

〈Regular Article〉

**A Possible Mechanism Underlying the Hypersensitivity of Dry Skin to Sensory Stimuli:  
Low Humidity Modulates the Imbalance between Nerve Growth Factor and  
Semaphorin3A through Oxidative Stress**

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**Abstract**

Skin exposed to low humidity often shows hypersensitivity to sensory stimuli. The aim of this study was to identify the mechanism underlying such hypersensitivity to sensory stimuli using reconstructed epidermal equivalents (RHEEs) exposed to low humidity.

RHEEs exposed to low humidity were identified to be an appropriate model of dry skin by their secretion of interleukin (IL)-1 $\alpha$  and carbonylated proteins (CPs). Oxidative situations and protein expression levels of nerve growth factor (NGF) and semaphorin3A (Sema3A) in RHEEs exposed to low humidity were compared with control RHEEs. It was found that RHEEs exposed to low humidity synthesized superoxide anion radicals ( $\cdot\text{O}_2^-$ ) in a higher level. RHEEs exposed to low humidity also showed a higher level of NGF and a lower level of Sema3A compared to those of control RHEEs. In addition, treatment with the conditioned medium of RHEEs exposed to low humidity stimulated axon elongation in N1E-115 neuroblastoma cells. These phenomena were abolished by superoxide dismutase.

Thus,  $\cdot\text{O}_2^-$  generated in RHEEs exposed to low humidity caused an imbalance of NGF and Sema3A, which can result in creating a higher susceptible conditions against sensory stimuli.

**Key words:** dryness, reactive oxygen species, NGF, semaphorin3A, epidermis.