

ARTICLE

***Lactobacillus*-derived artificial extracellular vesicles for skin  
rejuvenation and prevention of photo-aging**

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**Supplementary information**

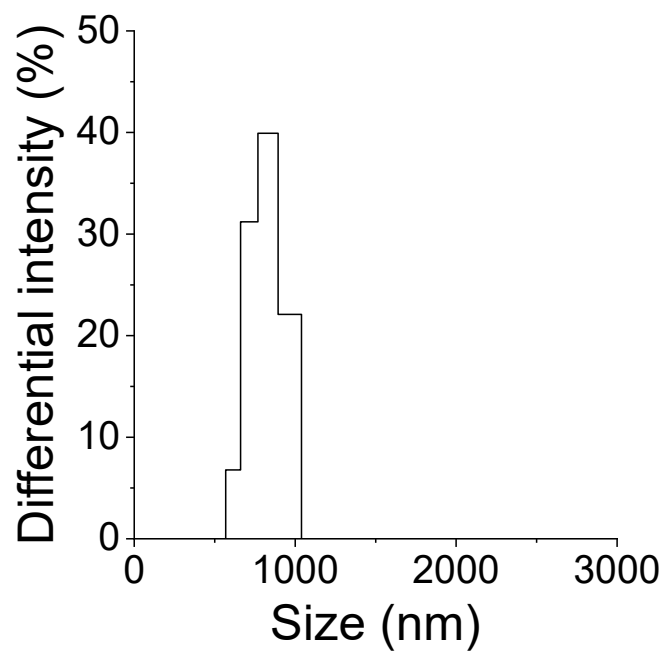


Fig S1. Particle size distribution (DLS) for CLSM analysis

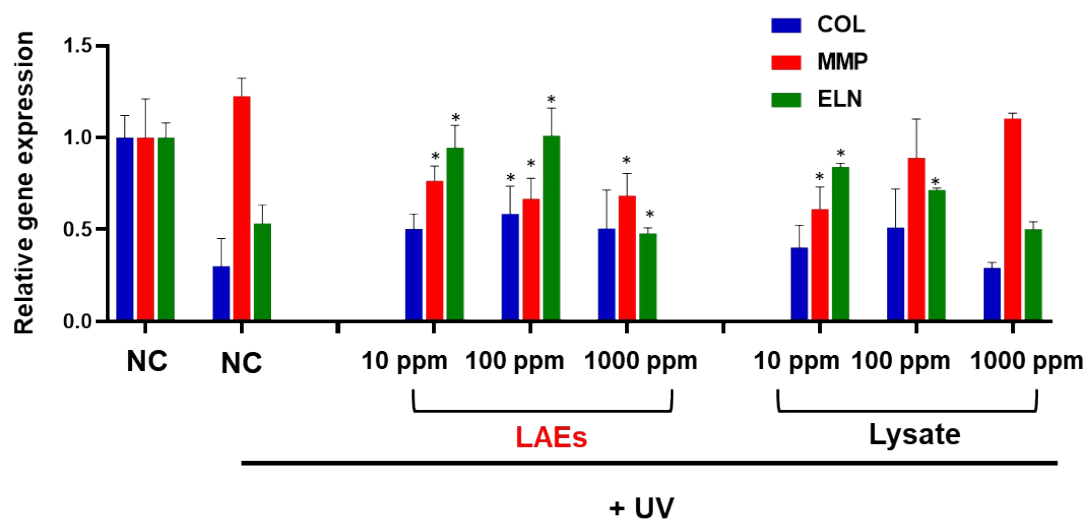


Fig S2. Gene expression of COL1A1 (COL), MMP, and ELN of fibroblasts under UV irradiation. RT-qPCR was performed. All measurements were performed in triplicate. Student's t-test was performed for comparison between control group (0 ppm) and experimental groups (\* Significantly different results ( $p < 0.05$ )).

	No UV	UV	UV+100ppm	UV+1000ppm
LMNA	0	0.393696	1.908567	0.179003
C5AR1	0	-2.24027	-0.33952	-1.59707
CASP1	0	-0.44965	1.853615	0.628426
TFB2M	0	-2.17373	0.077595	-1.08405
C1QA	0	-1.93757	0.934542	-1.42207
SMAD2	0	-0.23726	1.238085	-0.29718
EML1	0	0.708452	2.336575	2.175983
TMEM33	0	-2.22203	0.603945	-1.24911
POT1	0	-1.56445	-0.22534	-1.86902
BUB1B	0	0.245068	0	-0.06495
PDCD6	0	-0.61371	1.80419	0.779917
TERF2	0	-4.60871	1.839054	-1.52106
CALB1	0	-13.7575	-7.5	-5.99578
FCGR1A	0	-2.93017	-0.85729	-2.12224
FCGR3B	0	-9.0596	-2.3	-1.5
TFAM	0	-2.15424	-0.96249	-2.65236
CXCL16	0	-2.62188	0.070005	-1.97138
LMNB1	0	-0.48942	0.797792	0.20299
CDKN1C	0	-2.10603	0.646767	-1.31615
FCGBP	0	-3.41858	-1.07859	-2.19099
S100A9	0	-8.027	-4.84119	1.037235
SCN2B	0	-4.875	-0.20408	-1.96187
RNF144B	0	-6.77066	-0.13368	-0.93057
ZMPSTE24	0	-1.13549	-0.01107	-0.96479
ANXA5	0	-2.73955	1.160156	-0.62058
CD14	0	-2.24914	-0.77305	-1.61155
GFAP	0	-5.28468	-1.18341	2.432816
LMNB2	0	-1.29758	1.35607	-0.94436
TPP1	0	0.02029	1.658588	-0.04313
TERF1	0	-1.80374	0.345474	-1.38372
S100A8	0	-5.66393	-1.79742	-2.7568
C1QC	0	-3.67566	-0.05229	-2.19043
C3AR1	0	-1.32591	-0.44468	-1.90716
C3	0	1.286354	1.061121	1.032917
ANXA3	0	-2.18901	1.889889	-0.62079
SIRT6	0	-3.35358	-0.32077	-1.25388
ZNF25	0	-5.14189	2.192438	2.265619
ARID1A	0	-4.66077	1.349262	-2.16828
FOXO1	0	-1.04588	0.640257	0.70331
NDUFB11	0	-2.3941	1.151772	-0.77268
ELP3	0	-1.54299	2.6329	0.645229
ARL6IP6	0	-0.18482	1.301407	-0.33871
CLU	0	-2.90402	0.454887	-1.32731
COL3A1	0	-0.31445	2.338247	0.778629
TXNIP	0	-0.24236	5.021284	1.693569
COL1A1	0	0.416454	2.215582	1.016754
ANGEL2	0	-0.00722	1.72805	0.641045
ZFR	0	-2.69256	0.862247	-1.06368
C1S	0	-1.13413	1.621946	0.093973
PHF3	0	-1.33777	0.448582	-1.13161
TLR4	0	-2.18286	0.414967	-1.44843
RAP1A	0	-2.31905	0.786427	-1.16147
MRPL43	0	-2.2184	-0.0522	-1.43079
CCR1	0	-2.38281	-0.61624	-2.01722
CD163	0	-4.0012	-0.10423	-2.55899
POLRMT	0	-3.21143	0.33884	-1.43044
TOLLIP	0	-2.2796	1.009134	-0.77496
ZBTB10	0	-3.06334	0.025511	-1.49576
CX3CL1	0	-5.12134	-0.03137	-3.0864
TLR2	0	-2.72143	0.007557	-1.55689
ELAVL1	0	-0.45701	0.978327	-0.84974
TMEM135	0	1.530552	3.990757	3.06439
VWA5A	0	-1.71552	-0.77044	-1.77803
PANX1	0	-1.67533	-0.01301	-1.73992
TFB1M	0	-0.78034	0.88903	0.113352
SIRT3	0	0.461281	4.95635	4.579897
WRN	0	-0.03937	3.389839	1.856697
SNAP23	0	-0.87273	3.48185	1.996395
EP300	0	-1.07166	0.274616	-0.23037
LTF	0	-7.42984	-3.85805	-7.94579
LSM5	0	-2.56866	2.432156	0.644379
HSF1	0	-1.03703	1.171293	-0.08578
VPS13C	0	-0.50426	4.211584	2.448631
SIRT1	0	-2.79076	-0.15395	-1.63955
MBP	0	-2.04049	0.197905	-0.94444

Table S 1. Aging-related gene expression profile. The fold changes ( $\Delta\Delta\text{CT}$ ) were demonstrated.

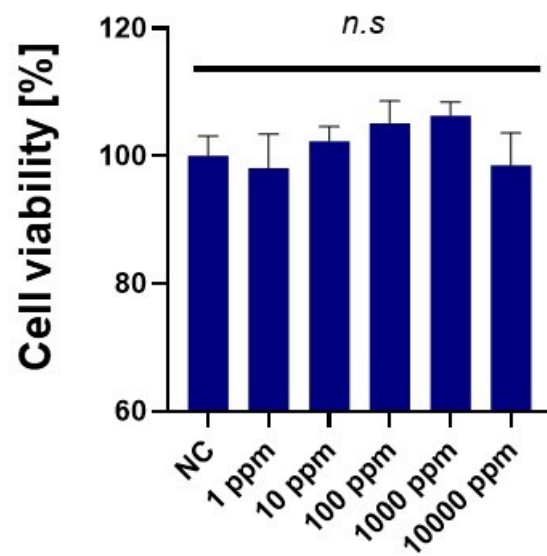


Fig S3. Cell viability examined by CCK-8 Hs68 was treated with LAEs for 24h.

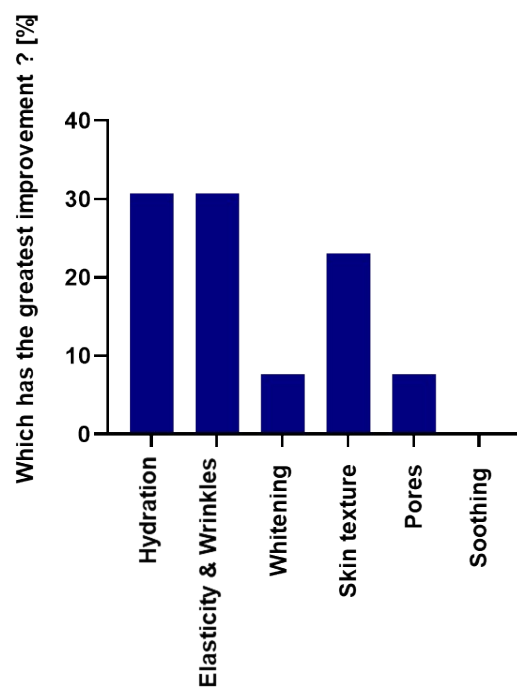


Fig S4. Self-questionnaire for the most perceived effect.

## Original raw data

Figure 2a

	COL1A1		MMP-1		ELN	
	Expression	SEM	Expression	SEM	Expression	SEM
<b>NC</b>	1		1		1	
<b>Control</b>	0.44	0.12	1.2254	0.05	0.4031	0.121
<b>TGF-beta</b>	0.59	0.12	0.8	0.0412	0.4985	0.098
<b>1 ppm</b>	0.49	0.05	0.9	0.11	0.41251	0.08
<b>10 ppm</b>	0.68	0.11	0.765	0.08	0.4031	0.12
<b>100 ppm</b>	0.77	0.08	0.667916	0.01	0.512	0.098
<b>1000 ppm</b>	0.41	0.078	0.683958	0.098	0.2921	0.07
<b>10000 ppm</b>	0.51	0.105	0.7125	0.121	0.3125	0.12

Figure 2b

	Wound area [%]	SEM
<b>NC</b>	100	
<b>1 ppm</b>	85	8.45
<b>10 ppm</b>	89	10.12
<b>100 ppm</b>	61	5.12
<b>1000 ppm</b>	53	9.812
<b>10000 ppm</b>	89	7.12

Figure 2c

	HA synthesis [%]	SEM
<b>RA</b>	14.6	2.12
<b>1 ppm</b>	-1.5	0.15
<b>10 ppm</b>	-2.9	0.5
<b>100 ppm</b>	0.51	0.98
<b>1000 ppm</b>	1.52	0.19
<b>10000 ppm</b>	4.3	0.85

Figure 2d

	IL 6 expression [%]	SEM
<b>NC</b>	100	
<b>Dex</b>	43.08	3.15
<b>1 ppm</b>	68.31	4.12
<b>10 ppm</b>	81.12	5.12
<b>100 ppm</b>	78.01	6.12

<b>1000 ppm</b>	101.05	8.15
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Figure 2e

	<b>IL 1<math>\alpha</math> expression [%]</b>	<b>SEM</b>
<b>NC</b>	100	
<b>Dex</b>	80.57	8.12
<b>1 ppm</b>	70.53183	11.52
<b>10 ppm</b>	69.50509	12.85
<b>100 ppm</b>	72.153	15.32
<b>1000 ppm</b>	80.0092	9.85

Figure 2f

		<b>-LAEs</b>			<b>+LAEs</b>	
			Expression	SEM	Expression	SEM
		noUV	1.563	0.12		
		NC	1	0.05	1.3	0.12
<b>+ UV</b>	Adenosine	10 ppm	1.740761	0.09	1.842663	0.21
		50 ppm	1.555623	0.11	1.946609	0.15
		100 ppm	1.561269	0.21	1.982155	0.098
	HSA	1 ppm	1.602539	0.15	2.005773	0.11
		5 ppm	1.503391	0.21	2.154826	0.19

Figure 3a

		<b>Senescence</b>	<b>SEM</b>
		NC (no UV)	1
<b>+UV</b>	0 ppm	1.504714	0.081
	1 ppm	1.58512	0.08
	10 ppm	1.676436	0.152
	100 ppm	1.215	0.053
	1000 ppm	1.3125	0.0412



Figure 4b

	SC	Epidermis	Dermis	Reservoir	Total	
						SEM
Free-FITC	0.21	0.51	0.61	0.94	2.27	0.152
Artificial EV 0.5 X	0.26	0.96	0.83	0.83	2.88	0.325
Artificial EV 1 X	0.18	1.07	0.66	0.83	2.74	0.198

Figure 5a

	Frontal eye wrinkle		Lateral eye wrinkle (Crow's feet)		Nasolabial folds	
	Improvement [%]	SEM	Improvement [%]	SEM	Improvement [%]	SEM
2 weeks	9.61	5.815	12.26	4.85	4.48	4.52
4 weeks	9.08	2.31	12.97	5.12	8.7	3.42
8 weeks	11.49	3.12	20.23	4.52	11.43	3.42

Supplementary figure 1

		COL		MMP		ELN		
		Expression	SEM	Expression	SEM	Expression	SEM	
+UV	NC	1	0.12	1	0.21	1	0.08	
	NC	0.300448	0.15	1.225429	0.098	0.533713	0.1	
	EV	10 ppm	0.50496	0.08	0.765571	0.08	0.946234	0.12
		100 ppm	0.585071	0.15	0.667916	0.11	1.01054	0.15
		1000 ppm	0.505688	0.21	0.683958	0.12	0.479323	0.03
	Lysate	10 ppm	0.403137	0.12	0.611998	0.12	0.840001	0.02
		100 ppm	0.51	0.21	0.891	0.21	0.7152	0.01
		1000 ppm	0.292169	0.03	1.102848	0.03	0.502162	0.04