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Subcommittee on Wellness and Human Rights
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Thank you, Mr. Chairman, for inviting the National Cancer Institute (NCI), an agency of the National Institutes of Health, Department of Health and Human Services, to appear before the subcommittee today. I am Robert Hoover, M.D., a physician-epidemiologist, currently the Director of the Epidemiology and Biostatistics Program of the Division of Cancer Epidemiology and Genetics (DCEG). Accompanying me today is my colleague, May Wong, Ph.D., a program director from the NCI's Division of Cancer Biology. We are pleased to be here, particularly since the NCI has historically been and continues to be responsible for a substantial proportion of the research into the role of simian virus 40 (SV40) in carcinogenesis.

Both my written and oral remarks today will be brief, since the NCI did contribute substantial testimony at the last meeting of the subcommittee on this topic in September, and we have responded to your additional questions following that hearing. Also, the Institute of Medicine (IOM) of the National Academy of Sciences recently issued a comprehensive summary and critical review of the research in this area, at the request of the National Institutes of Health and the Centers for Disease Control and Prevention.

Overview of the Research Field

SV40 was discovered initially in monkey kidney cells used as culture media to grow polio virus for the original Salk and Sabin polio vaccines. This, and the subsequent discovery that this virus had the capacity to cause multiple different tumors in rodents exposed as newborns, caused concern about what effect vaccination with contaminated polio vaccine might have had on human populations. Laboratory reports in the 1990s of possible detection of SV40 virus in some human malignancies heightened these concerns. The NCI has been supporting research directed at understanding SV40 carcinogenesis in several areas. Most of this support has been in the area of laboratory studies of molecular virology and carcinogenesis, and other efforts have been focused in epidemiology.

Research Line of Inquiry: Molecular Virology and Carcinogenesis

In the area of molecular virology and carcinogenesis, much work by extramural scientists, funded in part by NCI, has focused on the question of (1) whether SV40 is present in some human tumors; and (2) what the biological role of this virus might be. In the past decade, multiple investigators from independent laboratories have identified

SV40 DNA in tumor samples from mesotheliomas, brain tumors, osteosarcomas, and non-Hodgkin's lymphoma.

Some research groups have described unique characteristics of these SV40 DNA sequences and the detection of viral proteins in tumors, both of which argue against laboratory contamination as an explanation. However, when detected, SV40 appears to be present in very low amounts, which has complicated our understanding of what this detection means. Additionally, using the same highly sensitive molecular techniques, other research groups have not detected any SV40 in the same tumor types.

The reasons for these discrepancies are unclear. Recognizing some of the difficulties and the limitations of current approaches, the Institute of Medicine recommended the "development and use of sensitive and specific standardized techniques for SV40 detection." Those who have found evidence of SV40 infection in human tumors have also begun the more difficult task of attempting to discern whether this infection actually plays a role in the development of these cancers.

Research Line of Inquiry: Epidemiology

The other line of scientific inquiry - studying the question of whether SV40 causes human cancer - is provided by epidemiological studies, which examine the relationship between SV40 exposure or infection and the risk of cancer in human populations. Most of these studies have relied on large population-based cancer registries, such as the NCI's SEER registry program or the Danish cancer registry, to examine the incidence of cancer in people who had a high probability of receiving SV40-contamined polio vaccine as children.

Up through the 1990's, these studies have failed to detect an increased risk of those cancers suggested by the molecular virology work. The epidemiologic studies are important because, together, they indicate that it is unlikely that there is an "epidemic" of cancer that might be attributed to SV40-contaminated polio vaccine. Nonetheless, as pointed out by the Institute of Medicine, it has not been possible in these studies to be certain precisely which individual persons were actually infected with SV40 through receipt of contaminated vaccines. Thus, to answer the question of whether there is any increased risk of cancer from such exposure will require more epidemiologic research using specific data on exposure for individuals.

Some attempts have been made to do this by testing for antibodies to SV40 in cancer cases and controls. To date, these studies also have not indicated any increased risk for those with such antibodies. However, because of limitations in our current technologies, these studies cannot be considered definitive. Here again, the development of accurate tests for SV40 infection, called for by the Institute of Medicine, will facilitate future epidemiological research on the question of whether SV40 causes cancer in humans. Specifically, the Institute of Medicine report recommended "development of sensitive and specific serologic tests for SV40."

Future Research

As I have discussed, two parallel lines of research investigation - molecular virology and epidemiology - have been moving forward in an effort to answer important questions about the role of SV40 in human cancer. The scientific process of developing an hypothesis, conducting studies, publishing in peer-reviewed journals, reviewing different perspectives from the research, and then designing new investigations, is working well. With the remarkable progress we are making in understanding the molecular basis of disease, I anticipate that a clearer picture of the potential role of SV40 in human malignancy should emerge from this process. The course of future progress should also be enhanced by taking account of the research recommendations of the IOM report.

Summary

In summary, we agree with the Institute of Medicine, as stated in their report, that "the evidence is inadequate to accept or reject a causal relationship between SV40-containing polio vaccines and cancer." At the moment, there is no consensus in the scientific community on whether SV40 causes cancer in humans. When working at the cutting edge of science, this situation is neither unusual nor surprising. Different disciplines and different groups, using a variety of approaches and technologies, frequently come up with contrasting results. Indeed, it is in pursuing the scientific answers for such differences that our knowledge is enhanced and we are able to move the science forward.

Harald zur Hausen, an eminent virologist, and Editor-in-Chief of the International Journal of Cancer, recently summed up the situation as follows: "The truth [about whether SV40 causes cancer in humans] will hopefully come out in the future... In the meantime, it is clearly premature to label SV40 as a human carcinogen; a healthy skepticism stimulates more experiments and certainly does not harm scientific progress." At NCI, we are committed to supporting and conducting the scientific research that will lead to the answer. We are particularly optimistic that improved tools for the accurate detection of SV40 infection can be developed, and thus allow the power of molecular virology to be combined with the rigor of the epidemiologic method in addressing these important questions.

I would be pleased to answer your questions.