Synopsis of Original Research Paper

A role of stress response kinase ASK1 in the inflammatory skin disease.

Hidenori Ichijo, Junya Mizukami

Graduate School of Pharmaceutical Sciences, The University of Tokyo

The skin provides a first line of defense against various physicochemical and biological stresses such as wound and microbial pathogens and induces inflammatory response. The adaptive responses to these stresses are essential for the maintenance of homeostasis and dependent on the stress recognition mechanism and intracellular signaling systems. Apoptosis signal-regulating kinase 1 (ASK1) is activated in response to various stimuli such as oxidative stress and a mitogen activated protein kinase kinase kinase (MAPKKK) family member that activates both the p38 and JNK signaling cascades. Recent studies revealed that ASK1 is required for the production of inflammatory cytokines and migration of macrophages and induces apoptosis of keratinocytes in the skin.

Contact hypersensitivity (CHS) is a form of delayed-type hypersensitivity, an immune response to a variety of reactive contact sensitizers, such as metals, preservatives, and hair dyes. Whereas the sensitization phase of CHS has been focused on as a model for investigating T-cell-dependent immune response by immunologists, the elicitation phase in which allergic contact dermatitis is clinically manifested has received much attention from clinicians. Even in the mouse model of CHS, however, it is difficult to distinguish between the role of a certain molecule involved in the CHS response in the sensitization phase and that in the elicitation phase. Here we show, using a chemical genetic approach, that ASK1 plays an important role in the both sensitization and elicitation phase of the CHS response and would be a therapeutic target for the inflammatory skin diseases.