

DIETARY FAT AND UV INDUCED CARCINOGENESIS

V.E. REEVE, M. MATHESON, G.E. GREENOAK, P.J. CANFIELD and C.H. GALLAGHER

There is well-founded epidemiological evidence for the enhancement of various cancers in man by high dietary fat. There is also experimental evidence in rodents that high fat diets enhance the incidence of spontaneous and chemical carcinogen-induced mammary cancers. However, there is controversy concerning the effect of the degree of saturation of lipids on carcinogenesis. It is claimed that the high fat enhancement of chemically induced tumours in rats requires the inclusion of a minimal concentration (3%) of unsaturated fat (Carroll and Khor 1971), but others have evidence that the enhancement is proportional to the unsaturated fat content and not dependent only on the minimal dietary requirement being satisfied (Clinton et al. 1954). However, little is known of the effects of dietary fat on cancers induced by UV light, the most ubiquitous of environmental carcinogens (Black 1987).

We have examined the role of dietary fat content and saturation on the induction of skin tumours in the HRA/Skh hairless mouse by chronic mild exposures to simulated solar UV light and have found that:-

a) In mice fed isocaloric semi-purified diets containing low (5%) or high (20%) sunflower oil as the sole fat source, there was no effect on UV induced tumorigenesis. However, if mice were fed commercial mouse pellets soaked in sunflower oil (8-12% total fat) an enhancement of UV tumorigenesis was observed compared with mice fed normal pellets. This implies that high dietary fat does not increase UV tumorigenesis unless fed as a supplementary caloric source to the normal diet, and that an altered metabolic balance must underlie this effect.

b) Mice fed 20% saturated fat were entirely protected from UV induced tumour expression, whereas 20% unsaturated fat resulted in 100% tumour incidence. Refeeding normal pellets, or topical application of the tumour promoter, croton oil, revealed that saturated fat fed mice were harbouring latent tumours. Therefore a dietary deficiency of unsaturated fat had prevented the promotion phase of UV tumorigenesis.

c) Mice fed 20% fat required less than 1% unsaturated fat to overcome the inhibited tumour growth.

d) Dietary fat did not influence the localised immune suppression normally induced by chronic low-dose UV exposure (Elmets et al. 1985) by which mechanism initiated tumour cells escape recognition and rejection in the epidermis.

We postulate that the dietary fat regulation of UV tumour outgrowth occurs not at the initiation but rather the promotion phase of carcinogenesis, and that a deficiency of unsaturated fatty acids is reflected in a reduced availability of arachidonic acid for the further metabolism to critical immunogenic compounds, such as prostaglandins of the E series. These are increased in UV irradiated skin and may mediate the defect in antigen presentation which results in systemic immunosuppression after high doses of UV and permits tumour proliferation in the skin (Noonan et al. 1981).

CARROLL, K.K. and KHOR, H.T. (1971). *Lipids* 6:415.

CLINTON, S., MULLOY, A. and VISEK, W. (1984). *J.Nutr.* 114:1630.

BLACK, H.S. (1987). *Fed.Proc.* 46:1901.

ELMETS, C., LEVINE, M. and BICKERS, D. (1985). *Photochem. Photobiol.* 42:391.

NOONAN, F., DEFABO, E. and KRIPKE, M. (1981). *Photochem. Photobiol.* 34: 683.