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Crucial role of phospholipase C ϵ in ultraviolet B irradiation-induced skin inflammation and skin tumor development

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We have investigated the role of phospholipase C (PLC) ϵ in ultraviolet B (UVB) irradiation-induced skin inflammation and skin tumor development using $PLC\epsilon$ knockout mice. We irradiated wild-type mice and $PLC\epsilon$ knockout mice with a single shot of UVB at doses of 1.0 and 2.5 kJ/m² and pathologically examined the skin. Assessment of apoptosis by TUNEL assay showed that skin cells such as keratinocytes, fibroblasts, and endothelial cells in $PLC\epsilon$ knockout mice exhibited marked resistance to UVB-induced apoptosis on days 1 and 2. Also, the extent of neutrophil infiltration into the epidermis in $PLC\epsilon$ knockout mice was smaller than in wild-type mice on days 1 and 2. We next irradiated wild-type mice (n = 10), $PLC\epsilon$ heterozygous mice (n = 10), and $PLC\epsilon$ knockout mice (n = 10) with UVB at doses of 2.5 kJ/m² and 10 kJ/m² thrice a week for 40 and 25 weeks, respectively, and observed tumor formation until at 45 and 50 weeks, respectively. In the 2.5 kJ/m²-irradiated mice 1 of the 10 mice developed papilloma in each group. In the 10 kJ/m²-irradiated $PLC\epsilon$ knockout mice 5 types of tumor (papilloma, squamous cell carcinoma, spindle cell tumor, hemangioma, and angiosarcoma) developed in 6 mice. Also, 1 papilloma developed in wild-type mice, and 1 papilloma and 1 hemangioma developed in $PLC\epsilon$ heterozygous mice. Our results indicate that $PLC\epsilon$ plays a crucial role in UVB-induced skin inflammation and suggest that resistance to UVB-induced apoptosis conferred by the absence of $PLC\epsilon$ promotes UVB-induced fibroblast- and endothelial cell-derived tumor development.