

Infectious Causes of Human Cancer: Results and Perspectives

Harald zur Hausen, Deutsches Krebsforschungszentrum, Im Neuenheimer Feld 280,
69120 Heidelberg, Germany

During the past 30 years up to 21% of the global cancer incidence has been linked to infectious events, involving specific viral, bacterial and parasitic agents. Particularly the discovery of a role of Hepatitis B virus in hepatocellular carcinomas and of high risk human papillomaviruses (HPV) in cervical, other anogenital and oropharyngeal cancers triggered novel approaches in cancer prevention by vaccination. A global application of these vaccines theoretically could reduce the cancer risk in females by 12-14%, in males by 4-5%. The analysis of mechanisms of cell transformation by infectious agents revealed that some of them act as direct carcinogens. Here persistence of specific virus genes within each tumor cell emerges as a precondition to maintain the malignant state. Other agents act indirectly by either inducing immunosuppression and frequently then the activation of other latent tumor-linked infection, or by the chronic induction of inflammatory events. Even when infectious agents act as direct carcinogens, additional modifications within specific host cell signalling cascades essentially contribute to the eventual malignant proliferation. Considerations will be presented to analyze even cancers experimentally not yet linked to infectious events for a possible involvement of exogenous agents in their etiology. This involves in part cancers increased under immunosuppression, but also those with a reduced or not elevated incidence after immunosuppression. Malignant tumors arising either in the sequence of other basically non-transforming infections will also be discussed. Infections deserve additional attention which seem to protect against the subsequent risk for specific human cancers (acute lymphoblastic leukemia and other hematopoietic malignancies). Finally, potential synergistic effects of nutritional carcinogens with virus infections will be discussed.