SUPPLEMENTARY INFORMATION
FOR THE ARTICLE OF Y. N. ANTONENKO et al.

S1: Structures, Methods of Synthesis, and Certain Physicochemical Properties of Cationic Quinone Derivatives

Figures S1 and S2 show formulas of $CoQH_2$, plastoquinol, vitamin E, vitamin K_1, and compounds synthesized in our group, respectively. It is noteworthy that plastoquinol and vitamin K_1 inherent in chloroplasts, as well as the "professional" antioxidant vitamin E, in contrast to CoQ, contain no methoxy groups.

Plastoquinone differs from ubiquinone by (i) substitution of methyl for methoxy groups and (ii) absence of methyl group at fifth position of the quinone ring. SkQ3 contains no methoxy groups but retains, like ubiquinone, methyl at the fifth position. In SkQ2M, methylated carnitine substitutes for the phosphonium cation. In SkQ4 and SkQR1, decyltriphenylphosphonium cation was replaced by cations of decyltributylammonium and rhodamine 19, respectively. As shown in our group, the cation of ethyl rhodamine can penetrate through the lipid bilayer [1]. SkQR1 is unique among other SkQs since it is strongly fluorescing, so its fate in mitochondria, cells and the organism can be easily followed. SkQ5, containing a C_5 linker instead of C_{10}, was used as an example of a compound of lower hydrophobicity than the others. As to DMQ, it was tried as a compound, which, like SkQ3, has a structure intermediate between ubi- and plastoquinone (one methoxy group instead of two in ubiquinone). This compound was of certain interest since partial substitution of demethoxy-CoQ for CoQ was shown to prolong life of *C. elegans* and mice [2].

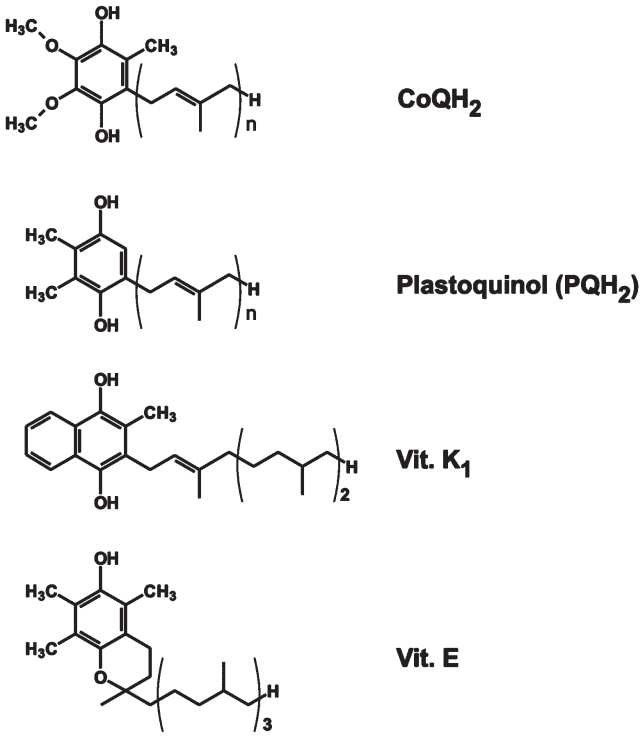


Fig. S1. Formulas of $CoQH_2$, plastoquinol, vitamins K_1, and E.

A number of antioxidative lipophilic compounds (SkQ1 (3a), SkQ3 (3b), MitoQ (3c), DMQ (3d), and SkQ5 (3e) in Fig. S3) were synthesized. In all of them, triphenylposphonium cation was covalently attached to the substituted 1,4-benzoquinone via an aliphatic carbon chain of 10 (or 5) methylene groups. Benzoquinones (1a, 1b) were prepared from corresponding benzoquinols by their oxidation by aqueous solution of $KBrO_3$.

General procedure of synthesis of alkyl-1,4-benzoquinones (1a-1d). Alkylhydroquinone (9 mmol), $KBrO_3$ (3 mmol), 9 ml H_2O, and 0.45 ml 5 N H_2SO_4 were stirred at 40-50°C for 30 min. The solution was extracted with diethyl ether. The organic extracts were dried over Na_2SO_4 and evaporated *in vacuo*. The yellow solid was purified by column chromatography on silica gel using chloroform as the eluent. *2,3-Dimethyl-1,4-benzoquinone* (1a): the yield, 63%; TLC: R_f ($CHCl_3$) 0.46; HPLC: t_R = 17.4 min (4.6 × 250 mm column Luna 5 μm C18(2), 1 ml/min, 25°C, 0-90% B for 26.4 min; A: 10 mM H_3PO_4 in water; B: 10 mM H_3PO_4 in MeCN), m. p. 58°C (56.5-57.5°C) [3]; UV (CH_3OH): λ_{max} – 209, 256, and 344 nm; ESI MS: m/z calculated for $C_8H_8O_2$ 136.15; found 136.2.

2,3,5-Trimethyl-1,4-benzoquinone (1b), yield, 74%; TLC: R_f (CH_2Cl_2) 0.67; HPLC: t_R = 7.8 min (4.6 × 150 mm column Luna 5 μm C18(2), 1.5 ml/min, 25°C, 5-95% B for 11 min; A: 0.05% aqueous TFA; B: 0.05% TFA in MeCN). UV (CH_3OH): λ_{max} – 198, 258, and 344 nm; ESI MS: m/z calculated for $C_9H_{10}O_2$ 150.18; found 150.4.

2,3-Dimethoxy-5-methyl-1,4-benzoquinone (1c) was from Aldrich (USA).

2-Methoxy-5-methyl-1,4-benzoquinone (1d) was obtained by refluxing methanol solution of *p*-toluquinone and $ZnCl_2$ [4]. Yield, 27.8%, m.p. 172°C.

Radical alkylation of the quinones (1a-1d) was done using the bromoalcanoic acid–ammonium persulfate–silver nitrate system [5].

General procedure of the synthesis of bromoalkylquinones (2a-2e). 11-Bromoundecanoic acid (2.1 mmol), 1a-1d (2 mmol), $AgNO_3$ (1 mmol) were dissolved in 7 ml of AcCN and H_2O (2 : 1) mixture at 80°C. Solution of $(NH_4)_2S_2O_8$ (2 mmol) in 3 ml of H_2O was added drop-wise with stirring at 70-89°C for 1.5 h. After dilution with water, the mixture was extracted with ether. The ether layer was washed with water, dried over Na_2SO_4 and evaporated *in vacuo*. The residue was applied to a silica gel column (225 × 35 mm) using chloroform as eluent. *10-(4,5-Dimethyl-3,6-dioxocyclohexa-1,4-dien-1-yl)decylbromide* (2a): yield, 29.7%; TLC: R_f ($CHCl_3$) 0.62; HPLC: t_R = 23 min (4.6 × 250 mm column Luna 5 μm C18(2), 1 ml/min, 25°C, 0-90% B for 26.4 min; A:

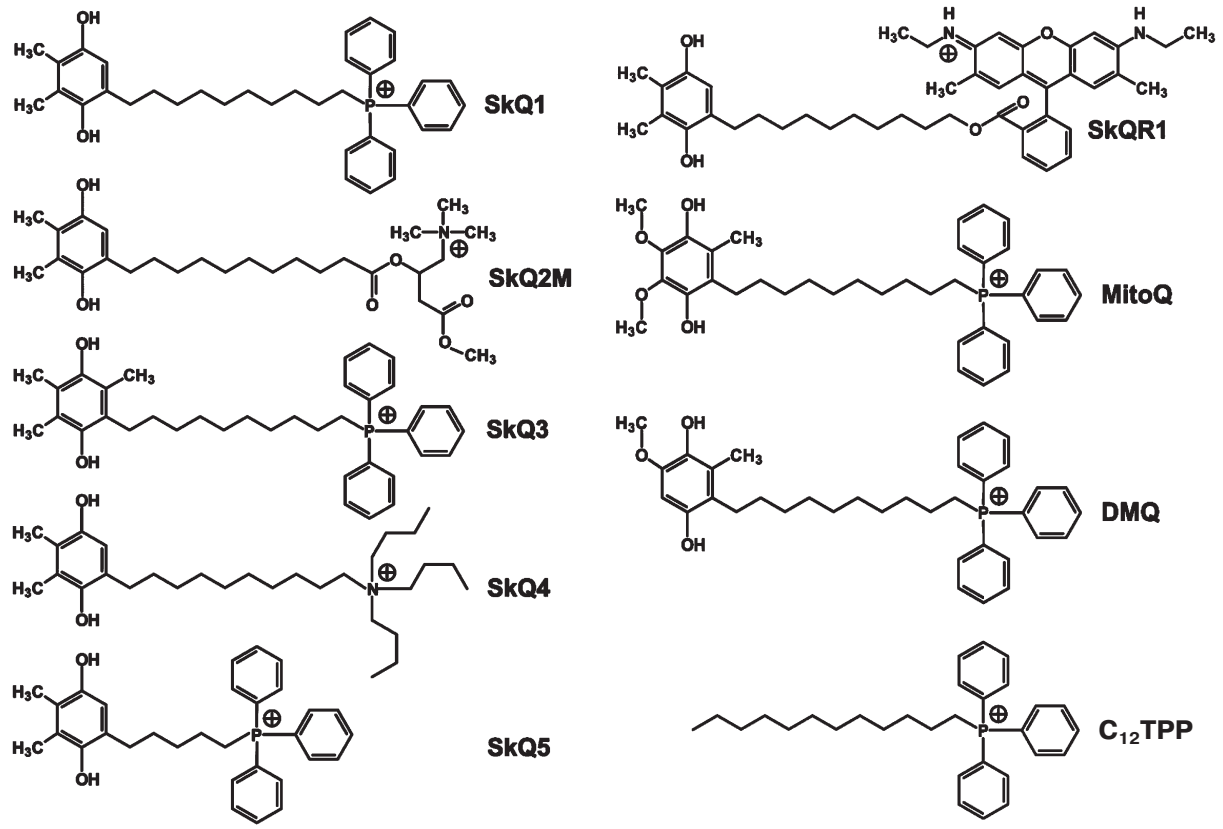
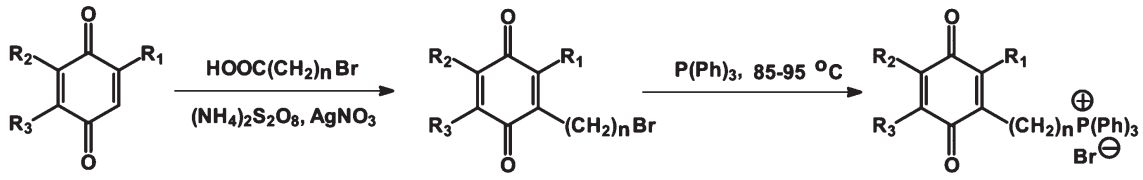


Fig. S2. Formulas of certain compounds synthesized in our group. Reduced forms of quinones are shown.



1a: R_1=H, R_2=R_3=CH_3	2a: R_1=H, R_2=R_3=CH_3, n=10	3a: R_1=H, R_2=R_3=CH_3, n=10	(SkQ1)
1b: R_1=R_2=R_3=CH_3	2b: R_1=R_2=R_3=CH_3, n=10	3b: R_1=R_2=R_3=CH_3, n=10	(SkQ3)
1c: R_1=CH_3, R_2=R_3=OCH_3	2c: R_1=CH_3, R_2=R_3=OCH_3, n=10	3c: R_1=CH_3, R_2=R_3=OCH_3, n=10	(MitoQ)
1d: R_1=CH_3, R_2=H, R_3=OCH_3	2d: R_1=CH_3, R_2=H, R_3=OCH_3, n=10	3d: R_1=CH_3, R_2=H, R_3=OCH_3, n=10	(DMQ)
	2e: R_1=H, R_2=R_3=CH_3, n=5	3e: R_1=H, R_2=R_3=CH_3, n=5	(SkQ5)

Fig. S3. Method used for synthesis of cationic derivatives of quinones.

10 mM H_3PO_4 in water; B: 10 mM H_3PO_4 in MeCN); UV (CH_3OH): λ_{max} – 214, 258, and 344 nm. ESI MS: m/z calculated for $C_{18}H_{27}O_2Br$ (M^+ + H) 356.3; found 356.1. IR: 2928, 2336, 1600, 1496, and 1304 cm^{-1}.

10-(2,4,5-Trimethyl-3,6-dioxocyclohexa-1,4-dien-1-yl)decylbromide) (2b): yield, 42%; TLC: R_f ($CHCl_3$) 0.79, R_f ($CHCl_3$–hexane, 3 : 1) 0.45. HPLC: t_R = 14.9 min (4.6 × 150 mm column Luna 5 μm C18(2), 1.5 ml/min, 25°C, 35-95% B for 18 min; A: 10 mM H_3PO_4 in water; B: 10 mM H_3PO_4 in MeCN); UV (CH_3OH): λ_{max} – 214, 262, 268, and 352 nm; ESI MS: m/z calculated for $C_{19}H_{29}O_2Br$ 369.34; found 369.6.

10-(4,5-Dimethoxy-2-methyl-3,6-dioxocyclohexa-1,4-dien-1-yl)decybromide (2c): yield, 26%; TLC: R_f (CH_2Cl_2–Et_2O, 20 : 1) 0.45; HPLC: t_R = 12.7 min (4.6 × 150 mm column Luna 5 μm C18(2), 1.5 ml/min, 25°C,

35-95% B for 26.4 min; A: 10 mM H_3PO_4 in water; B: 10 mM H_3PO_4 in MeCN); UV (CH_3OH): λ_{max} 278 nm; ESI MS: m/z calculated for $C_{19}H_{29}O_4Br$ 401.34; found 402.

10-(5-Methoxy-2-methyl-3,6-dioxocyclohexa-1,4-dien-1-yl)decylbromide (2d): yield, 37%; TLC: R_f ($CHCl_3$) 0.59. Compound 2d was used for the next step without further purification.

5-(4,5-Dimethyl-3,6-dioxocyclohexa-1,4-dien-1-yl)pentylbromide (2e) was prepared as described for 2a with use of 1a (1 mmol), 6-bromhexanoic acid (1 mmol), $AgNO_3$ (1 mmol), and $(NH_4)_2S_2O_8$ (1 mmol) in aqueous AcCN. Yield, 30%. Compound 2e was used for the next step without further purification.

Compounds 3a-3e were synthesized from triphenylphosphine and corresponding bromoalkylquinones (2a-2e).

General procedure for the synthesis of the triphenylphosphonium bromides (3a-3e). Triphenylphosphine (0.2 mmol), 2a-2e (0.2 mmol), and benzene or ethanol (0.3 ml) were sealed under argon in glass tube and kept at 85-95°C for 72 h. The residue after removing the solvent was precipitated by diethyl ether from CH_2Cl_2. The crude product was purified by column chromatography on silica gel with the mixture of $CHCl_3$–CH_3OH (at different ratio) as eluent. *[10-(4,5-Dimethyl-3,6-dioxocyclohexa-1,4-dien-1-yl)decyl]triphenylphosphonium bromide*, *SkQ1* (3a): yield, 24%; TLC: R_f ($CHCl_3$–CH_3OH, 4 : 1) 0.66; HPLC: t_R = 10.1 min (4.6 × 150 mm column Luna 5 μm C18(2), 1.5 ml/min, 25°C, 5-95% B for 11 min; A: 0.05% aqueous TFA; B: 0.05% TFA in MeCN); UV (CH_3OH): λ_{max} – 198, 226, and 260 nm (ε_{260} = 18.652 $cm^{-1}\cdot M^{-1}$), 352 nm; ESI MS: m/z calculated for $C_{36}H_{42}O_2P$, 537.69; found, 537.3; ^{1}H-NMR: ($CDCl_3$, 300K, AC-200) 1.12-1.29 ppm (br. m, 12H, 3, 4, 5, 6, 7, 8 - $(CH_2)_6$); 1.34 ppm (quintet, J_q = 7 Hz, 2H, 2-CH_2); 1.48-1.56 ppm (m, 2H, 9-CH_2); 1.91 ppm (s, 6H, 4′,5′-$(CH_3)_2$); 2.33 ppm (t, J_t = 7.6 Hz, 2H, 10-CH_2); 3.31 ppm (m, 2H, 1-CH_2); 6.37 ppm (s, 1H, $H_{(2')}$); 7.57-7.82 ppm (m, 15H, Ph); ^{13}C-NMR: (CD_3OD, 303K): 11.90 and 12.29 ppm (4′ and 5′-$(CH_3)_2$); 22.48 ppm (d, J = 4.6 Hz, 2-CH_2); 23.67 ppm (d, J = 49.8 Hz, 1-CH_2); 27.64 (10-CH_2); 28.87, 28.97, 28.99, 29.04, 28.09, and 29.14 ppm (4, 5, 6, 7, 8, and 9-$(CH_2)_6$); 30.28 ppm (d, J = 15.6 Hz, 3-CH_2); 118.11 ppm (d, J = 86.4 Hz, C_i of Ph); 130.44 ppm (d, J = 12.7 Hz, C_m of Ph); 131.89 ppm ($C_{2'}$); 133.49 ppm (d, J = 10.0 Hz, C_o of Ph); 134.98 ppm (d, J = 2.3 Hz, C_p of Ph); 140.32 and 140.86 ppm ($C_{4'}$ and $C_{5'}$); 148.95 ppm ($C_{1'}$); 187.43 and 187.57 ppm ($C_{3'}$ and $C_{6'}$).

[10-(2,4,5-Trimethyl-3,6-dioxocyclohexa-1,4-dien-1-yl)decyl]triphenylphosphonium bromide, *SkQ3* (3b): yield, 18%; TLC: R_f ($CHCl_3$–CH_3OH, 4 : 1) 0.60, R_f ($CHCl_3$–C_2H_5OH–CH_3COOH, 85 : 10 : 5) 0.29; HPLC: t_R = 10.2 min (4.6 × 150 mm column Luna 5 μm C18(2), 1.5 ml/min, 25°C, 5-95% B for 11 min; A: 0.05% aqueous TFA; B: 0.05% TFA in MeCN); UV (CH_3OH): λ_{max} – 200, 226, and 268 nm (ε_{268} = 18,006 $cm^{-1}\cdot M^{-1}$); ESI MS: m/z calculated for $C_{37}H_{44}O_2P$, 551.72; found, 551.3; ^{1}H-NMR: (CD_3OD, 300K, AV-600) 1.26-1.40 ppm (br. m, 12H, 4, 5, 6, 7, 8, 9 - $(CH_2)_6$); 1.548 ppm (quintet, J_q = 7.58 Hz, 2H, 3-CH_2); 1.671 ppm (sextet, J_{sx} = 8.0 Hz, 2H, 2-CH_2); 1.971 ppm (quintet, J_q = 1.07 Hz, 3H, 4′(5′)-CH_3); 1.985-1.989 ppm (m, 6H, 5′(4′)-CH_3 and 2′-CH_3); 2.461 ppm (t, J_t = 7.67 Hz, 2H, 10-CH_2); 3.350-3.405 ppm (m, 2H, 1-CH_2); 7.71-7.81 ppm (m, 12H, H_o and H_m of Ph); 7.87-7.90 ppm (m, 3H, H_p of Ph); ^{13}C-NMR: (CD_3OD, 303K): 12.21, 12.31, and 12.33 ppm (2′,4′, and 5′-$(CH_3)_3$); 22.78 ppm (d, J = 50.9 Hz, 1-CH_2); 23.56 ppm (d, J = 4.6 Hz, 2-CH_2); 27.40 (10-CH_2); 29.74 ppm (8-CH_2); 29.82 ppm (d, J = 1.2 Hz, 4-CH_2); 30.28, 30.33, and 30.35 ppm (5, 6, and 7-$(CH_2)_3$); 30.82 ppm (9-CH_2); 31.56 ppm (d, J = 16.0 Hz, 3-CH_2); 120.05 ppm (d, J = 86.5 Hz, C_i of Ph); 131.56 ppm (d, J = 13.1 Hz, C_m of Ph); 134.85 ppm (d, J = 9.9 Hz, C_o of Ph); 136.31 ppm (d, J = 3.0 Hz, C_p of Ph); 141.35, 141.57, and 141.66 ppm ($C_{2'}$, $C_{4'}$, and $C_{5'}$); 145.58 ppm ($C_{1'}$); 188.36 and 188.55 ppm ($C_{3'}$ and $C_{6'}$).

[10-(4,5-Dimethoxy-2-methyl-3,6-dioxocyclohexa-1,4-dien-1-yl)decyl]triphenylphosphonium bromide, *MitoQ* (3c) was described earlier [6]: the yield, 21%; HPLC: t_R = 9.32 min (4.6 × 150 mm column Luna 5 μm C18(2), 1.5 ml/min, 25°C, 5-95% B for 11 min; A: 0.05% aqueous TFA; B: 0.05% TFA in MeCN); UV (C_2H_5OH): 275 nm (ε_{275} = 15,950 $cm^{-1}\cdot M^{-1}$ proved to be slightly higher than that reported by Murphy [6] (10,400 $cm^{-1}\cdot M^{-1}$); ESI MS: m/z calculated for $C_{37}H_{44}O_4P$, 583.3; found, 583.3; IR: 3357, 2927, 2857, 1650, 1609, 1438, 1266, 1113 cm^{-1}; ^{1}H-NMR: ($CDCl_3$, 303K, AV-600) 1.15-1.28 ppm (br. m, 14H, 2, 3, 4, 5, 6, 7, 8 - $(CH_2)_8$); 1.320 ppm (qt., 2H, J = 7.7 Hz, 9-CH_2); 1.964 ppm (s. 3H, 2′-CH_3); 2.389 ppm (t., J_t = 7.70 Hz, 2H, 10-CH_2); 3.66-3.76 ppm (m., 2H, 1-CH_2); 3.946, 3.949 ppm (s, s, 6H, $(OCH_3)_2$); 7.66-7.83 ppm (m., 15H, Ph). ^{13}C-NMR: ($CDCl_3$, 303K, AV-600): 11.82 ppm (CH_3); 22.61 ppm (d, J = 4.7 Hz, 2-CH_2); 22.76 ppm (d, J = 49.4 Hz, 1-CH_2); 26.28 (10-CH_2); 28.58, 29.04, 29.05, 29.13, 29.20, and 29.64 ppm (4, 5, 6, 7, 8, 9-$(CH_2)_6$); 30.31 ppm (d, J = 15.5 Hz, 3-CH_2); 61.04 and (4′, 5′-$(OCH_3)_2$); 118.38 ppm (d, J = 85.3 Hz, C_i of Ph); 130.44 ppm (d, J = 12.8 Hz, C_m of Ph); 133.63 ppm (d, J = 9.9 Hz, C_o of Ph); 134.94 ppm (d, J = 2.8 Hz, C_p of Ph); 138.62 ppm ($C_{2'}$); 142.97 ppm ($C_{1'}$); 144.28 and 144.31 ppm ($C_{4'}$ and $C_{5'}$); 184.07 and 184.60 ppm ($C_{3'}$ and $C_{6'}$).

[10-(5-Methoxy-2-methyl-3,6-dioxocyclohexa-1,4-dien-1-yl)decyl]triphenylphosphonium bromide, *DMQ* (3d): yield, 25%; TLC: R_f ($CHCl_3$–CH_3OH–H_2O, 65 : 25 : 4) 0.61; HPLC: t_R = 9.11 min (4.6 × 150 mm column Luna 5 μm C18(2), 1.5 ml/min, 25°C, 5-95% B for 11 min; A: 0.05% aqueous TFA; B: 0.05% TFA in MeCN); UV (CH_3OH): λ_{max} – 224, 274, and 374 nm; ESI MS: m/z calculated for $C_{36}H_{42}O_3P$, 553.69; found, 554.2; ^{1}H-NMR: ($CDCl_3$, 303K, DRX-500) 1.08-

1.32 ppm (br. m, 12H, 4, 5, 6, 7, 8, 9 - $(CH_2)_6$); 1.58-1.69 ppm (br. m, 12H, 2, 3 - $(CH_2)_2$); 1.93 ppm (s, 3H, 2′-CH_3); 2.47 ppm (t, J_t = 7.7 Hz, 2H, 10-CH_2); 3.58-3.63 ppm (m, 2H, 1-CH_2); 5.80 ppm (s, 3H, $H_{4'}$); 7.62-7.79 ppm (m, 15H, Ph); ^{13}C-NMR: (CD_3OD, 303K): 12.17 ppm (2′-CH_3); 22.68 ppm (d, J = 4.5 Hz, 2-CH_2); 22.87 ppm (d, J = 49.2 Hz, 1-CH_2); 26.26 (10-CH_2); 28.46, 29.12, 29.20, 29.27, 29.30, and 29.67 ppm (4, 5, 6, 7, 8, and 9-$(CH_2)_6$); 30.40 ppm (d, J = 15.3 Hz, 3-CH_2); 107.05 ppm ($C_{2'}$); 118.47 ppm (d, J = 86.0 Hz, C_i of Ph); 130.49 ppm (d, J = 12.3 Hz, C_m of Ph); 133.74 ppm (d, J = 10.1 Hz, C_o of Ph); 134.98 ppm (d, J = 2.7 Hz, C_p of Ph); 141.22 and 143.04 ppm ($C_{1'}$ and $C_{2'}$); 158.29 ppm ($C_{5'}$); 182.09 ($C_{6'}$); 187.73 ppm ($C_{3'}$).

The compound SkQ5 (3e) was identified as the corresponding quinol, *[5-(3,6-dioxy-4,5-dimethyl-phen-1-yl)pentyl]triphenylphosphonium bromide* (4), and prepared by reduction of 3e with $NaBH_4$ in CH_3OH. The yield (of 4) 18%; TLC: R_f ($CHCl_3$–CH_3OH–H_2O, 65 : 25 : 4) 0.59. HPLC; t_R = 7.0 min (4.6 × 150 mm column Luna 5 μm C18(2), 1.5 ml/min, 25°C, 5-95% B for 11 min; A: 0.05% aqueous TFA; B: 0.05% TFA in MeCN); UV: λ_{max} – 268, 276, and 290 nm; ESI MS: m/z calculated for $C_{31}H_{34}O_2P$, 469.57; found, 470.2; ^{1}H-NMR: (DMSO-D_6, 303K, AC-200) 1.45-1.62 ppm (br. m, 6H, 2, 3, and 4 - $(CH_2)_3$); 1.97 and 2.04 ppm (s and s, 3H and 3H, 4′- and 5′-$(CH_3)_2$); 2.41 ppm (br. t, J_t = 7 Hz, 2H, 5-CH_2); 3.46-3.53 ppm (m, 2H, 1-CH_2); 6.37 ppm (s, 1H, $H_{2'}$); 7.06 (br. s, 1H, OH); 7.69-7.92 ppm (m, 15H, Ph); 8.13 ppm (br. s, 1H, OH); ^{13}C-NMR: (DMSO-D_6, 303K): 11.89 and 12.72 ppm (4′ and 5′-$(CH_3)_2$); 20.34 ppm (d, J = 49.5 Hz, 1-CH_2); 21.74 ppm (d, J = 4.3 Hz, 2-CH_2); 28.75 and 29.56 (4- and 5-CH_2); 29.51 ppm (d, J = 16.4 Hz, 3-CH_2); 113.01 ppm ($C_{2'}$); 118.46 ppm (d, J = 85.6 Hz, C_i of Ph) 120.22 ppm ($C_{1'}$); 124.84 and 126.61 ppm ($C_{4'}$ and $C_{5'}$); 130.09 ppm (d, J = 12.5 Hz, C_m of Ph); 133.41 ppm (d, J = 10.1 Hz, C_o of Ph); 134.71 ppm (d, J = 2.7 Hz, C_p of Ph); 144.65 and 147.83 ppm ($C_{3'}$ and $C_{6'}$).

Triphenyl(dodecyl)phosphonium iodide (5a) was synthesized from triphenylphosphine and 1-iododododecane by a similar procedure with 3a, the treatment of 5a by HCl/dioxane solution gave corresponding chloride (5b, C_{12}TPP): yield, 62.5%; TLC: R_f ($CHCl_3$–CH_3OH, 4 : 1) 0.73, R_f ($CHCl_3$–CH_3OH, 9 : 1) 0.55; HPLC: t_R = 10.5 min (4.6 × 150 mm column Luna 5 μm C18(2), 1.5 ml/min, 25°C, 5-95% B for 11 min; A: 0.05% aqueous TFA; B: 0.05% TFA in MeCN); UV (CH_3OH): λ_{max} – 200, 224, and 268 nm; ESI MS: m/z calculated for $C_{30}H_{40}P$, 431.6; found, 431.4; ^{1}H-NMR: (CD_3OD, 303K, AV-600) 0.883 ppm (t, J_t = 7.07 Hz); 1.23-1.36 ppm (br. m, 16H, 4, 5, 6, 7, 8, 9, 10, 11 - $(CH_2)_8$); 1.569 ppm (quintet, J_q = 7.50 Hz, 2H, 3-CH_2); 1.671 ppm (sextet, J_{sx} = 8.0 Hz, 2H, 2-CH_2); 3.41-3.48 ppm (m, 2H, 1-CH_2); 7.74-7.78 ppm (m, 6H, H_m of Ph); 7.80-7.85 ppm (m., 6H, H_o of Ph); 7.87-7.90 ppm (m., 3H, H_p of Ph);

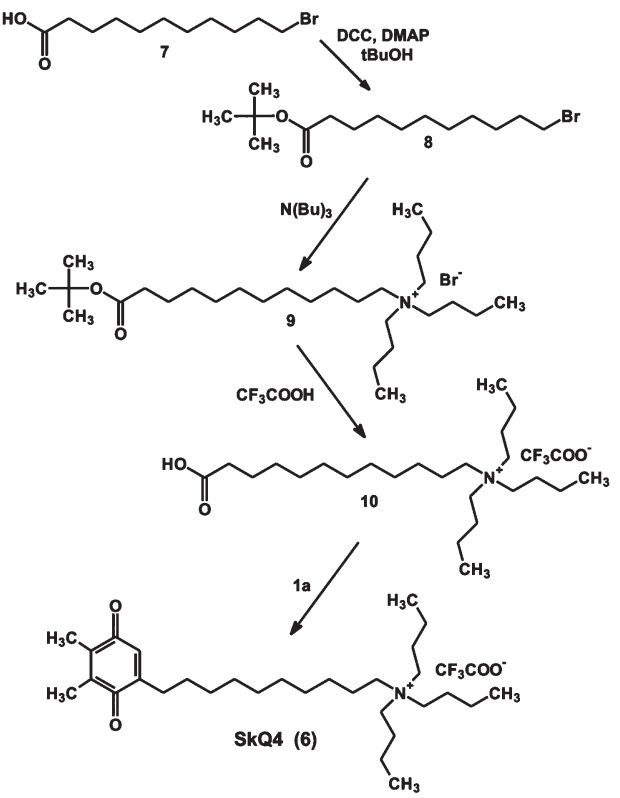


Fig. S4. Synthesis of SkQ4.

^{13}C-NMR: (CD_3OD, 303K): 14.43 ppm (CH_3); 22.84 ppm (d, J = 50.9 Hz, 1-CH_2); 23.55 ppm (d, J = 4.3 Hz, 2-CH_2); 29.89 (4-CH_2); 30.34, 30.39, 30.51, 30.66, and 30.67 ppm (5, 6, 7, 8, and 9-$(CH_2)_5$); 31.55 ppm (d, J = 16.0 Hz, 3-CH_2); 33.01 ppm (10-CH_2); 119.98 ppm (d, J = 86.2 Hz, C_i of Ph); 131.52 ppm (d, J = 12.7 Hz, C_m of Ph); 134.84 ppm (d, J = 9.9 Hz, C_o of Ph); 136.21 ppm (d, J = 2.8 Hz, C_p of Ph).

The synthesis of *[10-(4,5-dimethyl-3,6-dioxocyclohexa-1,4-dien-1-yl)decyl]tributylammonium trifluoroacetate*, *SkQ4*, (6) is outlined in Fig. S4.

11-Bromoundecanoic acid (7) was esterified with *tert*-butanol in the presence of N,N′-dicycloxehylcarbodiimide and N,N-dimethylaminopyridine to give *tert*-butyl ester (8), which was used for the synthesis of (9) followed by acid hydrolysis giving (10). Alkylation of 2,3-dimethyl-1,4-benzoquinone (1a) under the conditions described for 2a afforded crude SkQ4 (6), which was purified using a semi-preparative HPLC 10 × 250 mm column Ultrasphere 5 μm ODS, 5 ml/min, 25°C, 40-70% B for 20 min (A: 0.05% aqueous TFA; B: 0.05% TFA in MeCN): yield 5.4%; TLC: R_f (n-C_4H_9OH–H_2O–CH_3COOH, 4 : 1 : 1) 0.55; HPLC: t_R = 10.06 min (4.6 × 150 mm column Luna 5 μm C18(2), 1.5 ml/min, 25°C, 5-95% B for 11 min; A: 0.05% aqueous TFA; B: 0.05% TFA in MeCN); UV (CH_3OH): λ_{max} – 202, 260, and 242 nm; ESI MS: m/z calculated for $C_{30}H_{54}NO_2$, 460.75; found,

460.7; ^{1}H-NMR: (CD_3OD, 300K, AV-600): 1.019 ppm (t, $J_т$ = 7.42 Hz, 9H, CH_3 of Bu); 1.27-1.40 ppm (m, 12H, 3, 4, 5, 6, 7, and 8-$(CH_2)_6$); 1.416 ppm (sextet, J_{sx} = 7.41 Hz, 6H, 3″-CH_2 of Bu); 1.502 ppm (quintet J_{qt} = 7.46 Hz, 2H, 9-CH_2); 1.70-1.63 ppm (m, 8H, 2″-CH_2 of Bu and 2-CH_2); 1.992-2.013 ppm (m, 6H, 4′ and 5′-$(CH_3)_2$); 2.402 ppm (dt, J_d = 1.36; J_t = 7.70 Hz, 2H, 10-CH_2); 3.233 ppm (m, 8H, 1″-CH_2 of Bu and 1-CH_2); 6.510 ppm (t, J_t = 1.40 Hz, 1H, $H_{(2')}$); ^{13}C-NMR: (CD_3OD, 300K): 11.93 and 12.33 ppm (4′ and 5′-$(CH_3)_2$); 13.93 ppm (4″-CH_3 of Bu); 20.73 ppm (3″-CH_2 of Bu); 22.76 ppm (2-CH_2); 24.83 ppm (2″-CH_2 of Bu); 27.33 ppm (3-CH_2); 29.17 ppm (9-CH_2), 30.05 and 30.07 ppm (8- and 10-$(CH_2)_2$); 30.31, 30.36, 30.37, and 30.39 ppm (4, 5, 6, and 7-$(CH_2)_4$); 59.55 ppm (1′-CH_2 of Bu); 59.75 ppm (1-CH_2); 133.18 ppm ($C_{2'}$); 141.64 and 142.30 ppm ($C_{4'}$ and $C_{5'}$); 150.56 ppm ($C_{1'}$); 188.97 and 188.65 ppm ($C_{3'}$ and $C_{6'}$).

Synthesis of lipophilic methyl carnitine-containing cation *2-{[11-(4,5-dimethyl-3,6-dioxocyclohexa-1,4-dien-1-yl)undecanoyl]oxy}-N,N,N-trimethyl-4-oxobutan-1-aminium chloride*, *SkQ2M* (11) is shown in Fig. S5.

1,10-Decanedicarbonic acid (14) reacted with the oxalyldichloride to give (15), which was used for acylation of hydroxyl group of carnitine methyl ester. The derivative obtained (16) reacted with 1a under the conditions described above for the synthesis of 2a to afford SkQ2M (11). The product 11 was purified by silica gel column chromatography with $CHCl_3$–CH_3OH–H_2O (65 : 25 : 4) as eluent, the final purification was done with a preparative HPLC; SkQ2M (11): the yield, 6.2%; TLC: R_f ($CHCl_3$–CH_3OH–H_2O, 65 : 25 : 4) = 0.41; t_R = 9.59 min (4.6 × 150 mm column Luna 5 μm C18(2), 1.5 ml/min, 25°C, 5-95% B for 11 min; A: 0.05% aqueous TFA; B: 0.05% TFA in MeCN); UV (CH_3OH): λ_{max} – 204, 260, and 346 nm; ESI MS: m/z calculated for $C_{27}H_{44}NO_6$, 478.64; found, 478.4; ^{1}H-NMR (CD_3OD, 303K, AV-600): 1.27-1.35 ppm (br. m, 12 H, 4, 5, 6, 7, 8, and 9 - $(CH_2)_6$); 1.495 ppm (quintet, J_{qt} = 7.0 Hz, 2H, 10-CH_2); 1.615 ppm (quintet, J_{qt} = 7.0 Hz, 2H, 3-CH_2); 1.987 ppm (quartet, J = 1.14 Hz, 3H, 5′-CH_3); 2.015 ppm (q, J_q = 1.12 Hz, 3H, 4′-CH_3); 2.381 ppm (t, J_t = 7.57 Hz, 2H, 2-CH_2); 2.397 ppm (dt, J_d = 1.36, J_t = 7.96, 2H, 11-CH_2); 2.771 and 2.806 ppm (m [AB-part of ABMXY-system: J_{AB} = 16.76 Hz, J_{AM} = 6.96 Hz, J_{BM} = 5.44 Hz]; 2H, 3″-CH_2); 3.196 ppm (s, 9H, -$^+$N$(CH_3)_3$); 3.689 ppm (m [X-part ABMXY-system: J_{MX} = 1.07 Hz, J_{XY} = 14.46 Hz], 1H, $H_{(1''X)}$); 3.860 ppm (m [Y-part ABMXY-system: J_{MY} = 8.51 Hz, J_{XY} = 14.46 Hz], 1H, $H_{(1''Y)}$); 5.639 ppm (q [M-part of ABMXY-system: J_q = 6.80 Hz], 1H, $H_{(2'')}$); 6.513 ppm (t, J_t = 1.36 Hz, 1H, $H_{(2')}$).

Rhodamine derivative *N-[(3Z)-9-[2-({[10-(4,5-dimethyl-3,6-dioxo-cyclohexa-1,4-dien-1-yl)decyl]oxy}carbonyl)phenyl]-6-(ethylamino)-2,7-dimethyl-3H-xanten-3-ylidene]ethanaminium chloride*, SkQR1 (12), was obtained starting from 2a and Cs-salt of rhodamine 19 (12a) and then converted to chloride by aqueous HCl treatment as indicated in Fig. S6. Yield, 65%; TCL: R_f (CH_3Cl–CH_3OH, 4 : 1) 0.68; R_f ($CHCl_3$–CH_3OH–H_2O, 65 : 25 : 4) 0.80; HPLC: t_R = 24.4 min (4.6 × 250 mm column Luna 5 μm C18(2), 1 ml/min, 25°C, 0-90% B for 26.4 min; A: 100 mM H_3PO_4 in water; B: 100 mM H_3PO_4 in MeCN); M. p. 178-180°C (degr.); element anal.: calculated for $C_{44}H_{53}ClN_2O_5$: C, 72.86; H, 7.36; Cl, 4.89; N, 3.86; found: C, 72.53; H, 7.21; Cl, 4.22; N, 3.61; UV (C_2H_5OH): λ_{max} – 250, 350, and 535 nm (ε = 80,000 $cm^{-1}\cdot M^{-1}$); ESI MS: m/z (MH+) calculated for $C_{44}H_{51}N_2O_5$, 688.89; found, 689.4; IR(film): 3200, 2928, 2336, 1700, 1685, 1600, 1496, 1304 cm^{-1}; ^{1}H-NMR (DMSO-D_6, 303K, AV-400): 0.95-1.25 ppm (br. m, 14H, 2, 3, 4, 5, 6, 7, 8 - $(CH_2)_7$); 1.24 ppm (t, J_t = 6.8 Hz, 6H, CH_3 of -NHEt); 1.41 ppm (quintet, J_{qt} = 7.5 Hz, 2H); 1.92 and 1.94 (s and s, 3H and 3H, 4′ and 5′-$(CH_3)_2$); 2.09 ppm (s, 6H, 2, 7-$(CH_3)_2$); 3.48 ppm (quintet, $J_q \approx 7$ Hz, 4H, CH_2 of -NHEt); 3.85 ppm (t, J_t = 6.3 Hz, 2H, 1-CH_2); 6.57 ppm (s, 1H, H_3); 6.80 and 6.91 ppm (s and s, 2H and 2H, $H_{(1''')}$, $H_{(4''')}$, $H_{(5''')}$, and $H_{(8''')}$); 7.44 ppm (dd, J_d = 7.8 Hz, J_d = 1.0 Hz; 1H, $H_{(6'')}$); 7.74 ppm (t, J_t = 5.8 Hz, 2H, NH of -NHEt); 8.60-8.70 ppm (m, 2H, $H_{(4'')}$ and $H_{(5'')}$); 8.22 ppm (dd, 1H, J_d = 8.2 Hz, J_d = 1.1 Hz, $H_{(3'')}$); ^{13}C-NMR (δ, ppm, DMSO-D_6, 303K): 11.59 and 11.98 (4′ and 5′ - $(CH_3)_2$); 13.45 (CH_3 of -NHEt); 17.29 (2′ and 7′-$(CH_3)_2$); 25.07, 27.29, 27.57, 28.25, 28.39, 28.51, 28.55, 28.56, and 28.65 (2, 3, 4, 5, 6, 7, 8, 9, and 10 - $(CH_2)_9$); 37.86 (CH_2 of -NHEt); 64.96 (1-CH_2); 93.45 ($C_{(4''')}$-$C_{(5''')}$); 112.78 ($C_{(1''')}$-$C_{(8''')}$); 125.32 ($C_{(4'')}$); 128.38 ($C_{(6'')}$); 129.78 and 130.75 ($C_{(1'')}$ and $C_{(2'')}$); 130.20 and 130.22 ($C_{(5'')}$ and $C_{(8a''')}$-$C_{(9a''')}$); 131.77 ($C_{(2''')}$ and $C_{(7''')}$); 132.85 ($C_{(9''')}$); 132.88 ($C_{(3'')}$); 139.79 and 140.36 ($C_{(4')}$ and $C_{(5')}$); 148.40 ($C_{(1')}$); 155.71 and 156.6 ($C_{(4a''')}$-$C_{(10a''')}$ and $C_{(3''')}$-$C_{(6''')}$); 164.98 (-COO-); 186.91 and 187.000 ($C_{(3')}$ and $C_{(6')}$).

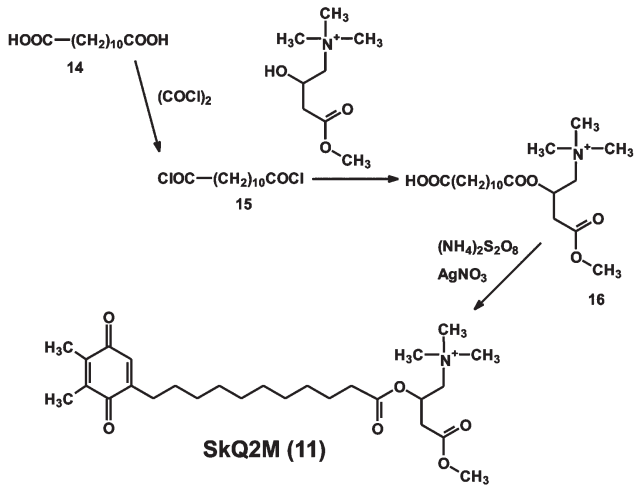


Fig. S5. Synthesis of SkQ2M.

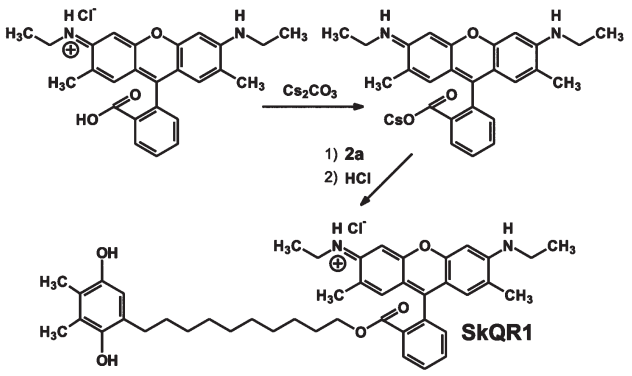


Fig. S6. Synthesis of SkQR1.

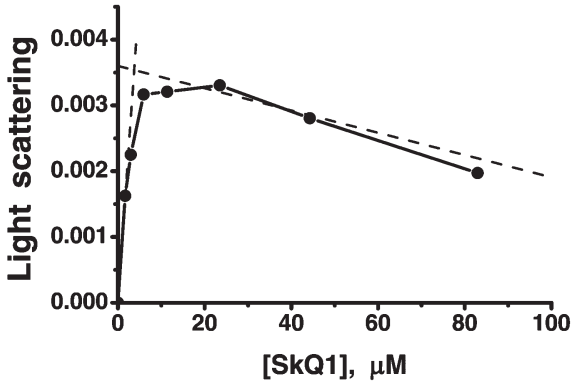


Fig. S7. Estimation of critical micelle formation concentration for SkQ1.

Stability of synthesized compounds in water solution at pH 6.5 and 37°C was found to decrease in the range MitoQ > SkQ3 > SkQ1 > SkQR1. A 50% decomposition of 0.1 mM SkQ1 took 54 h. For SkQR1, this value was 3.5 h. The stability decreased with increasing pH. All the compounds studied were stable in ethanol solution as well as in the solid state. In the latter case, $t_{1/2}$ for SkQ1 decomposition at 20°C was 4 months. Concentration of diluted water solution of all the above compounds was strongly affected by their sorption on the surface of some kinds of glass or plastic vessels where they were stored. Such an effect was absent if ethanol substituted for water by not less than 50%. Moreover, like other hydrophobic cations, decyltriphenylphosphonium derivatives of quinones are prone to occupy the air/water interface, so their solutions should be strongly shaken before use. The critical concentration for SkQ1 micelle formation measured with a Photocor Complex scattered laser goniometer (Photocor Instr., USA) was shown to be about 1.1 μM (Fig. S7).

Electronic spectra of oxidized and reduced SkQ1 are shown in Fig. S8a. The extinction coefficient for SkQ1 in ethanol at 267 nm was 21,730 $cm^{-1} \cdot M^{-1}$.

In the next series of experiments, we compared the ESR spectra of semiquinone species of different ubiquinone and plastoquinone derivatives: MitoQ, CoQ_1, SkQ1, decyl-PQ, PQ_0, SkQ3, and 2,3,5-trimethyl-1,4-benzoquinone. Some of these spectra are shown on Fig. S8b. The quinones were dissolved in ethanol and reduced by $NaBH_4$. The semiquinones were formed due to autooxidation of the corresponding quinols by O_2 at pH 8.

The EPR spectra of radical ions of MitoQ and short-chain analog of ubiquinol (CoQ_1) were found to be very similar. In both cases, the unpaired electron interacted with three protons of the methyl group at C5 and two protons of the methylene group at C6. However, hyperfine splitting due to methyl protons was about two times greater than hyperfine splitting due to methylene protons,

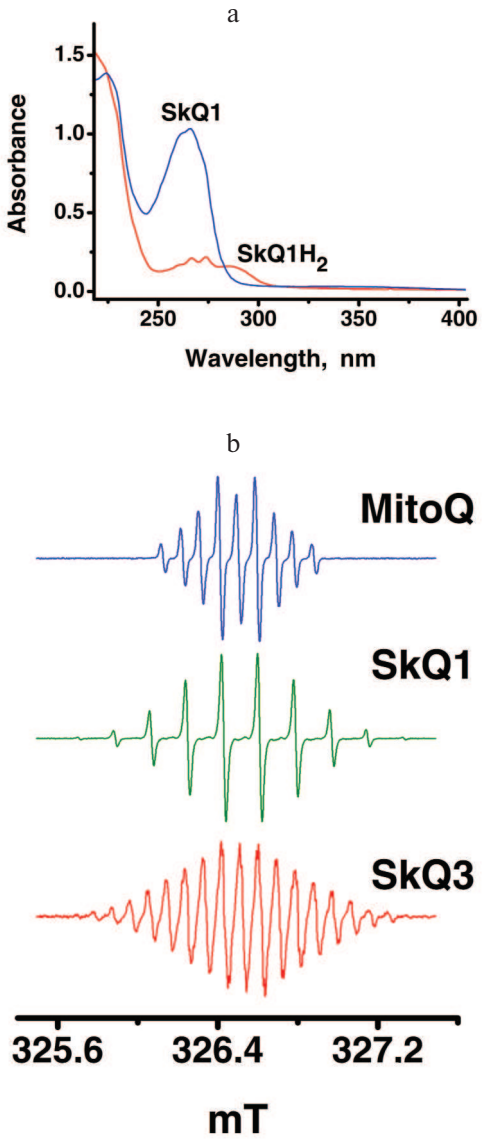


Fig. S8. Light absorption spectra of SkQ1 and $SkQ1H_2$ (a) and EPR spectra of semiquinones of MitoQ, SkQ1, and SkQ3 (b).

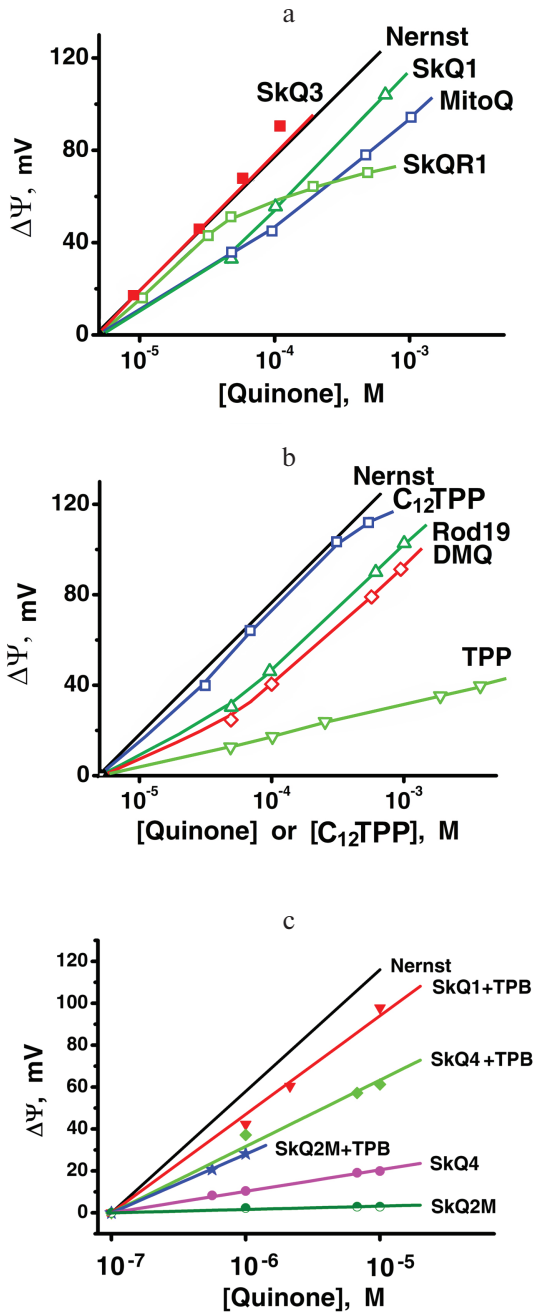


Fig. S9. Diffusion potentials generated across thick planar phospholipid membrane by some SkQ derivatives. For conditions, see Fig. 2, but pH 7.0.

i.e. a(3H) = 0.19 mT, a(2H) = 0.097 mT. This means that unpaired electron density at C5 and C6 atoms of the quinone ring of both MitoQ and CoQ_1 differed also about twofold. In the case of Q_0, unpaired electron density at C5-C6 atoms was shown to be equal to a(3H) = 0.236 mT and a(1H) = 0.197 mT.

The ESR spectra of SkQ1 and decyl-PQ can be characterized by almost identical interaction of unpaired electron with all nine protons of the quinone ring: six methyl group protons at C2 and C3, one proton at C5 and two protons of methylene group at C6: a(9H) = 0.18 mT. The ESR spectrum of decyl-PQ was practically the same. Consequently, in both cases all carbon atoms of the quinone ring equally shared the unpaired electron.

The hyperfine structure of the ESR spectra mentioned above clearly demonstrates that the semiquinones of both MitoQ and SkQ1 exist predominantly in the form of anion radicals, which could be stabilized by hydrogen bonding.

The ESR spectrum of SkQ3 was more complicated than that of SkQ1. Replacement of the proton at C5 with a methyl group resulted in a situation when the unpaired electron became more unequally shared by the carbon atoms of the quinone ring: a(9H) = 0.18 mT, a(2H) = 0.09 mT. A similar result was observed in the case of PQ_0 and 2,3,5-trimethyl-1,4-benzoquinone. The ESR spectra of these short-chain analogs of SkQ1 and SkQ3, respectively, demonstrated that unpaired electron density at C1-C6 atoms of the quinone ring were quite different (for PQ_0, a(6H) = 0.18 mT, a(2H) = 0.27 mT; for 2,3,5-trimethyl-1,4-benzoquinone, a(6H) = 0.181 mT, a(3H) = 0.225 mT, a(1H) = 0.191 mT).

S2: SkQs in BLM and Isolated Mitochondria

When studied in BLM, the SkQ derivatives synthesized were found to destabilize the membrane at concentrations higher than about $5 \cdot 10^{-5}$ M. To study such high concentrations, thick planar phospholipid membrane (which is more stable than BLM) was used (Fig. S9). On

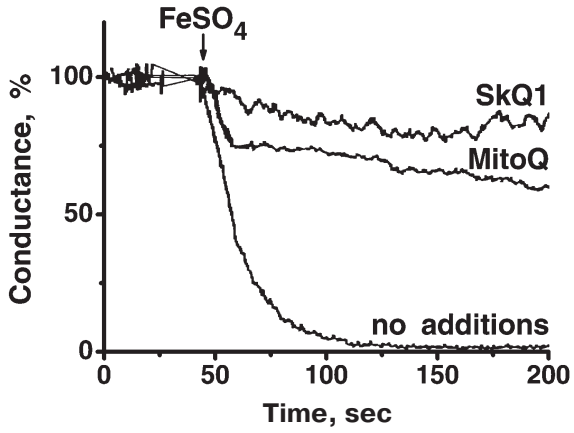


Fig. S10. Protective effects of SkQ1, SkQ3, and MitoQ upon inactivation of gramicidin channel by Fe^{2+}, ascorbate, and *tert*-butyl hydroperoxide. BLM was formed from a decane solution of diphytanoyl phosphatidylcholine and diphytanoyl phosphatidylglycerol (70 and 30%, respectively). Incubation mixture (see Fig. 3a) was supplemented with 0.5 mM ascorbate and 0.5 mM *tert*-butyl hydroperoxide. Additions: 5 μM SkQ1 or MitoQ and 20 μM $FeSO_4$.

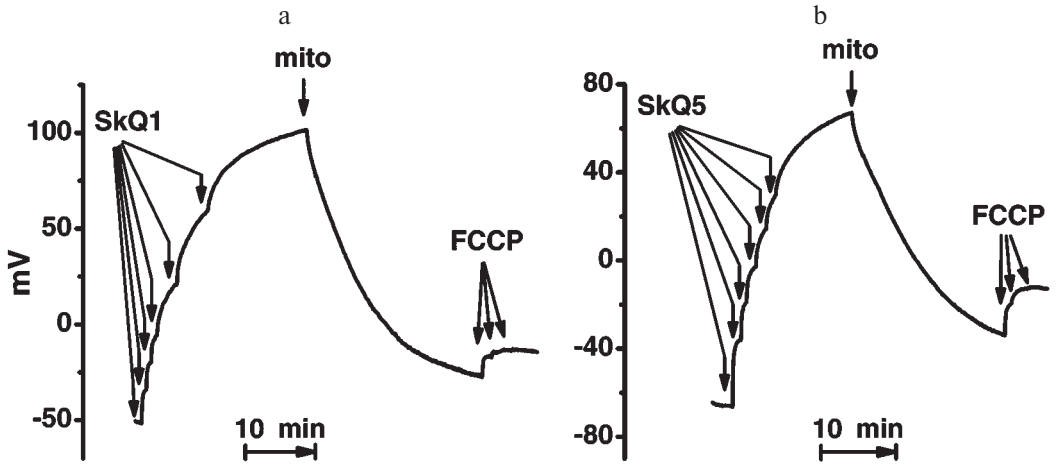


Fig. S11. Uptake of SkQ1 (a) and SkQ5 (b) by rat liver mitochondria. Incubation mixture, 250 mM sucrose, 5 mM Mops-KOH, 1 mM EGTA, BSA (0.2 mg/ml), 5 mM succinate, pH 7.4. Additions: each addition of SkQ1 or SkQ5 was 0.25 μM; mitochondria, 1.2 mg protein/ml; 100 nM FCCP (each addition).

such membranes, the SkQ concentrations could be increased to 10^{-3} M. Under these conditions, Nernstian diffusion potentials were obtained with SkQ1, SkQ3, MitoQ, C_{12}TPP, and DMQ. As to SkQR1 (Fig. S9a), diffusion potential decreased below Nernstian at its concentrations above $5 \cdot 10^{-5}$ M (most probably due to protonophorous activity of SkQR1). For SkQ2M and SkQ4, Nernstian potential was not observed even at high concentrations of these cations. However, it was increased in the presence of a penetrating anion, tetraphenyl borate (Fig. S9c).

In BLMs modified by gramicidin D, SkQ1 was shown to prevent inactivation of the gramicidin channels in the presence of a $FeSO_4$, ascorbate, and *tert*-butyl hydroperoxide (Fig. S10).

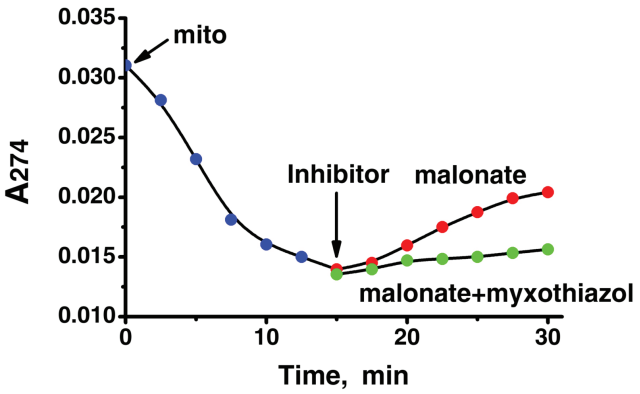


Fig. S12. SkQ1 can be reduced and oxidized by the mitochondrial respiratory chain. Reduction of SkQ1 was followed by measuring decrease in the light absorbance at 274 nm. For incubation mixture, see Fig. 4a. Additions: rat heart muscle mitochondria, 0.25 mg protein/ml; 2 mM malonate, 1 μM myxothiazol.

Accumulation of SkQ1 by mitochondria *in vitro* is shown in Fig. S11. The SkQ1 concentration was measured by a TPP electrode [7]. One can see that the SkQ1 import by mitochondria takes about 15-20 min. Subsequent addition of uncoupler FCCP induces rather small but measurable release of SkQ1. Since the octanol/water partition coefficient for SkQ1 was about 13,000 : 1, a large portion of the SkQ1 uptake could be explained by a $\Delta\psi$-independent, uncoupler-insensitive, passive sorption of SkQ1 by mitochondrial membranes, whereas the rest (uncoupler-sensitive portion) was due to the electrophoretic SkQ1 accumulation inside mitochondria. In line with this reasoning, substitution of SkQ1 by less hydrophobic SkQ5 (pentane instead of decane as a linker between triphenylphosphonium and plastoquinone; octanol/water partition coefficient about 500) decreased energy-independent uptake whereas energy-dependent uptake was increased (cf. Fig. S11, a and b).

Experiments showed that SkQ1 can be reduced by the mitochondrial respiratory chain. In the cases of succinate as reductant (Fig. S12), malonate added 15 min after succinate induced oxidation of $SkQ1H_2$, which was much slower than the preceding reduction of SkQ1 by succinate. This oxidation was inhibited by myxothiazol, indicating that Complex III is competent in the $SkQ1H_2$ oxidation, the rate of oxidation being lower than the rate of SkQ1 reduction by succinate.

Similar relationships were revealed when glutamate and malate substituted for succinate as the SkQ1 reductant (Fig. 4a (main text; here and further figures designated without "S" refer to the main article)). Rates of reduction of SkQ1 and MitoQ by succinate were found to be similar (not shown). The data of Fig. S12 indicate that SkQ1 added to mitochondria should be maintained mainly in the quinol form, a feature favorable for antiox-

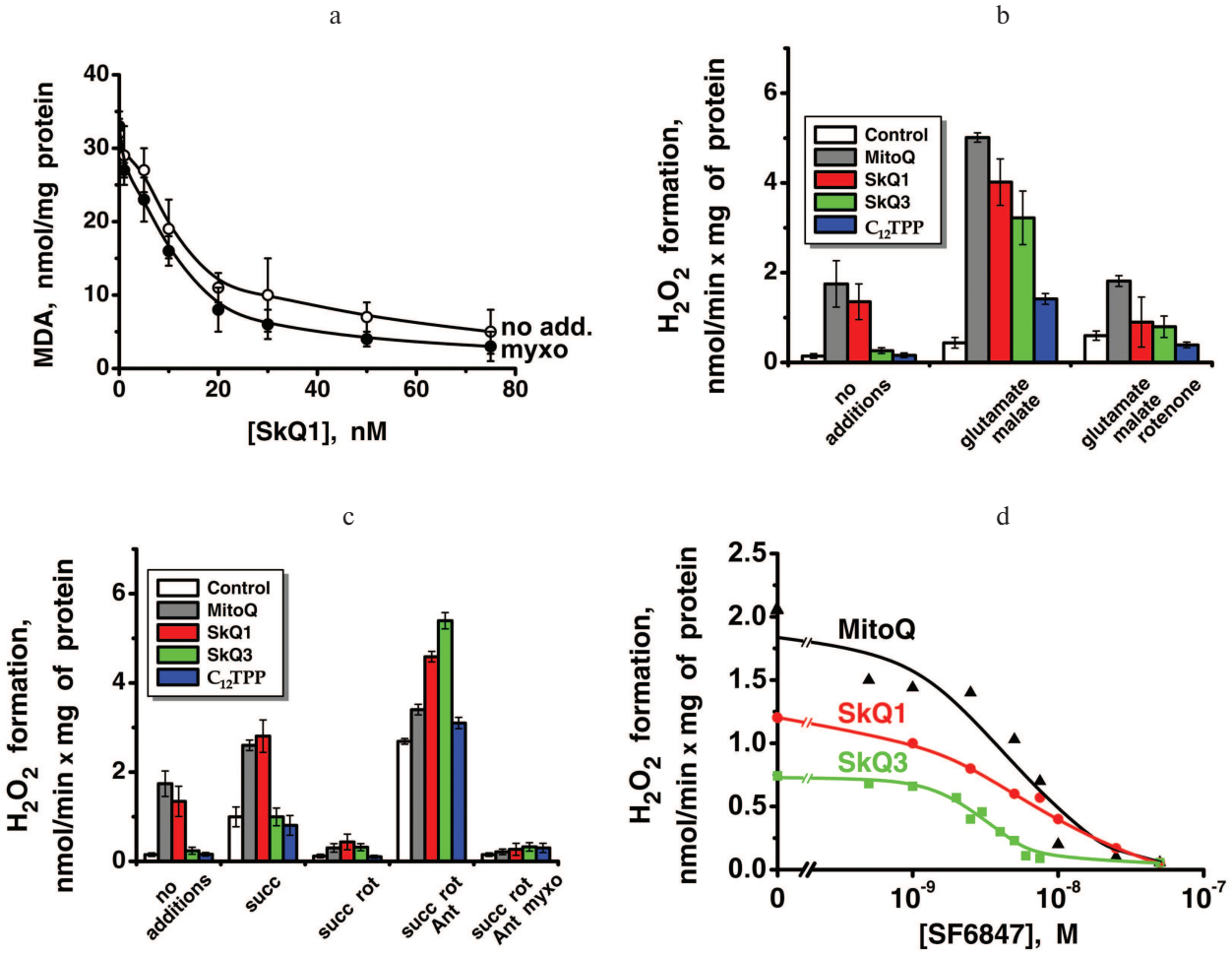


Fig. S13. Anti- and prooxidant effects of SkQ and MitoQ. a) Myxothiazol is without effect on antioxidant activity of SkQ1. For incubation mixture, see Fig. 4a. Substrate, 2.5 mM succinate. Addition, 1 μM myxothiazol. b-d) Effects of MitoQ, SkQ1, SkQ3, and C_{12}TPP on the H_2O_2 production by rat heart muscle mitochondria under various conditions. Incubation mixture as in Fig. 4b. Additions: 4 mM glutamate, 1 mM malate, 2 μM rotenone, 2 mM succinate, 1 μM antimycin A, 1 μM myxothiazol, and 1 μM MitoQ, SkQ1, SkQ3, and C_{12}TPP.

idant activity of this compound. In line with such a conclusion, we found that addition of myxothiazol, preventing quinol oxidation by the respiratory chain, increased only slightly the antioxidant activity of SkQ1 under the Fenton reaction conditions (Fig. S13a).

Results of a study of prooxidant activity of the cationic quinones are shown in Fig. S13, b-d. As follows from the data (Fig. S13, b and c), addition of μmolar MitoQ, SkQ1, or SkQ3 to mitochondria oxidizing glutamate and malate or succinate in State 4 strongly stimulates H_2O_2 production. C_{12}TPP fails to reproduce such an effect. The H_2O_2 generation is strongly inhibited by rotenone (Fig. S13, b and c) or uncoupler SF6847 (Fig. S13d). In the latter case, very low ($C_{1/2} = 6 \cdot 10^{-9}$ M) concentration of uncoupler is required. This value is close to that for inhibiting reverse electron transfer in Complex I and much smaller than that inducing half-maximal decrease in the $\Delta\psi$ level. This fact as well as the complete inhibition by rotenone of H_2O_2 formation with succinate indicate that ROS generation induced by cationic quinones is coupled to reverse electron transfer via Complex I. As to partial rotenone inhibition of H_2O_2 formation with NAD-substrates, it can be explained by a $\Delta\psi$ collapse (due to arrest of respiration), which prevents accumulation of cationic quinones in mitochondria.

S3: SkQ1 in Human Cell Cultures

As shown in the present paper, SkQ1 arrests apoptosis induced by low [H_2O_2] in cell cultures (Fig. 6, b and c). However, addition of large H_2O_2 amounts was shown to overcome the SkQ1-induced inhibition of apoptosis (Fig. S14a). As to a SkQ1-sensitive apoptosis induced by low [H_2O_2], it can be accounted for by the principle of ROS-induced ROS release when small amounts of ROS stimu-

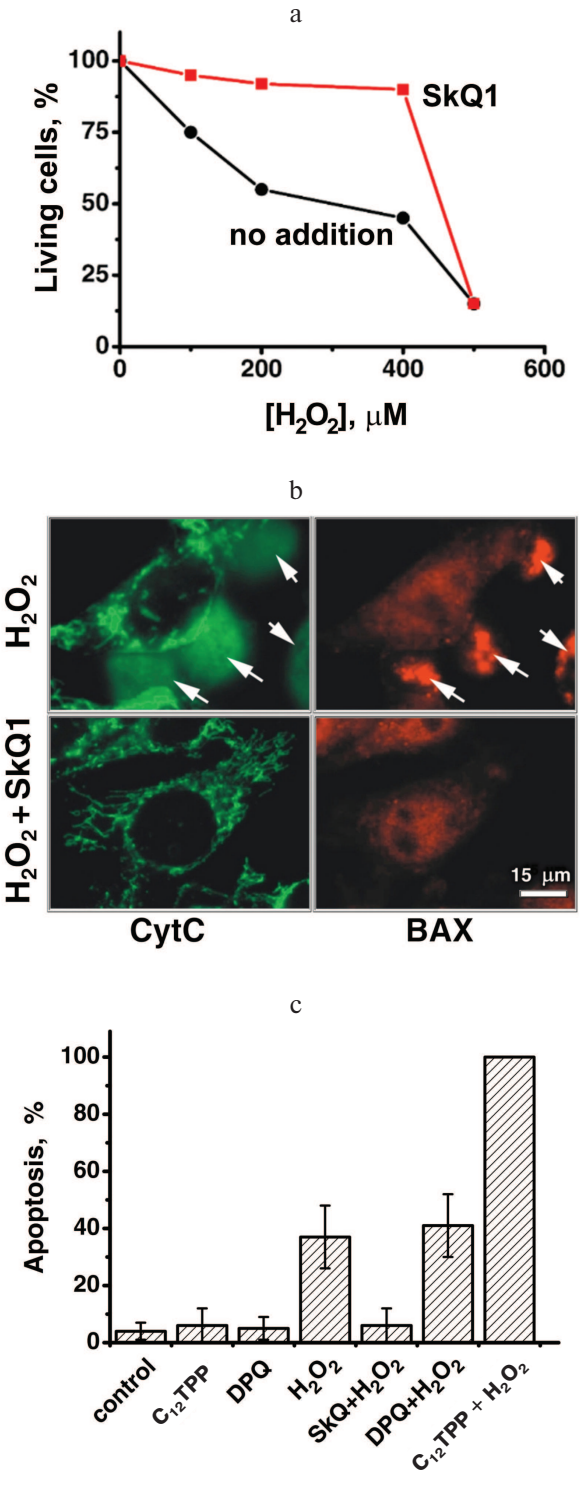


Fig. S14. a) Dependence of apoptosis of human fibroblasts upon the H_2O_2 concentration with and without SkQ1 pre-treatment. Where indicated, cells were pre-treated with 20 nM SkQ1 for 7 days. b) Effect of SkQ1 pre-treatment on localization of cytochrome *c* (green) and BAX (red) in HeLa cells treated with 200 μM H_2O_2 for 7 h. SkQ1 as in (a). Cytochrome *c* and BAX were stained with specific antibodies (Pharmingen). Arrows indicate apoptotic cells. c) Effect of 20 nM SkQ1, DPQ, and C_{12}TPP on the H_2O_2-induced apoptosis of human fibroblasts. Cells were pre-treated with SkQ1, C_{12}TPP, or DPQ for 7 days. Where indicated, 400 μM H_2O_2 was added. Apoptosis was measured after 24 h.

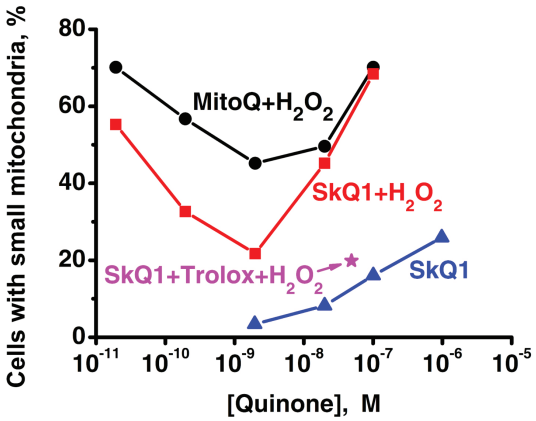


Fig. S15. H_2O_2-induced fission of elongated mitochondria in HeLa cells. SkQ1, MitoQ, or 0.1 mM Trolox was added 2 h before the 350 μM H_2O_2 treatment. Number of cells with small mitochondria was measured 20 h after the H_2O_2 treatment.

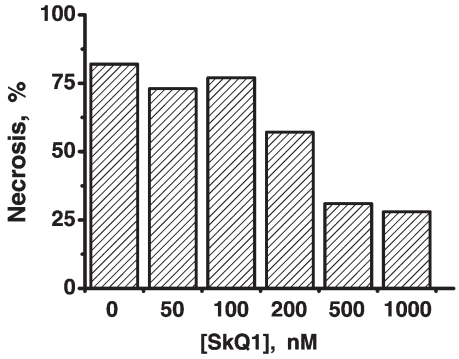


Fig. S16. SkQ1 protects against a light-induced necrosis. SkQ1 was added 1 h before illumination. Conditions as in Fig. 6f.

late formation of large ROS amounts (Fig. 6d). Quite recently, Pinton et al. described a molecular mechanism of such kind of event [8]. They reported that added H_2O_2 stimulates phosphorylation of p66shc, a "lifespan-shortening protein", by protein kinase C_β. Phosphorylated protein (P-p66shc) becomes a target for proline isomerase Pin1, which converts P-p66shc to a conformer imported by mitochondria. In the mitochondrial intermembrane space, P-p66shc combines with cytochrome *c*, an event most probably resulting in that cytochrome *c* acquires ability to reduce O_2 to $O_2^{\cdot-}$ [9]. This, in turn, increases mitochondrial [ROS] and opens the permeability transition pore in the inner mitochondrial membrane. The latter event leads to release of cytochrome *c* and other pro-apoptotic proteins from mitochondria to cytosol, thereby initiating apoptosis.

One of steps of the above cascade, namely, H_2O_2-induced cytochrome *c* release, was already confirmed in our group (Fig. S14b). In the same experiment, the proapoptotic protein BAX was shown to migrate to mitochondria in the H_2O_2-treated cells. Both processes were

arrested by SkQ1. Identification of p66shc as a possible player in this episode is now under investigation.

Figure S14c shows that antiapoptotic effect of SkQ1 on the H_2O_2-treated cells cannot be reproduced by C_{12}TPP and decylplastoquinone (DPQ), compounds of similar hydrophobicity but lacking either quinone or cationic residue. Even more, C_{12}TPP proved to stimulate the H_2O_2-induced apoptosis.

Figure S15 shows that SkQ1 is more effective than MitoQ in protection against H_2O_2-induced fragmentation of mitochondria in HeLa cells. Prooxidant effect of SkQ1 was observed at higher concentrations and was prevented by Trolox.

In Fig. S16, concentration dependence of antinecrotic SkQ1 effect is seen, $C_{1/2}$ being within $(2\text{-}5)\cdot10^{-7}$ M SkQ1.

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