The IARC Monographs: Biological Agents and Cancer

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Evaluations and challenges
The IARC Monographs programme started evaluating the carcinogenicity of biological agents in 1993:
- In 2009, Volume 100B considered 11 biological agents.
- In 2011, Volume 104 considered Niflurin and 4 polymavirus SV40, and the human BIV, JCV and MCV.

Concerns with animal cancer bioassays
Due to species specificity, the use of animals as surrogate hosts has not proven very useful for assessing the carcinogenicity of human viruses in humans.
- Cancer bioassays in the context of natural infection cannot be feasible: most human tumour viruses e.g. HPV, HBV, HCV cannot infect rodents or other animals.
- When infection is feasible, results obtained in cancer bioassays rarely reflect what would happen in humans: e.g. the human BK and JC polymavirus have not been demonstrated to induce tumours in humans but are very tumorigenic in rodents.

Specificities in epidemiological studies
- Specific tropism of the infectious agents leads to very specific cancers (e.g. “extranodal NKT-cell lymphoma (nasal type)” caused by EBV).
- Difficulty of assessing causally for certain cancer types in which presence of a specific infection is part of the diagnostic criteria (e.g. HTLV-I and ATLL; KSHV and primary effusion lymphoma).
- Choice of good markers of infection is critical importance; requires clear knowledge of the lifecycle of the agent (e.g. P. falciparum).
- Widespread presence of certain viruses in a healthy population (e.g. EBV and some polymavirus): a major problem when studying the potential association of these viruses with human cancer.
- Specificity of the detection methods is critical (e.g. cross-reactivity between human JC and BK polymavirus and with SV40).

Major findings

Three major mechanisms of carcinogenesis
- Direct carcinogens: HPV, HTLV, EBV, KSHV, MCV
- Indirect carcinogens: Chronic inflammation or immune suppression or deregulation

Involvement of co-factors in infection-related cancers
Infection with carcinogenic agents does not always lead to cancer. This feature common to all Group 1 biological agents strongly suggests the involvement of co-factors in the carcinogenic process. Carcinogenesis would result from the interaction of multiple risk factors, including:
- Host-related factors (e.g. gene polymorphism, immune status)
- Environmental co-factors
  - that may lead to reactivation of latent oncogenic viruses such as EBV or KSHV (e.g., chemicals, immunosuppressive drugs, food, plants or another infection)
  - acting through other mechanisms (e.g. HPV and UV)

Outcomes and Impact
- Recognition of Opisthorchis viverrini as a cancer-associated agent in South-East Asia by WHO
- Estimation of the global burden attributable to infections based on the evaluations of the Vol. 100B
- More than 270 citations in PubMed for Vol. 100B
- Further epidemiological studies: Chordoma and aetiology update focusing on risk factors

Research needs
- Role of multiple infections in cancer (e.g. in sub-Saharan Africa)
- Role of host-related factors (e.g. gender polymorphism, immune status)
- Potential importance of viral subtypes of the infectious agents (e.g., replication-deficient mutants of Merkel cell polymavirus in human cancer)
- Role of infection in cancers associated with exposure to chemicals or other agents (e.g., nasopharyngeal carcinoma; salted fish and EBIV in southern China)

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