Meeting Summaries

The First International Workshop on Molecular Epidemiology and Evolutionary Genetics of Pathogenic Microorganisms

Under the auspices of the Centers for Disease Control and Prevention (CDC), ORSTOM (the national French agency for scientific research in developing countries), and CNRS (the national French agency for basic research), the First International Workshop on Molecular Epidemiology and Evolutionary Genetics of Pathogenic Microorganisms was held in Atlanta, from June 16 to 19, 1996. The workshop was cosponsored by the National Institutes of Health (NIH), the Burroughs Wellcome Fund, the National Foundation for CDC, Boehringer Mannheim, the French Ministry of Foreign Affairs, and Emory University. Five hundred participants (health care providers, public health professionals, and laboratory scientists) from 25 countries attended the 3-day workshop, whose purpose was to exchange information on the use of molecular tools and approaches in areas of molecular epidemiology and evolutionary genetics in studies of emerging, reemerging, and endemic diseases. The workshop provided an opportunity for CDC, NIH, the World Health Organization, the Walter Reed Army Institute of Research, the Kenya Medical Research Institute, and ORSTOM to present jointly their perspectives on meeting the challenges of emerging infectious disease.

During the workshop, public health and laboratory science-based presentations on parasitic, fungal, bacterial, and viral diseases identified information gaps in the areas of disease and pathogen detection; laboratory-based presentations focused on the use of molecular tools and approaches in pathogen identification and evolution; and other presentations focused on specialized themes, such as the definition of a strain, tools and approaches in molecular epidemiology, emerging infections, concomitant infections, insect disease vectors, opportunistic infections, and tropical parasites.

Many of the challenges of dealing with emerging and reemerging pathogens are common to parasitologists, virologists, bacteriologists, and mycologists. Many pathogens cannot be maintained or propagated in culture or in animal models often because the biology and physiology of these pathogens are not known. This difficulty highlights the advantage of moving directly to molecular probes, polymerase chain reaction amplification, and sequence-based identification for substantiating epidemiologic relationships. Infectious disease clinicians and epidemiologists are faced with whether the disease under investigation is caused by a recently acquired infection or a recrudescent infection and whether an infection is caused by multiple species/strains. In addition, host and pathogen genetic factors that influence susceptibility and pathogenesis and environmental factors that influence transmission of pathogens are critical in the assessment of risk factors for acquiring infections. Molecular approaches to identifying emerging, reemerging, and endemic pathogens were described as most likely to yield the tools needed by epidemiologists to assess the source and risk factors, thus allowing the formulation of needed prevention and control guidelines.

Various approaches and tools now used in detecting pathogens and in studying evolution were examined, and molecular biology and evolutionary genetics applications in the following areas were discussed: 1) diagnosis of known pathogens and development of rapid means to identify unknown pathogens; 2) strain characterization for epidemiologic tracking; 3) ecologic and biologic factors that influence emergence of pathogens; 4) reassessment of taxonomy using molecular biologic data; 5) evaluation of the impact of genetic diversity of microorganisms on vaccine, drug, and insecticide efficacies; 6) gene flow in natural populations of vectors and pathogens; and 7) the role of vectors in the evolution of pathogens. Regardless of the organism under study, a unified approach in evolutionary genetics and population biology was recommended.

Two other topics related to emerging infections were also examined. The first concerned the risk for infection of human recipients of xenogeneic agents through xenotransplantation (and the subsequent transmission of these pathogens to the general population). The second concerned the role of immune activation caused by chronic infections (parasitic and bacterial) and immunization (pneumococcal and influenza) in HIV-infected persons in promoting the replication of HIV and associated progression of disease manifestations. The former is a concern in areas of sub-Saharan Africa and Asia where HIV coexists

with parasitic (e.g., malaria and schistosomiasis) and bacterial (e.g., tuberculosis) infections; the latter is a concern in the United States, where pneumococcal and influenza vaccinations are recommended for HIV-infected persons. Field-based, prospective, and longitudinal studies are needed for a complete picture of the extent of interaction between vaccination and pathogen-induced immune activation, HIV replication, and associated rapid progression to AIDS.

The need for a global partnership to facilitate a more rapid identification of infectious agents in a manner that discriminates among closely related strains and species and uses genetic information to study evolution, emergence, and dispersal of infectious agents was emphasized. To address emerging infectious disease threats, CDC has a strategic plan that emphasizes surveillance and applied research for a strong public health-based defense against infectious disease. A goal of this plan is the integration of laboratory science and epidemiology to develop and use tools to detect and promptly identify emerging and reemerging pathogens and investigate factors that influence their emergence. To promote international collaborations and interaction between clinicians, epidemiologists, and laboratory scientists, CDC, ORSTOM, and CNRS will cosponsor the 2nd International Workshop on Molecular Epidemiology and Evolutionary Genetics of Pathogenic Microorganisms at ORSTOM, Montpellier, France from May 26 to 28, 1997.

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Simian Virus 40 (SV40), a Possible Human Polyomavirus (Workshop Held at NIH)

During the past 4 years, polymerase chain reaction (PCR) assays have detected DNA sequences related to SV40 (an oncogenic simian polyomavirus) in a variety of human tissues, especially choroid plexus tumors, ependymomas, mesotheliomas, and osteosarcomas (1-7). These findings were supported by the isolation of infectious SV40 from a choroid plexus tumor (8). Although another paper reported the failure to detect SV40 DNA in mesotheliomas (9), these studies have reawakened interest in inadvertent human exposure to SV40 in the late 1950s and early 1960s when polio and adenovirus vaccines prepared in rhesus monkey cells containing SV40 were used (10,11). In response to the implications of detecting SV40 DNA in human tumors, the Food and Drug Administration, National Institutes of Health, National Vaccine Program Office, and Centers for Disease Control and Prevention sponsored a workshop on SV40 on January 27-28, 1997 at the National Institutes of Health to examine the possibility that SV40 is an infectious agent in humans.

The workshop first reviewed the biology of SV40 and the human polyomaviruses JC and BK and the data associating SV40 DNA with human tumors. In addition to tumors, SV40 DNA sequences have been detected in human pituitary gland tissue, peripheral blood mononuclear cells, and seminal fluids from healthy persons (3,5,7). Two laboratories were unable to detect SV40 DNA by PCR assays in human tissue, including mesothelioma; researchers noted the ability of the PCR primers used in these assays to amplify DNA sequences from JC and BK viruses as well as from SV40 and discussed whether each set of primers in the PCR reaction requires specific conditions to amplify virus-specific DNA. Furthermore, preliminary data suggested that primers considered to be SV40-specific could, under certain conditions, amplify what appeared to be host DNA sequences. Two laboratories demonstrated that the sensitivity of different PCR primers to detect SV40 DNA was 1-10 to 10-1,000 SV40 genomes. These discussions emphasized the need for caution in interpreting PCR data and the need for standardized, quantitative PCR assay procedures.

National Institute for Biological Standards Control scientists described the use of PCR assays to search for SV40 DNA in current and early lots of polio vaccines and concluded that polio vaccines used in the United Kingdom in 1971 to 1996 did not contain SV40 DNA, while early vaccines prepared in rhesus monkey cells contained easily detectable amounts of SV40 DNA. To evaluate the relationship between exposure to SV40 in the early polio vaccines and the development of tumors (choroid plexus tumors, ependymomas, mesotheliomas, and osteosarcomas), scientists described epidemiologic surveys