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PHOTOBIOLOGY AND PHOTOPROTECTION

## NEW DEVELOPMENT IN PHOTOCARCINOGENESIS

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The number of patients with skin cancers is increasing woprldwide. In this session first of all, state of skin cacers are summarized briefly and present new insights in photocarcinogenesis. Photocarcinogenesis is multistage process of initiation, promotion and progression. It is also known that UV induced immunesuppression is strongly involved in photocarcinogenesis. A conventional knowledge demonstrated that genetic mutation caused by UVB induces initiation and UVB-inflammation (sunburn) induces promotion. However recent findings revealed that photocarcinogenesis pathway is more complex consequences where each process of initiation, promotion and UV induced immunesuppression is closely related. DNA damage itself trigers the signaling pathway in inflammation or immunesuppresion. In Ogg1 knockout mice the presence of 8-oxo-7,8-dihydroguanine (8-oxoG), oxidative DNA damage, upregulate inflammatory genes. Pyrimidine dimers, major DNA photolesions, have been shown to cause UV induced immunesuppression, partly by upregulation of IL-10, immunesuppresive cytokine. UVB (and UVA) causes the formation of dipyrimidine photoproducts or oxidative DNA damage in skin cells, resulting in the alteration of the genes involved in cell cycle, apoptosis or inflammation. Oxidative stress caused by UV also modify cell signaling by redox regulation. Epidemiological studies have shown that intermittent severe inflammation caused by acute sunburn is a major risk factor in the development of skin cancers. Sunburn is elicited by oxidative stress caused by UV at or near the membrane. We found that anti-inflammatory dietary food, Spirulina platensis (Sp) can reduce the development of UVB-induced skin tumors in mice. The inhibitory effect of Sp on acute UV response, "sunburn", was confirmed macroscopically and microscopically along with a significant decrease in the proinflammatory cytokines expressions such as IL-1 $\beta$  and Cxcl-1 in mice irradiated with UVB. Sp has an antioxidant effect as it had reduced the formation of 8-oxoG, whereas it had little effect on the amount of pyrimidine photoproducts. We have shown that TLR4 is also involved in this photocarcinogenesis process. These results indicated not only cumulative dose but intensity of UV is considered for skin cancer prevention. Furthermore a inhibition of CXCL1 by using neutralising antibody suppressed the development of skin cancers in mice model of photocarcinogenesis, indicating a close correlation between inflammatory processes and photocarcinogenesis.





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