positive regulation of endocytosis	31/999	6.05E-10
GO:0007159	leukocyte cell-cell adhesion	46/999	7.74E-10
GO:0002757	immune response-activating signal transduction	44/999	7.84E-10
GO:0050707	regulation of cytokine secretion	34/999	9.26E-10
GO:0030100	regulation of endocytosis	40/999	1.53E-09
GO:0002821	positive regulation of adaptive immune response	24/999	1.97E-09
GO:0042098	T cell proliferation	35/999	2.51E-09
GO:1903555	regulation of tumor necrosis factor superfamily cytokine production	28/999	2.68E-09
GO:0002705	positive regulation of leukocyte mediated immunity	26/999	3.65E-09
GO:0071706	tumor necrosis factor superfamily cytokine production	28/999	4.53E-09

GO:0050766	positive regulation of phagocytosis	18/999	4.53E-09
GO:0071674	mononuclear cell migration	19/999	6.33E-09
GO:1903037	regulation of leukocyte cell-cell adhesion	41/999	6.44E-09
GO:0006911	phagocytosis, engulfment	16/999	8.32E-09
GO:0032680	regulation of tumor necrosis factor production	27/999	8.37E-09
GO:0002446	neutrophil mediated immunity	13/999	1.00E-08
GO:0050900	leukocyte migration	146/3441	1.19E-30
GO:0050778	positive regulation of immune response	205/3441	5.97E-29
GO:0060326	cell chemotaxis	122/3441	1.09E-24
GO:0001819	positive regulation of cytokine production	164/3441	1.41E-24
GO:0002274	myeloid leukocyte activation	97/3441	9.33E-24
GO:0097529	myeloid leukocyte migration	91/3441	2.70E-22
GO:0030595	leukocyte chemotaxis	96/3441	5.67E-22
GO:0002253	activation of immune response	141/3441	1.19E-21
GO:0031349	positive regulation of defense response	130/3441	1.33E-21
GO:0030335	positive regulation of cell migration	184/3441	8.32E-21
GO:0002250	adaptive immune response	143/3441	1.80E-20
GO:0002685	regulation of leukocyte migration	91/3441	4.28E-20
GO:0045088	regulation of innate immune response	108/3441	1.82E-19
GO:0002443	leukocyte mediated immunity	128/3441	2.17E-19
GO:0002764	immune response-regulating signaling pathway	123/3441	2.74E-19
GO:0002521	leukocyte differentiation	183/3441	4.29E-19
GO:0097530	granulocyte migration	69/3441	4.45E-19
GO:0006909	phagocytosis	86/3441	1.87E-18
GO:0002757	immune response-activating signal transduction	117/3441	2.09E-18
GO:0050663	cytokine secretion	95/3441	2.12E-18
GO:0050727	regulation of inflammatory response	120/3441	2.83E-17
GO:0002687	positive regulation of leukocyte migration	71/3441	4.62E-17
GO:0002694	regulation of leukocyte activation	169/3441	5.72E-17
GO:0071216	cellular response to biotic stimulus	86/3441	6.29E-17
GO:0019221	cytokine-mediated signaling pathway	130/3441	8.14E-17
GO:0098542	defense response to other organism	153/3441	8.33E-17
GO:0050707	regulation of cytokine secretion	84/3441	1.61E-16
GO:0002460	adaptive immune response based on somatic recombination of immune receptors built from immunoglobulin superfamily domains	102/3441	2.38E-16
GO:0032103	positive regulation of response to external stimulus	111/3441	3.13E-16
GO:0009611	response to wounding	155/3441	3.40E-16
GO:1990266	neutrophil migration	57/3441	3.64E-16
GO:0042110	T cell activation	159/3441	7.36E-16
GO:0032635	interleukin-6 production	67/3441	8.39E-16
GO:0045089	positive regulation of innate immune response	88/3441	9.07E-16
GO:0007159	leukocyte cell-cell adhesion	117/3441	1.20E-15
GO:0032675	regulation of interleukin-6 production	64/3441	2.09E-15

GO:0002688	regulation of leukocyte chemotaxis	58/3441	7.25E-15
GO:0050715	positive regulation of cytokine secretion	64/3441	1.50E-14
GO:0002697	regulation of immune effector process	126/3441	1.52E-14
GO:0071621	granulocyte chemotaxis	56/3441	1.85E-14
GO:0002366	leukocyte activation involved in immune response	93/3441	2.68E-14
GO:0002263	cell activation involved in immune response	94/3441	3.29E-14
GO:0070661	leukocyte proliferation	111/3441	4.90E-14
GO:0032943	mononuclear cell proliferation	107/3441	8.72E-14
GO:0046651	lymphocyte proliferation	106/3441	1.33E-13
GO:0002224	toll-like receptor signaling pathway	50/3441	1.75E-13
GO:0002690	positive regulation of leukocyte chemotaxis	48/3441	2.49E-13
GO:0030198	extracellular matrix organization	88/3441	3.41E-13
GO:1903555	regulation of tumor necrosis factor superfamily cytokine production	64/3441	3.53E-13
GO:0002573	myeloid leukocyte differentiation	84/3441	3.99E-13
GO:0042060	wound healing	119/3441	4.35E-13
GO:0051249	regulation of lymphocyte activation	136/3441	7.27E-13
GO:0043410	positive regulation of MAPK cascade	164/3441	1.11E-12
GO:0071706	tumor necrosis factor superfamily cytokine production	64/3441	1.23E-12
GO:0002699	positive regulation of immune effector process	81/3441	1.52E-12
GO:0032680	regulation of tumor necrosis factor production	62/3441	2.08E-12
GO:0002218	activation of innate immune response	64/3441	2.75E-12
GO:0002449	lymphocyte mediated immunity	90/3441	3.00E-12
GO:1902105	regulation of leukocyte differentiation	101/3441	4.18E-12
GO:0032612	interleukin-1 production	43/3441	4.50E-12
GO:0032640	tumor necrosis factor production	62/3441	4.69E-12
GO:0030593	neutrophil chemotaxis	45/3441	5.49E-12
GO:0032611	interleukin-1 beta production	37/3441	1.08E-11
GO:0002758	innate immune response-activating signal transduction	57/3441	2.15E-11
GO:0002703	regulation of leukocyte mediated immunity	77/3441	3.13E-11
GO:0001776	leukocyte homeostasis	51/3441	4.33E-11
GO:0034612	response to tumor necrosis factor	70/3441	5.49E-11
GO:0032609	interferon-gamma production	52/3441	6.43E-11
GO:0032649	regulation of interferon-gamma production	48/3441	7.28E-11
GO:0072593	reactive oxygen species metabolic process	92/3441	7.71E-11
GO:0050729	positive regulation of inflammatory response	51/3441	1.03E-10
GO:1903037	regulation of leukocyte cell-cell adhesion	96/3441	1.12E-10