51.Topical tacrolimus treatment does not facilitate UV-induced carcinogenesis in a mouse model.

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Tacrolimus is an immunosuppressive drug mainly through down-regulation of T cell activation. Topical application of tacrolimus is therapeutically effective on chronic inflammatory skin diseases. However, there has been a concern about increased risk of UV exposure-induced skin cancer facilitated by topical tacrolimus, because of its potential suppression of anti-tumor immunity. The aim of this study was to examine whether topical tacrolimus treatment facilitated UV-induced carcinogenesis using K5.Stat3C mice. K5.Stat3C mice expressed constitutively activated Stat3 in epidermis and therefore were prone to skin cancers, induced by the carcinogenesis regimen of UVB irradiation. To verify immunosuppressive potential of tacrolimus, an experiment of contact hypersensitivy (CH) by dinitrofluorobenzene (DNFB) was conducted. Four days after sensitization of DNFB in the back skins of K5.Stat3C mice, DNFB was challenged onto the ear skins twice weekly, with or without topical tacrolimus treatment. Tacrolimus significantly attenuated ear swelling and dermatitis induced by repeated application of DNFB, indicating that tacrolimus ameliorated the CH response as expected. Finally, K5.Stat3C mice were subjected to the UVB carcinogenesis regimen which induced epidermal atypia after 12 weeks and squamous cell carcinoma after 16 weeks. Immediately after every irradiation, we topically treated them with tacrolimus or vehicle onto the right ears and left ears, respectively. Histological examination revealed that there was no difference between the two groups in the latent period of onset of epidermal atypia, cancer development or histological appearance. Taken collectively, topical tacrolimus did not facilitate UVB-induced carcinogenesis, although it suppressed the CH response to hapten.