News Release

Progression from *in vivo* validation to *in vitro* screening in hazard assessment for leukoderma-inducible chemicals

Key Points

- 6 positive control chemicals with leukoderma in duction potencies and 3 negative control chemicals with leukoderma induction potencies were chosen based on human case studies.
- 6 positive control chemcals induced leukoderma while 3 negative control chemicals did not validated by in vivo assessment.
- 6 possitive and 3 negative control chemicals were correctly distinguished by the presence or absence of endoplasmic reticulum stress induction in immortalized normal melanocytes.

Summary

Chemicals are representative environmental factors that affect human health. Recently, external exposure to a chemical of rhododenol (RD) caused chemical leukoderma, an acquired patchy hypopigmentation, in about 20,000 Asian people. The development of a hazard assessment system for accurate determination of leukoderma-inducible chemicals is required for the prevention of such tragedies. Case studies in humans have shown 6 chemicals, including RD, with a constitutive leukoderma-inducible potency and 3 chemicals with a photosensitive but not a constitutive leukoderma-inducible potency. In this study, the 6 positive and 3 negative control chemicals with or without constitutive leukoderma-inducible potencies were investigated by our previously developed in vivo hazard assessment system using tail skin of mice. Based on the results of validation, this study aimed to develop an in vitro hazard assessment system to correctly determine chemicals with a constitutive leukoderma-inducible potency. As expected, external exposure to the 6 positive control chemicals, but not external exposure to the 3 negative control chemicals, resulted in development of constitutive leukoderma in mouse tail skin with a decreased level of skin melanin and decreased number of melanocytes. Moreover, the 6 positive and 3 negative control chemicals were correctly distinguished by the presence or absence of endoplasmic reticulum (ER) stress induction, but not by tyrosinase-dependent cell death or production of reactive oxygen species (ROS), in immortalized normal melanocytes. The

hazard assessment system using tail skin could be a solid in vivo tool to reliably determine the chemical potency of a chemical for constitutive leukoderma induction. The hazard assessment system focusing on ER stress induction in normal melanocytes might be a novel and convenient in vitro tool for accurately evaluating chemicals with leukoderma-inducible potencies. Thus, this study contributed to environmentology through the development of a screening system for preventing an environmental factor-related disease.

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