

# The role of alternative autophagy in atopic dermatitis and its therapeutic use

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We aimed to elucidate the role of autophagy in skin development. There are two types of autophagy, namely canonical autophagy and alternative autophagy, and we generated various skin-specific autophagy gene-knockout mice. Although simple knockout mice of canonical autophagy and alternative autophagy did not show any remarkable abnormalities, double-knockout (Beclin1-knockout) mice died within a day after birth owing to impairment of epidermal barrier. Furthermore, we found that Beclin 1 deficiency causes mislocalization of integrins, abnormal cell detachment of basal cells and their immature differentiation, and abnormal skin development.

We also screened a low-molecular weight compound library to identify chemicals with alternative autophagy-inducing activities and successfully identified candidate compounds. By the application of these compounds to atopic dermatitis model mice, we obtained TMD-AD129 compound which exhibited strong anti-dermatitis activity. At present, we are optimizing this compound for development as drugs.