Synopsis of Original Research Paper

Development of a novel therapeutic application for allergic skin diseases using intracellular proteases

Takayuki Tsukuba

Department of Dental Pharmacology, Graduate School of Biomedical Sciences, Nagasaki University

Cathepsin E is an endolysosomal aspartic proteinase predominantly expressed in immune related cells. In our previous study, cathepsin E-deficient mice displayed atopic dermatitis. In addition, macrophages derived from cathepsin E-deficient mice showed an accumulation of the lysosomal membrane sialoglycoproteins, LAMP-1 and LAMP-2, and, consequently, an elevation in lysosomal pH. However, the molecular mechanism by which cathepsin E deficiency causes atopic dermatitis remains unclear. In this report, we demonstrate that cathepsin E-deficient macrophages showed an increased reactive oxygen species production and up-regulation of oxidized peroxiredoxin-6, but decreased antioxidant glutathione. Moreover, cathepsin E-deficient macrophages displayed higher sensitivity to cell death by oxidative stress treated with H_2O_2 and paraquat. Higher-sensitivity of cathepsin E-deficient macrophages to infection with *Staphylococcus aureus* was observed. These results indicate that cathepsin E deficiency causes increased oxidative stress, suggesting that these abnormalities in cathepsin E-deficient cells are presumably involved in the abnormal host defense of these mice.