

Supplemental Table S1. Antibodies used in this study.

Antibodies	Supplier	Cat.	Usage
Nqo1	CST	#3187	Western Blotting
$\beta$ -Actin	MBL	M177-3	Western Blotting
Keratin 14	abcam	ab7800	Immunohistochemistry
Keratin 10	abcam	ab76318	Immunohistochemistry
Nqo1	CST	#62262	Immunohistochemistry
Anti-mouse IgG, HRP-linked Antibody	CST	#7076	Western Blotting
Anti-mouse IgG (H+L), F(ab') <sub>2</sub> Fragment (Alexa Fluor® 555 Conjugate)	CST	#4409	Immunohistochemistry
Anti-rabbit IgG (H+L), F(ab') <sub>2</sub> Fragment (Alexa Fluor® 555 Conjugate)	CST	#4413	Immunohistochemistry
Anti-mouse IgG (H+L), F(ab') <sub>2</sub> Fragment (Alexa Fluor® 488 Conjugate)	CST	#4408	Immunohistochemistry
Anti-rabbit IgG (H+L), F(ab') <sub>2</sub> Fragment (Alexa Fluor® 488 Conjugate)	CST	#4412	Immunohistochemistry

Supplemental Table S2. Normal human epidermal keratinocytes used in this study.

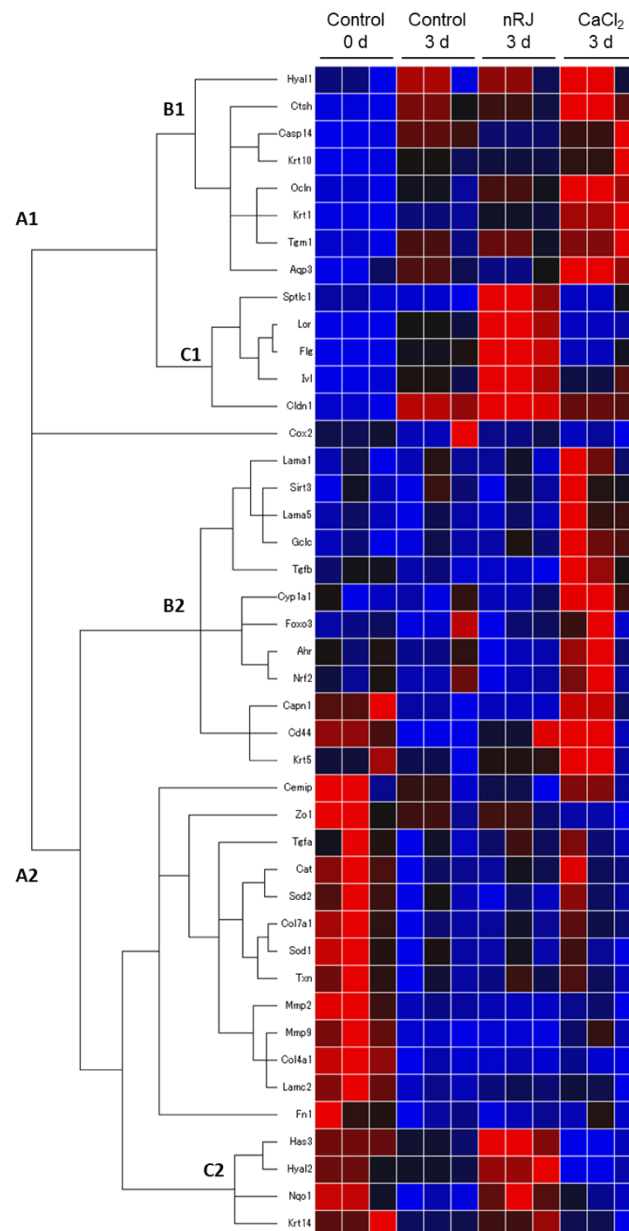
Supplier	Sex	Age	Race	Tissue		Lot number
PromoCell	female	31	Caucasian	skin		
	female	32	Caucasian	breast	Pooled	433Z033
	female	51	Caucasian	eyelid		
PromoCell	female	56	Caucasian	abdomen	Single	451Z0141
BIOPREDIC International	female	23	Caucasian	abdomen	Single	KER110016

Supplemental Table S3. The concentration of 10H2DA in royal jelly.

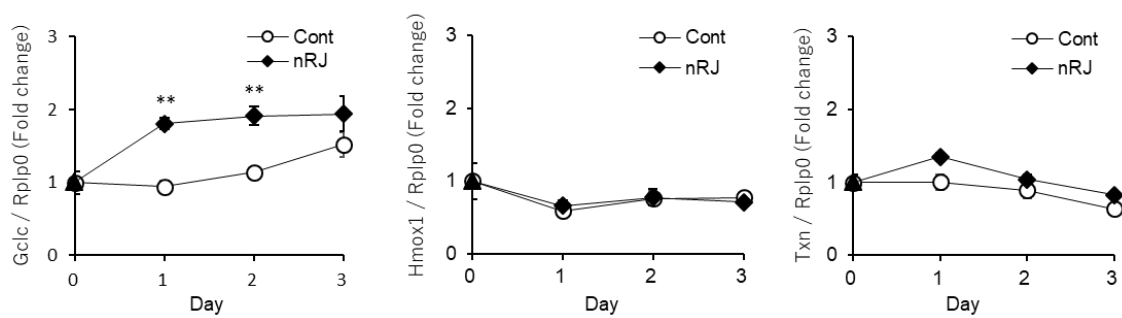
<b>Royal jelly</b>	<b>Lot</b>	<b>10H2DA (%)</b>	<b>Method</b>
Lyophilized raw royal jelly	YDP-M-180120	4.65	HPLC
Lyophilized raw royal jelly	YDP-M-190801	4.86	HPLC
Lyophilized raw royal jelly	YDP-M-200225	4.58	HPLC
Lyophilized protease-treated royal jelly	YRP-M-181030	4.06	HPLC

Supplemental Table S4. Primer pairs used in this study

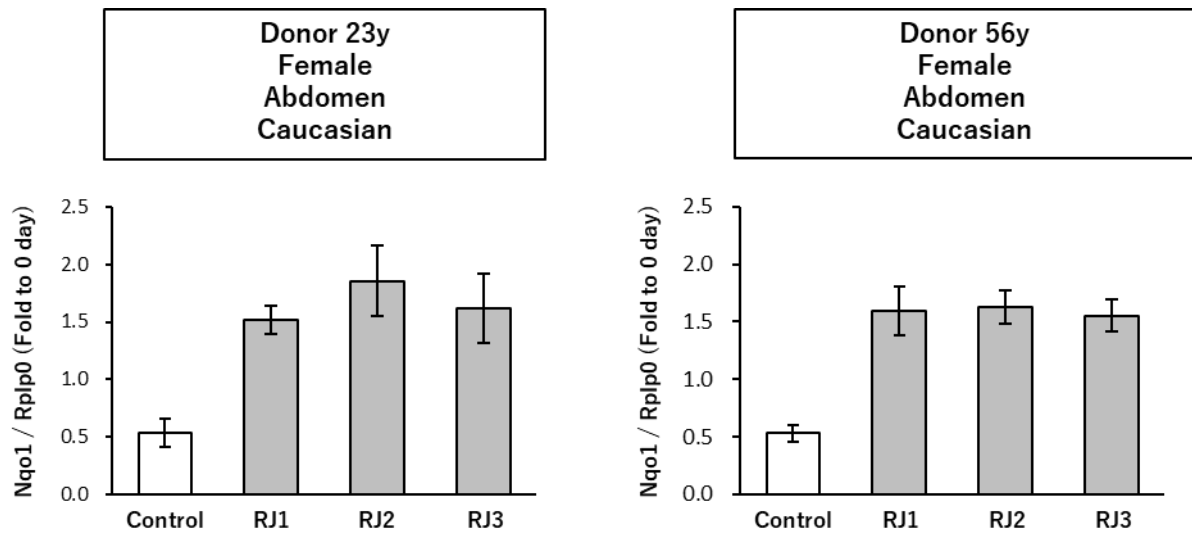
Symbol	Gene name	Forward, Sequence (5'→3')	Reverse, Sequence (5'→4')
<i>AHR</i>	Aryl hydrocarbon receptor	TGGTTGTGATGCCAAAGGAAGAA	ACTGGACCCAAGTCCATCGG
<i>AQP3</i>	Aquaporin 3	CCGTGACCTTTGCCATGTGCTT	TTGTGCGCGAAGTGCCAGATTG
<i>CAPN1</i>	Calpain-1	TTCGAGCCCAACAAGGAGGG	AGAGCACTTGCTCATCGGGG
<i>CASP14</i>	Caspase-14	CAGCCCACAAACCATCCCAAC	GTAGGCGATGTATCCCTCTACCGT
<i>CAT</i>	Catalase	AATGCTTCAGGGCCGCCTTT	ACTCGAGCACGGTAGGGACA
<i>CD44</i>	CD44 molecule	AGTGGTTTGGCAACAGATGGC	GAGGCTGCAGCTGTCCCTGT
<i>CEMIP</i>	Cell migration inducing hyaluronidase 1	GGAGCCGGCCATCATCAGAC	GGGAAGGTTCCACCACTGGC
<i>CLDN1</i>	Claudin 1	GTCTTTGACTCCTTGCTGAATCTG	CACCTCATCGTCTTCCAAGCAC
<i>COL17A1</i>	Collagen type XVII alpha 1 chain	CAGGACCTGTCACCACCATC	CGTACCCCGAAGTCCGTAAG
<i>COL4A1</i>	Collagen type IV alpha 1 chain	GAGTGCCTGGAAAGGACGGG	GGTGTTCCTGGCAAGCCCAT
<i>CTSH</i>	Cathepsin H	TCATGGATGTCTAAGCACCGT	GGTTCCTTCTGTTGTGGGCG
<i>CYP1A1</i>	Cytochrome P450 family 1 subfamily A member 1	GATTGAGCACTGTCAGGAGAAGC	ATGAGGCTCCAGGAGATAGCAG
<i>FNI</i>	Fibronectin 1	CAGCAGTACGGCCACCAAGA	ACGGTGTGCTGGTCACAGG
<i>FOXO3</i>	Forkhead box O3	TCGAGAGCTCCCCGGACAAA	GGATGGAGTTCTTCCAGCCG
<i>GCLC</i>	Glutamate-cysteine ligase catalytic subunit	TTCACACTGCCCGAGGTCAA	CTTGTTAAGGTACTGAAGCGAGGGT
<i>HAS3</i>	Hyaluronan synthase 3	ACCAACCGAGTCCTGAGCCT	TGGTTGAGCCACCGGAGGTA
<i>IVL</i>	Involucrin	CCAGGCCAGGTCCAAGACAT	CTGGACACTGCGGGTGGTTA
<i>KRT1</i>	Keratin 1	TGACAAGGTGAGGTTCTTGAG	AGTTGGTCCACTCTCCTTCGG
<i>KRT10</i>	Keratin 10	AGTCCCAACTGGCCTTGAAAC	AGCTGCACACAGTAGCGACC
<i>KRT14</i>	Keratin 14	TGCCGAGGAATGGTTCTTCACC	GCAGCTCAATCTCCAGGTTCTG
<i>KRT5</i>	Keratin 5	GCTGCCTACATGAACAAGGTGG	ATGGAGAGGACCACTGAGGTGT
<i>LAMA5</i>	Laminin subunit alpha 5	GAGGCTTTGAACCGGGCAGT	TCCTGCTTCCTTTGCAGGGC
<i>LOR</i>	Loricrin cornified envelope precursor protein	GTCTGCGGAGGTGGTTCCTCT	TGCTGGGTCTGGTGGCAGATC
<i>MMP2</i>	Matrix metalloproteinase 2	TGAGGGCGCTCTGTCTCCTG	TCAGGTATTGCACTGCCAACTC
<i>NQO 1</i>	NAD(P)H quinone dehydrogenase 1	CCTGCCATTCTGAAAGGCTGGT	GTGGTGATGGAAAGCACTGCCT
<i>Nrf2</i>	Nuclear factor, erythroid 2 like 2	CCAACTACTCCCAGGTTGCCC	GTGACTGAAACGTAGCCGAAGA
<i>OCN</i>	Occludin	ATGGCAAAGTGAATGACAAGCGG	CTGTAACGAGGCTGCCTGAAGT
<i>SIRT3</i>	Sirtuin 3	CCACCTGCACAGTCTGCCAA	CAGCGGCTCCCCAAAGAACA
<i>SOD1</i>	Superoxide dismutase 1	GCACACTGGTGGTCCATGAAA	CAAGCCAAACGACTTCCAGCG
<i>SOD2</i>	Superoxide dismutase 2	CCCAAAGGGGAGTTGCTGGAA	CCAAGCCAACCCCAACCTGA
<i>SPTLC1</i>	Serine palmitoyltransferase long chain base subunit 1	GCAGTGTTGAAGGAAAAGTGCGG	CAGTGCTCTCTTCCAGTTGTAGG
<i>TGFB1</i>	Transforming growth factor beta 1	GTTGTGCGGCAGTGGTTGAG	CCGGTAGTGAACCCGTTGATG
<i>TGM1</i>	Transglutaminase 1	GAACGACTGCTGGATGAAGAGG	CTTGATGGACTCCACAGAGCAG
<i>ZO1</i>	Zonula occludens-1	GTCCAGAATCTCGGAAAAGTGCC	CTTTCAGCGCACCATACCAACC



**Supplemental Figure S1. Comparison of the gene expression pattern in keratinocytes following stimulation with RJ or keratinocyte differentiation inducer, CaCl<sub>2</sub>.** Two major clusters, A1 and A2, were observed before (0 d) and after (3 d) stimulation. With CaCl<sub>2</sub>, there were two clusters, B1 and B2. B1 contained the keratinocyte differentiation markers *Krt1* and *Krt10*. On the other hand, nRJ-treated keratinocytes expressed another characteristic of gene expression that was classified into clusters C1 and C2. In cluster C1, both stratum spinosum and granular layer related genes such as *Flg* and *Lvl* were observed.



**Supplemental Figure S2. Changes in Nrf2 downstream genes following stimulation with nRJ**  
 Keratinocytes (pooled) were treated with 1 mg/ml nRJ for 3 days. Expression of *Gclc*, *Hmox1*, and *Txn* was analyzed using real-time PCR. Data represent mean  $\pm$  SEM,  $n = 3-4$ , \*\* $p < 0.01$ , vs. Control (Cont), Student's *t*-test.



**Supplemental Figure S3. Induction of NQO1 expression in keratinocytes (derived from 23y donor and 56 y donor) was comparable among different lots of nRJ.**

Keratinocytes were treated with 1 mg/ml nRJ (RJ1 Lot YDP-M-180120, RJ2 Lot YDP-M-190801, and RJ3 Lot YDP-M-200225) for 3 days. NQO1 mRNA expression was analyzed by real-time PCR. Data represent the mean  $\pm$  SEM, n=3.