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Skin cancer is a serious problem for many organ transplant recipients. Half of them develop skin cancer within 20 years after the transplantation. The main cause of this increased skin cancer risk is thought to be suppression of the immune system, a necessity to prevent rejection of the transplanted organ.

This thesis focuses on the effects of immunosuppressive drugs on the responses of skin cells to UV irradiation and how these altered responses would affect UV-induced skin cancer development. The goal was to compare several immunosuppressants and identify the least hazardous one. Human skin cultures and mice were used as experimental models to study short and long term effects in successive stages of tumor development.

These studies have yielded several unexpected findings. Foremost, none of the tested immunosuppressants increased skin cancer development in mice when administrated in the diet; remarkably, cyclosporin even delayed tumor onset. And furthermore, seemingly discordant effects of the drugs on different putative stages of tumor development evoked a new perspective on the step-wise process leading up to skin cancer.

More specifically and contrary to the prevailing consensus, this study showed that UV-induced early microscopic clusters of skin cells overexpressing the mutant-p53 tumorsuppressor protein are not early stages or precursors of ensuing skin carcinomas with mutant-p53. Surprisingly, some immunosuppressants affected the number of these clusters without corresponding effects on tumor onset.

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PIETER VOSKAMP Local effects of immunosuppressants in the skin and impact on UV carcinogenesis

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