6. Song, F., Li, B. & Stocum, D.L. Amphibians as research models for regenerative medicine. *Organogenesis* **6**, 141–150 (2010).
7. Ramos, M.L., Gragnani, A. & Ferreira, L.M. Is there an ideal animal model to study hypertrophic scarring? *J. Burn Care Res.* **29**, 363–368 (2008).
8. Golberg, A.Y. & Yarmush, M.L. Nonthermal irreversible electroporation: Fundamentals, applications, and challenges. *IEEE Trans. Biomed. Eng.* **60**, 707–714 (2013).
9. Narayanan, G. Irreversible electroporation for treatment of liver cancer. *Gastroenterol. Hepatol.* **7**, 313–316 (2011).
10. Maor, E., Ivorra, A., Leor, J. & Rubinsky, B. The effect of irreversible electroporation on blood vessels. *Technol. Cancer Research & Treatment* **6**, 307–312 (2007).
11. Phillips, M.A., Narayan, R., Padath, T. & Rubinsky, B. Irreversible electroporation on the small intestine. *Br. J. Cancer* **106**, 490–495 (2012).
12. Charpentier, K.P. *et al.* Irreversible electroporation of the pancreas in swine: A pilot study. *HPB (Oxford)* **12**, 348–351 (2010).
13. Rubinsky, B., Onik, G. & Mikus, P. Irreversible electroporation: A new ablation modality — clinical implications. *Technol. Cancer Res. Treat.* **6**, 37–48 (2007).
14. Golberg, A., Bei, M., Sheridan, R.L. & Yarmush, M.L. Regeneration and control of human fibroblast cell density by intermittently delivered pulsed electric fields. *Biotechnol. Bioeng.* **110**, 1759–1768 (2013).
15. Moloney, T.C., Hoban, D.B., Barry, F.P., Howard, L. & Dowd, E. Kinetics of thermally induced heat shock protein 27 and 70 expression by bone marrow-derived mesenchymal stem cells. *Protein Sci.* **21**, 904–909 (2012).

SUPPLEMENTARY INFORMATION 1: TEMPERATURE EFFECTS OF PULSED ELECTRIC FIELDS

To evaluate the temperature effects of pulsed electric fields (PEF) we developed a following electo-thermal model.

Geometry

PEF was delivered using contact electrodes we ablated a surface area (A) of 0.0001 m^2 of a dorsal skin of Sprague Dawley female rats. During the treatment, the skin was clamped between the electrodes as appears on **Fig. 1a**. The distance between the electrodes (L) was 0.002 m. Skin density was approximately 1100 (kg m^{-3}); therefore, the mass of a treated skin section was calculated as follows in Equation (S1):

$$m = A\rho L. \tag{S1}$$

Electro-thermal model of skin heating by pulsed electric fields

The heat supplied to the skin by each electric pulse is calculated as appears in Equation (S2):

$$Q = I(n)Vt_p \tag{S2}$$

where Q (Joule) is the heat supplied to the skin by each pulse (n); I(Amp) is the current during the pulse, V (Volt) is the applied voltage. Currents during each pulse were measured for the 40 animals (**Fig. 1c**). To model the effects of electric fields, we used non-parametric regression (described in the Methods section) to construct the equation that described current (I) as a function of pulse number (n). The derived expression appears in Equation (S3):

$$I(n) = 0.482n^{0,352}. \tag{S3}$$

The temperature increase of a treated skin section, immediately after the application of electric field is calculated using Equation (S4):

$$T_{pn} = \frac{Q}{mc_p} + T_{in} \tag{S4}$$

where m (gr) is the mass of a skin section on which electric fields are applied; c_p is the heat capacitance of skin; T_{pn} (K) is the temperature of the treated section of skin immediately after the treatment; T_{pi} (K) is the temperature of the treated section of skin immediately after pulse delivery.

The thermal properties of skin used in this model, and the initial conditions appear in Table 1S.

Next, to decide on the heat conduction model, we calculated the Biot number as appears in Equation (S5):

$$Bi = \frac{hL}{2k}. \tag{S5}$$

The calculated Biot number in this problem is 0.01; therefore, we used Lumped Capacitance Heat Conduction approximation as follows:

$$T_{cn} = T_{env} + (T_{pn} - T_{env})e^{-BiFo} \tag{S6}$$

where T_{cn} (K) is the temperature of the treated skin (with N pulses) section after a cooling period; T_{env} (K) is the environmental temperature; Bi is Biot number and Fo is Fourier number, calculated as appears in Equation (S7):

$$Fo = \frac{kt}{\rho c_p (L/2)^2}. \tag{S7}$$

To obtain the temperature of skin during PEF treatment we solved Equations (S2)–(S4) and (S6) simultaneously for 180 pulses, delivered in groups of 45 at 2 Hz with a pause of 30 s between the groups.

Table 1S Skin thermal properties and environmental conditions during the experiment.

Model parameter	Sign	Value	Ref.
Rat skin heat capacitance (J kg^{-1} K^{-1})	c_p	3000	based on[1,2]
Convection heat transfer coefficient (W m^{-2} K^{-1})	h	4	based on[3]
Skin thermal conductivity (W m^{-1} K^{-1})	k	0.4	based on[2,4,5]
Environmental temperature (K)	T_{env}	298	measured
Initial temperature of the skin before treatment (K)	T_{in}	303	measured

FURTHER READING

1. Holmes, K.R. in *Heat and Mass Transfer in Living Systems*. (ed. K.R. Diller) 18–20 (N.Y. Acad. Sci., 1998).
2. Holmes, K. Thermal properties. http://users.ece.utexas.edu/~valvano/research/Thermal.pdf. (1998).
3. Kurazumi, Y. *et al.* Radiative and convective heat transfer coefficients of the human body in natural convection. *Build. Environ.* **43**, 2142–2153 (2008).
4. Shuangxi, H., Chunli, F., Li, Y., Sun, F. & Wei, K. in *Advanced Computational Intelligence (IWACI)*, 2011 Fourth International Workshop on 447–451 (2011).
5. Stewart, D.A., Gowrishankar, T.R. & Weaver, J.C. Skin heating and injury by prolonged millimeter-wave exposure: Theory based on a skin model coupled to a whole body model and local biochemical release from cells at supraphysiologic temperatures. *IEEE Trans. Plasma Sci.* **34**, 1480–1493 (2006).

SUPPLEMENTARY INFORMATION 2: SKIN REGENERATION 1 WEEK AFTER NON-THERMAL PEF ABLATION

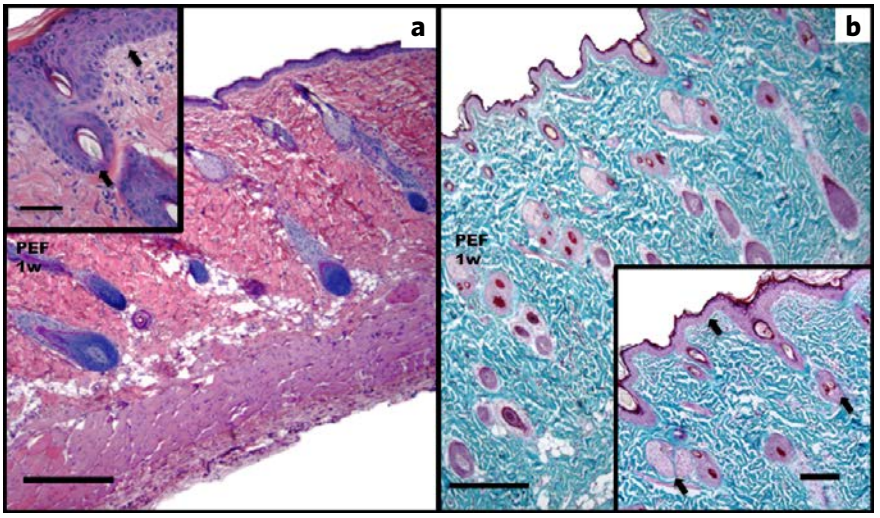

Figure S2 Histological analysis of rat skin 1 week after PEF. (**a**) H&E staining. Shown is regeneration of epidermis (insert arrows), hair follicles (insert arrows) and sebaceous glands (arrows). Epidermis is multilayer (insert arrows). No significant inflammatory infiltration is observed. Scale bars: 500 μm, insert 200 μm. (**b**) Masson's trichrome stain. The collagen network structure is similar to normal skin (**Fig. 3f**). Regenerating sebaceous glands and hair follicles are shown by arrows in the insert. Scale bars: 250 μm, insert 200 μm.