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Supplementary Material

High Glucose Enhances Skin Sensitizer-induced NRF2 Activation *In Vitro*

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Abstract:

Background:

Hyperglycemia has a potentially critical role in the promotion of sensitization, however, the clear mechanism of this phenomenon is unknown. The activation of NRF2 is a key event triggered by skin sensitizers. Therefore, we investigated the effects of high glucose on the activation of NRF2 by the skin sensitizers *in vitro*.

Methods:

The involvement of glucose levels in NRF2 activation by cinnamaldehyde, a skin sensitizer, was assessed in human MCF-7 breast cancer cells under normal glucose conditions (1.0 g/L D-glucose) and high glucose conditions (4.5 g/L D-glucose).

Results:

High glucose induced the NRF2 transactivation, *HMOX1* mRNA expression, and SOD-like activity. Nuclear NRF2 level was increased under high glucose conditions compared to normal glucose conditions. High glucose also enhanced the cinnamaldehyde-induced *HMOX1* mRNA expression and SOD-like activity.

Conclusion:

Oxidative stress caused by hyperglycemia induced additionally the activation of NRF2 signaling by skin sensitizers.

Keywords: Glucose, Skin sensitizer, Cinnamaldehyde, Oxidative stress, KEAP1-NRF2 signaling, ROS.

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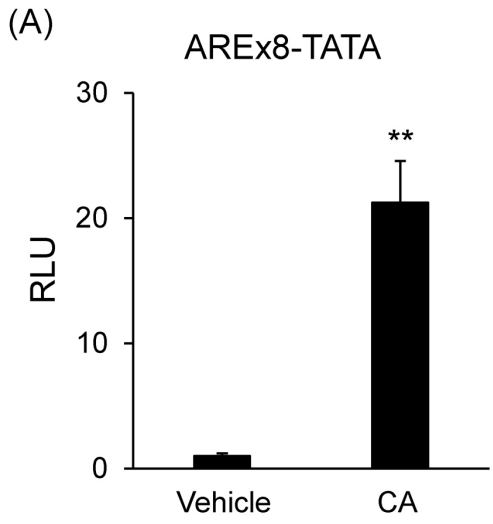

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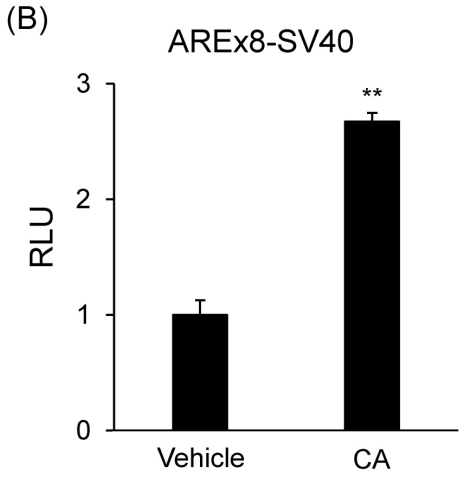

Fig. (S1). Supplement 1 Luciferase assay in MCF-7 cells transfected with pAREx8-TATA or pAREx8-SV40. MCF-7 cells were transfected with pAREx8-TATA (**A**) or pAREx8-SV40 (**B**) and further incubated in the absence or presence of 32 μM CA under normal glucose conditions for 24 hours. The luciferase activity was determined. Experiments were performed in triplicate, and values are indicated as mean ± S.D. Statistically significant differences are indicated by an asterisk (**$p < 0.01$ by Student's *t*-test).