

Pharmacological activation of the Nrf2 pathway attenuates UVB & LPS-induced damage

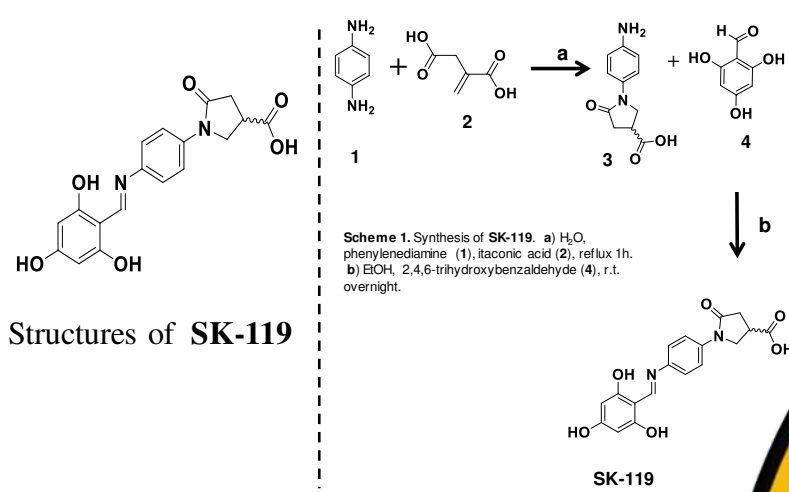
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Introduction: In order to protect the human body against environmental stress, such as UVB, a multifunctional enzymatic and antioxidant defense system is expressed in the skin. A key regulator of this pathway is the transcription factor Nrf2. We have speculated that targeted activation of this pathway may provide therapeutic options against oxidative stress-related disorders.

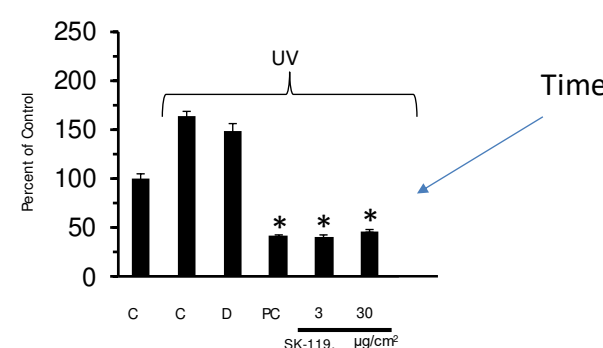
1 Synthesis of pharmacological Nrf2 activator (SK-119)

A novel pharmacological Nrf2 activator (E)-5-oxo-1-(4-((2,4,6-trihydroxybenzylidene)amino)phenyl)pyrrolidine-3-carboxylic acid (SK-119) was synthesized after in silico design

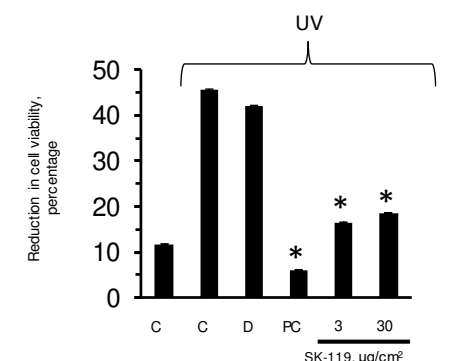


3 Sk-119 attenuates UVB-induced damage

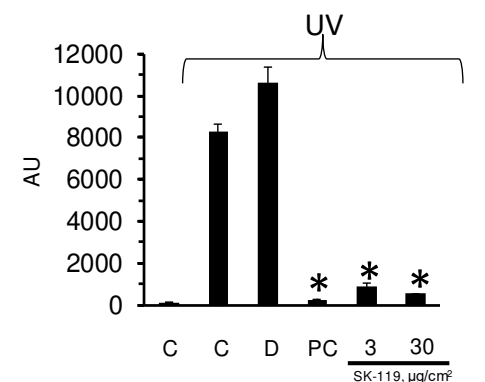
SK-119 Attenuates ROS generation



SK-119 Attenuates UVB-induced damage



SK-119 Attenuates DNA damage



Conclusions

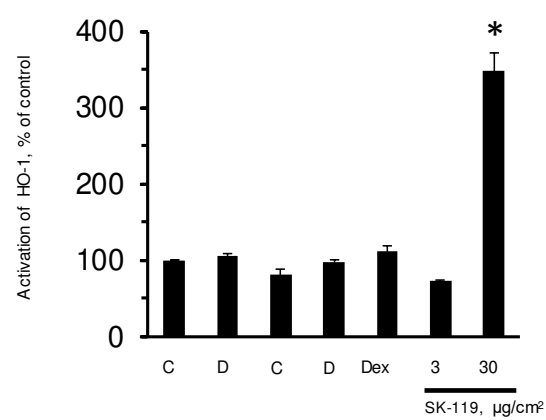
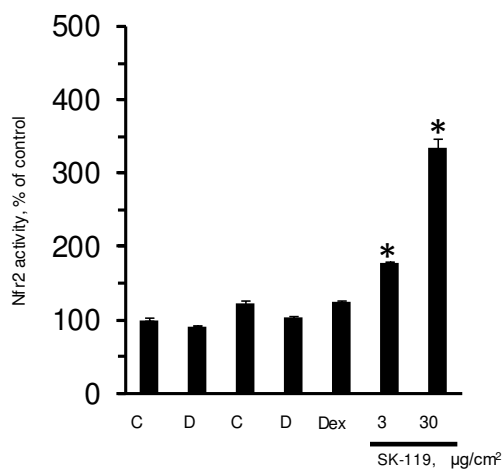
The results suggest that pharmacological activation of Nrf2 may be used as a therapeutic option by enhancing the endogenous protection of the skin.

NRF2 activation

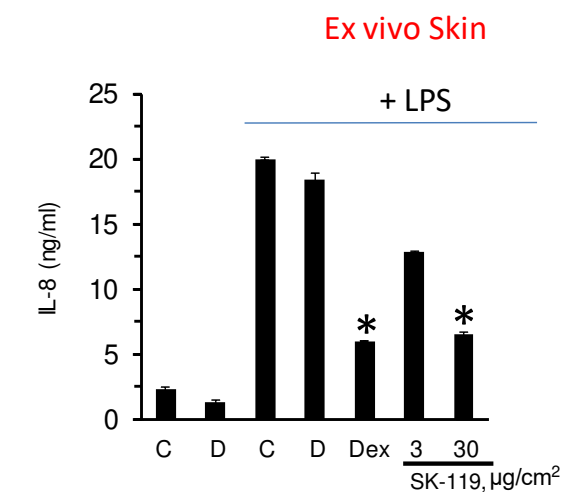
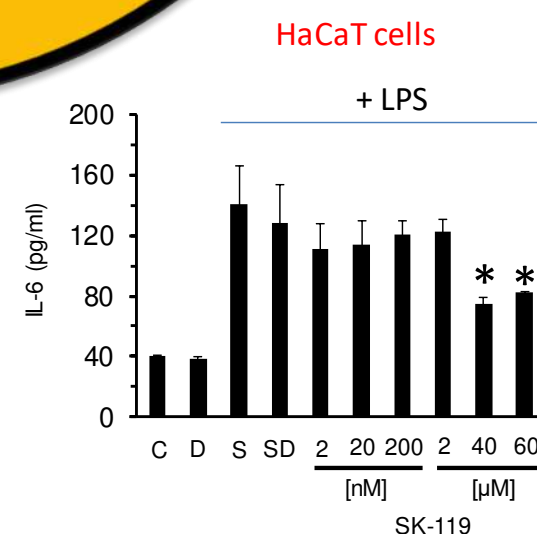


Endogenous protection against stress

2 Topical application of Sk-119 activates Nrf2 in ex vivo human skin



4 Sk-119 attenuates LPS-induced inflammation



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