

b

	Day 10				Day 14			Day 20			Day 40		
	Plg+/+	Plg+/-	Plg-/-										
Plg+/+	-	*	ns	-	*	ns	-	**	**	-	*	*	
Plg+/-	*	-	ns	*	-	ns	**	-	ns	*	-	ns	
Plg-/-	ns	ns	-	ns	ns	-	**	ns	-	*	ns	-	

Supplementary Fig. 1. A comparison of the quality of dorsal skin in plg+/+, plg+/- and plg-/- mice at different days after irradiation. (a) Skin scores for plg+/+, plg+/- and plg-/- mice at different days after irradiation. (b) Statistical analysis of skin scores between plg+/+, plg+/- and plg-/- mice at different days after irradiation. * p<0.05, ns= not significant.



Supplementary Fig. 2. The thickness of epidermis increases significantly after irradiation in plg+/+ mice, but not in plg-/- mice. Representative photographs of H&E stained skin sections from plg+/+ and plg-/- mice at diffrent days after irradiation. Magnification 100x.



Supplementary Fig. 3. The number of vessels increases significantly after irradiation in plg+/+ mice, but not in plg-/- mice. Representative photographs of CD31 (red) and DAPI (blue) staining of skin sections from plg+/+ and plg-/- mice at different days after irradiation. Magnification 100x.



Supplementary Fig. 4. The number of proliferating cells increases significantly after irradiation in plg+/+ mice, but not in plg-/- mice. Representative photographs of Ki67 (red) and DAPI (blue) staining of skin sections from plg+/+ and plg-/- mice at different days after irradiation. Magnification 200x.



Supplementary Fig. 5. Apoptosis in the skin of plg+/+ and plg-/- mice after irradiation. Representative photographs of TUNEL (green) and DAPI (blue) staining of skin sections from plg+/+ and plg-/- mice at different days after irradiation. Magnification 200x.



Supplementary Fig. 6. Reactive oxygen spicies (ROS) in the skin of plg+/+ and plg-/- mice after irradiation. Representative photographs of 8-Oxo-2´-deoxyguanosine (brown) and Hematoxylin (purple) staining of skin sections from plg+/+ and plg-/- mice at different days after irradiation. Magnification 200x.



Supplementary Fig. 7. Large numbers of neutrophils and NETS infiltrate irradiated skin in plg+/+ mice, but not in plg-/- mice. Representative photographs of immunostaining of neutrophils (red), DAPI (blue), and NETs (citrulinated histon 3, green) on skin sections from plg+/+ and plg-/- mice at different days after irradiation. Magnification 100x.



Supplementary Fig. 8. Macrophage accumulation in the skin of plg+/+ and plg-/- mice after irradiation. Representative photographs of (CD68) (red) and DAPI (blue) staining of skin sections from plg+/+ and plg-/- mice at different days after irradiation. Magnification 100x.

а	Cell extract from	Days after irradiation								
	HT-1080 Cells + <u>hTGF</u> β	<i>Plg-/-</i> Day 0	<i>Plg-/-</i> Day 3	<i>Plg-/-</i> Day 9	<i>Plg-/-</i> Day 16	<i>Plg+/+</i> Day 0	Plg+/+ Day 3 	<i>Plg+/+</i> Day 9 	<i>Plg+/+</i> Day 16	
P-Smad2	•		-	-	-		-	-	-	
Smad2	-	-	-	-	-	-	-	-	-	
β-actin	-	-	-	-	-	-	-	-	-	



Supplementary Fig. 9. Activation (phosphorylation) of Smad2 in the skin of *plg+/+* and *plg-/-* mice after irradiation. (a) Representative photograph of western blot of skin samples from *plg+/+* and *plg-/-* mice at different days after irradiation. β -actin was used as an internal control. HT-1080 cells induced by hTGF β were used as control for P-Smad2 antibody. (b) Quantification of P-Smad2 from the band intensity (n = 4 per time point).



Supplementary Fig. 10. Fibrin accummulation in the skin of plg+/+ and plg-/- mice after irradiation. Representative photographs of fibrin (orange) and DAPI (blue) staining of skin sections from plg+/+ and plg-/- mice at different days after irradiation. Magnification 100x.



Supplementary Fig. 11. Plasminogen activation is neccessary to induce inflammation after irradiation. Skin samples from WT, *tPA-/-;uPA-/-* and *plg-/-* mice were taken at different times after irradiation. Extracts were prepared and analyzed by ELISA ($n \ge 4$ per time point). (a) IL-6 levels , (b) TNF- α levels, (c) IL1- β levels and (d) IL-10 levels in the skin after irradiation.



Supplementary Fig. 12. TXA suppresses the accumulation of pro-inflammatory markers in the skin after irradiation. Skin samples from plg+/+ and plg-/- mice and plg+/+ mice treated with TXA (n \geq 4) were taken at different times after irradiation and extracts were prepared and analyzed by ELISA (n \geq 4 per time point). (a) IL-6 levels, (b) TNF- α levels, (c) IL1- β levels and (d) IL-10 levels in the skin after irradiation.

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Days after irradiation	Statistical significance between <i>plg+/+</i> and and p <i>lg+/+</i> with TXA
Day 10	*
Day 14	*
Day 20	ns

b

Days after irradiation	Statistical significance between <i>plg+/-</i> and and <i>plg+/-</i> with TXA
Day 10	**
Day 14	*
Day 20	ns

Supplementary Table 1. Statistical analysis of skin scores in irradiated mice treated with TXA (Figure 6b and 6d). (a) Statistical analysis of skin scores between plg+/+ and plg+/+ treated with TXA. (b) Statistical analysis of skin scores between plg+/- and plg+/- treated with TXA. * p<0.05. ns= not significant.