The IARC Monographs Workshops: Tumour Concordance between Humans and Experimental Animals and Mechanisms Involved in Human Carcinogenesis


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Background

• The IARC Monographs have been published continuously since 1971. For the 100th Volume of the Programme the evidence on all human carcinogens (Group 1) that have been identified to date has been updated.
• Nearly 150 experts from 28 countries contributed to Volume 100, which was developed in six meetings from October 2008 to October 2009: A: Pharmaceuticals, 23 agents; B: Biological agents, 11 agents; C: Metals, particles and fibres, 14 agents; D: Radiation, 14 agents; E: Personal habits and indoor combustions, 11 agents; F: Chemicals and related occupations, 34 agents.
• For each agent, evaluations of the evidence of carcinogenicity in humans and in experimental animals and an overall evaluation of the human cancer hazard have been developed.
• Tumour sites with sufficient evidence of carcinogenicity in humans or experimental animals, as well as those sites with limited evidence in humans were established.
• The available information on the established mechanistic events and other likely mechanisms for these agents known to cause cancer in humans was also specifically summarized.
• In the past, many IARC Monographs evaluations have been made for agents that had been tested in 2-year cancer bioassays in experimental animals, but for which epidemiological and mechanistic studies in humans are less likely to become available.
• Hence, insight into how relevant agents may cause cancer in humans will be particularly useful in future assessments of the IARC Monographs.
• In addition, identification of carcinogens based on cancer studies in experimental animals should be facilitated.

Objectives

• Two Workshops will synthesize the Volume 100 review information for related future IARC Scientific Publications on Tumour Concordance between Humans and Experimental Animals and Mechanisms Involved in Human Carcinogenesis.
• These publications will build on the analyses of two extensive databases (see upper right-hand corner) prepared from information collected in the Volume 100 review. These analyses should address important hazard- and risk-assessment questions and cut across individual agents to discern more general principles.

As for tumour concordance between humans and experimental animals, questions and goals are:

• To determine whether particular tumours in experimental animals have predictive value for human cancer (either at an analogous site or at other sites).
• What are the circumstances under which it is reasonable to expect analogous tumour sites to occur in different species?
• Identify human cancer sites without good animal models.
• To find out whether different tumour sites tend to occur together.
• The analyses may be restricted to subsets of carcinogenic agents (e.g., metals, physical agents, hormonal agents, biological agents) or they may be more general in nature.

As for mechanisms involved in human carcinogenesis, the Workshops will aim to:

• Compile these mechanisms that were identified in Volume 100; consider joint consideration of multiple agents that act through a similar mechanism could facilitate development of a more detailed description of that mechanism and its common mechanistic steps.
• Identify biomarkers that could be influential in future studies; this will part identify biomarkers that could be included in future studies to provide more reliable information about whether a particular mechanism is operating in other humans or experimental animals.
• Detailed information from advanced toxicological analyses and results on various predictive end-points and biomarkers in short-term animal assays may allow cancer-hazard identification in the absence of classical biossays and epidemiology.
• Identify susceptible populations and developmental stages. Because susceptibility often has its basis in a mechanism, this could also facilitate a more reliable and precise description of populations that may be susceptible to agents acting through each mechanism.
• Promote research that will lead to more reliable evaluations.

Excerpt from the databases

The Workshops

• Preparations to organize these two Workshops have been initiated in 2011 in consultation with a core group of experts. The development of the database with the Volume 100 Information on the two main topics is on-going (see above) and will be completed in April 2012. The Workshops are scheduled to take place 16–18 April and 28–30 November 2012 at the IARC. Workshop participants have been drawn largely, but not exclusively from the six Volume 100 Working Groups.
• The first meeting will discuss in subgroups and in plenary sessions:
  1) tumour concordance and mechanisms together, to see where the two topics can benefit from each other.
  2) the databases and whether further development and refinement with respect to content and structure are needed in order to allow more detailed analysis.
  3) which data analyses should be done by participants in the intervening period until the second Workshop with the same Working Group.
  4) how the ensuing publication(s) should be structured.
• During the first Workshop there will also be invited lectures on key issues and recent insights in toxicology and carcinogenesis (e.g., the hallmarks of cancer, inflammation and cancer, recent developments in toxicology, biological models for leukemia and lymphoma, tumour (site) concordance, previous analyses of tumour (site) concordance on the basis of IARC Monographs data).
• The second Workshop will discuss the results of the analyses and the interpretation of the data, and aim to reach consensus on the final form and content of the publication(s).

References


Recommended reading