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Milestones and controversies in skin cancer research

The skin represents one of the largest organ systems of the human body - constituting about one-twelfth of total body weight. Positioned as the interface between the internal systems of the body and its environment, the skin acts as a barrier to an expansive array of extrinsic agents and provides the foremost target for environmental insult. Thus, it is not surprising that skin cancer in some light skinned populations represents the most frequently occurring neoplastic disease. In the United States skin cancer accounts for over one million new cases annually. Major milestones in the study of cancer development have been achieved through investigations of the carcinogenic potential of various agents on skin. Indeed, Sir Percivall Pott (1775) associated exposure to soot in chimney sweeps to skin cancer. However, exposure to ultraviolet radiation (UVR) accounts for ~90% of non-melanoma skin cancer incidence. More than 100 years after Pott's observation, Unna (1894) associated the severe degenerative changes of sun-exposed areas of sailors' skin with the development of skin cancer, "Carcinome der Seemannshaut". Shortly after, Dubreuilh (1896) also found an association of "la lumiere solaire" (sunlight) exposure with keratoses and skin cancer exhibited by vineyard workers in southern France. Similarly, Shield (1899) observed the predisposition to skin cancer in light-skinned individuals, especially of Celtic origin, and living in geographical areas of high insolation. Experimental proof of the causal role of UVR in skin cancer was provided by Findlay (1928) when he demonstrated that UVR from a quartz-mercury vapor lamp induced skin cancer in mice. Roffo (1939) confirmed that observation and reported that natural sunlight also induced skin cancer in rats. He also was the first to recognize the importance of lipids in cancer development and to conduct an epidemiological study of skin cancer in humans, analyzing occurrence with respect to anatomical site, gender, nationality, and occupation. Roffo was the first to set an approximate limit of effectiveness in skin cancer induction to those wavelengths of <320nm. An action spectrum for UVR-induced skin cancer in humans has now been adopted by the CIE, although there still remains controversy regarding the role of UVA, especially with respect to melanoma. Once it was clearly established that UVR was the primary incitant of skin cancer, a number of studies examined factors that could modulate the disease. Baumann and Rusch (1939) observed that dietary fat influenced UVR induced skin cancer expression. Kripke and Fisher (1976) demonstrated the immunosuppressive nature of UVR and Black et al (1995) found that dietary fat level and source of fat exerted profound influence over specific immune responses. Black (1974) also provided evidence that specific dietary antioxidants could inhibit UVR-carcinogenesis. Questions exist regarding antioxidant supplementation versus consumption of foods that are naturally rich in antioxidants as a means of cancer prevention. A recent controversy has developed concerning levels of UVR exposure with respect to the risk of skin cancer development as opposed to the health benefits resulting from vitamin D synthesis.

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