Meeting Report

Formation of a Molecular Epidemiology Group?

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Initial Planning

At several formal and informal meetings in 1996, when discussing methodological issues and current problems in molecular epidemiology, it was frequently expressed that there was a need for an organized group dedicated specifically to this young discipline. Letters were sent to a number of researchers in epidemiology, toxicology, molecular biology, and carcinogenesis to determine the prevalence of interest in such a group. Response was resoundingly positive, and communications continued via E-mail regarding how such a group should be organized. On April 12, 1997, approximately 100–125 researchers from diverse fields gathered in San Diego, California, and put forth a mandate to begin a molecular epidemiology group. Supported by more than 100 additional interested scientists who were unable to attend the meeting, it was agreed unanimously that there are a number of issues that could be addressed by such a group.

Rationale for Establishment of the Group

Recent advances in technology and an understanding of disease etiology on a molecular level have enabled researchers to study determinants of disease risk at a new and different level, and for epidemiologists, molecular biologists, toxicologists, clinicians, and others to merge their efforts toward an integrated approach to molecular epidemiology. With this methodology, however, have come a number of problems and issues that, we believe, need to be addressed in a continued and ongoing manner. To date, there is not a coordinated and continuous forum for researchers from each of these disciplines to meet together and confront issues in the practice of molecular epidemiology, nor is there a consolidated venue for scientists working in molecular epidemiology to present their work to others with similar interests (other than at AACR meetings and special symposia). Furthermore, there are few opportunities for bench scientists to learn necessary fundamentals of epidemiology as they apply to molecular epidemiological studies or for epidemiologists to accommodate new findings in biochemistry and molecular biology that might be relevant to their work. Establishment of the group was proposed as a vehicle for communication and learning for all those interested in working together and merging their efforts to gain further insights into disease etiology. Initially, it was thought that the group could serve as a forum for discussion of current issues in the conduct and interpretation of molecular epidemiological studies through structured, roundtable discussion groups focused on specific issues. It was also proposed that the group sponsor regular instructional seminars in topics related to the broad range of disciplines in molecular epidemiology. These could include issues related to epidemiological study design, proper choice of a control group, power issues and sample size, and statistical analysis to evaluate gene-environment interactions, as well as seminars on recent advances in the field of carcinogen and hormone metabolism, molecular and cellular carcinogenesis, molecular biology and molecular techniques (e.g., PCR/RFLP methods, DNA/protein adduct measurements, and so forth).

Agenda Items

With these goals in mind, a meeting was held on April 12, 1997, to begin organization of the group. Initial issues to be addressed included the structure and function of the group as well as meeting formats. A mission statement was to be determined and a name given to the group. We were also interested in discussing the potential role of the group as a force to address issues of concern to researchers, such as proposed consent for use of archival tissue.

Proceedings

In a welcoming address, Dr. Fred F. Kadlubar thanked all for their encouragement and support in forming this group, particularly Dr. Louise Strong, current president of AACR; Dr. Margaret Spitz, incoming president of ASPO;2 Dr. Ken Olden, Director of the National Institute of Environmental Health Sciences; and the members of Division of Cancer Epidemiology and Genetics at the National Cancer Institute. Dr. Kadlubar reiterated the rationale for forming such a group, (a) to provide a forum for information regarding latest developments in fields relevant to epidemiologists, biostatisticians, laboratory scientists, and clinicians; (b) to organize seminars or continuing education courses; and (c) to provide a regular venue for research presentations in the field of molecular epidemiology. The floor was then yielded to Dr. Colin Garner for a description of a similar group formed in the United Kingdom in 1996, which constituted a molecular epidemiology group sponsored, in part, by the United Kingdom Environmental Mutagen Society. Membership of that group is 102, and a constitution was adopted formally earlier this year. Dr. Garner shared the mission statement of the group: "to promote a multidisciplinary approach to population-based molecular studies of environmental causes of human disease," as well as the objectives, which were quite similar to those suggested for the group in San Diego. The United Kingdom group also has as objectives to promote the application of quality control in molecular epidemiological studies, to encourage younger researchers to participate in the discipline through presentation of their work, to

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2 The abbreviation used is: ASPO, American Society of Preventive Oncology.

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produce position papers as appropriate, and to represent the United Kingdom on issues relating to molecular epidemiology. Dr. Garner also shared formats for previous meetings of the group (three) and their future plans.

A group devoted to molecular epidemiology is also being organized in Italy, and Dr. Riccardo Puntoni spoke about the rationale for forming a group there, their purposes, and some of the mechanics of merging two groups who are already working in this interdisciplinary field in Italy.

Dr. Peter Shields next led the discussion concerning the structure and organization of the group, as well as possible meeting formats, and offered several options. It was proposed that the Molecular Epidemiology Group could exist as a free-standing, independent group. This group could operate in an informal manner with minimal structure and possible dues paid, which would be deposited into an interest-free account. Another alternative would be to organize formally and incorporate as a nonprofit organization with a formal board, constitution, and by-laws.

It was also suggested that the Molecular Epidemiology Group formally link itself with another professional society, in a manner similar to the relationship between Women in Cancer Research and AACR. Dues would be collected by the broader society for use by the society in part and the Molecular Epidemiology Group in part. The group could also attach to another society with nonprofit status to serve as a fiscal sponsor. The groups could hold joint meetings, which would take advantage of group discounts and reduce organization workload for all. A key issue for the possibility of attaching to another group would be deciding to which society it would be best to link ourselves. Dr. Christine Ambrosone noted that a number of organizations had expressed interest in working with our group, particularly for the purpose of sponsoring joint programs, both officially and unofficially, including the American College of Epidemiology, ASPO, and the International Society for Environmental Epidemiology. Dr. Margaret Spitz spoke, noting that she had presented the possibility of joint meetings to the Board of Directors of ASPO and there was an enthusiastic positive response. This organization is a multidisciplinary group with more than 350 members, which has been in existence for more than 20 years. The ASPO meetings are for 2 days, and Dr. Spitz suggested that the afternoon of the 2nd day could include a symposium on molecular epidemiology, and then the Molecular Epidemiology Group could meet on a 3rd day. Dr. Christopher Amos spoke for meeting with the International Genetic Epidemiology Society, and it was also suggested that the group either hold a meeting on the day preceding or following the AACR meetings or approach AACR to allow dedication of one afternoon or day to molecular epidemiology.

Because one of the goals of the Molecular Epidemiology Group is to serve as a forum for education and discussion, it was also proposed that we not hold a traditional meeting but rather hold biannual alternating meetings. The first meeting could be a continuing education series on specific topics that are not obtainable elsewhere, such as talks on evaluating statistical interactions, problems with molecular epidemiological study designs, and the latest methods for biomarker assays, as examples. It was further suggested that these courses be offered for a fee, which would supply a financial base for other group activities. During the alternate year, we could apply to hold a Gordon Research Conference to promote discussion and the free exchange of ideas at the frontiers of the biological, chemical, and physical sciences. Scientists with common interests in a particular field come together for a week of intense examination of the most advanced aspects of their field. These Conferences have a long record of stimulating advanced research in industrial laboratories, colleges and universities, research institutes, and government laboratories. An alternative to a Gordon Conference would be an AACR Special Conference. With meetings in alternate years, people could choose which meeting they would prefer to attend and not have yet another annual meeting to attend.

A great deal of conversation was generated regarding the structure and organization of the group as well as the meeting format. Resolution of these issues also hinged, somewhat, on the mission of the group and if it were to be focused primarily on cancer as a disease end point. It was pointed out that many of the same issues are relevant for molecular epidemiological studies of several disease end points, and a decision to limit the group to cancer researchers would be biased, because the Molecular Epidemiology Group meeting was being held in conjunction with the AACR meeting. It was felt that, perhaps, clarification of the mission of the group would facilitate decision-making regarding these other aspects of the group.

A mission statement, drafted by Drs. Rashmi Sinha and Christine Ambrosone, was presented by Dr. Ambrosone. It read as follows:

"The Molecular Epidemiology Working Group is a professional organization dedicated to an interdisciplinary approach to the study of chronic disease etiology. The Molecular Epidemiology Working Group promotes the incorporation of molecular and biochemical concepts and techniques into well-designed epidemiological studies by providing a forum for discussion and development of sound approaches to the conduct and interpretation of molecular epidemiological studies, sponsoring of educational activities, and fostering of partnerships between scientists in different disciplines. The Molecular Epidemiology Working Group is an organization for epidemiologists, molecular biologists, toxicologists, nutritionists, statisticians, clinicians, and all other scientists who are interested in working together and merging their efforts toward an integrated approach to gain further insights into disease etiology and to promote public health."

This statement was adopted with minor changes suggested, particularly that we add "and to inform public health policy" in the last sentence. It was suggested that a goal should be "advancing the science of molecular epidemiology," and being a resource for training of young researchers. It was also suggested that the mission include a statement regarding the importance of genetics to epidemiological studies. Participants briefly discussed the choice of a name, and it was agreed that we would call ourselves the Molecular Epidemiology Group.

Dr. John Potter next summarized recommendations resulting from a recent workshop that he cochaired with Dr. Sinha, "Diet and Genetic Susceptibility," the aims of which could be relevant for issues to be addressed by this group. These included technical issues related to study design, laboratory procedures, quality control, and data management. It was suggested that research approaches include hypothesis-driven epidemiological study designs with joint participation of all collaborators in every phase of the study, such that applications of basic research can be applied to public health. It was recommended that scientists pursue anomalies rather than discard them as null studies and that more negative studies should be published, even if in a specialized abbreviated form. It was further suggested that these issues be raised at the upcoming editorial board meeting of Cancer Epidemiology, Biomarkers & Prevention.

Looming issues include those related to ethics and informed consent, with serious implications for population-based
Dr. Paul Strickland suggested that the Molecular Epidemiology Group be a force to encourage support from the National Cancer Institute, AACR, and ASPO for the formation of a NIH study section dedicated to molecular epidemiology and biomarker studies.

Dr. David Hunter addressed current issues regarding informed consent for genetic studies, which is summarized below in an earlier statement written by Dr. Hunter.

Many molecular epidemiology studies are collecting samples for testing DNA adduct levels or possible genetic markers of disease risk. Sample size calculations suggest that for low-penetrance genes or studies of gene-environment interactions, sample sizes need to be very large, frequently on the order of thousands of cases. Prospective studies may be particularly valuable, as a wide variety of disorders can be studied, information on environmental exposures should be free of recall bias, and the influence of a single genotype on multiple outcomes can be determined. The level of informed consent that should be given by participants in these studies is uncertain.

Similarly, many case-control studies also have stored biological specimens, including sources of DNA, for future analyses. In many of these studies, consent statements request consent for future study of gene-environment interactions, including polymorphisms that have yet to be identified.

Whether participants can be asked for broad generic consent for future studies of any gene or disease is controversial. If this is not deemed appropriate, however, participants in studies would need to be asked frequently to reconsent to each new hypothesis, an infeasible approach particularly in large studies. The obligations of investigators who have linkable genetic information of varying degrees of clinical utility are uncertain. The option of anonymizing specimens, often used in studies of high-penetrance genes, is often not available in studies of gene-environment interaction, in which extensive, potentially identifying information must be retained.

Bills before Congress and statements from societies such as the American Society for Human Genetics propose very rigorous consent procedures and are motivated largely by concerns about potential for insurance discrimination for subjects in studies of high-penetrance genes. Can we distinguish between studies of high- and low-penetrance genes? Can we gain approval for consent procedures that acknowledge the need for large, population-based studies and the difficulties of applying the intensive counseling models from smaller, family studies?

These issues were discussed in depth, and it was proposed that the Molecular Epidemiology Group form a committee/working group to review the issues of appropriate consent in molecular epidemiology studies and to advocate high ethical standards consistent with the feasibility of conducting population-based research. A number of individuals volunteered to be on this committee, and it was suggested that this committee should include one or more patient advocates as well as an ethicist.

As proceedings of the meeting were summarized by Dr. Ambrosone, it was agreed that, for now, The Molecular Epidemiology Group would maintain an informal structure and make no definitive decisions regarding organization. A steering committee was appointed, including those who had organized the initial meeting (Drs. Kadlubar, Ambrosone, Shields, Potter, Sinha, Rothman, and Hunter). Drs. Boffetta, Spitz, Amos, and P. Yang also expressed interest in participating in this group. The steering committee will meet and delineate issues and options for the group to vote on electronically. The foremost issue at hand is determination of the location and time of the next meeting of the Molecular Epidemiology Group, if it should be affiliated with another organization and, if so, with whom. Those interested in additional information regarding the group may contact Dr. Christine Ambrosone in the Division of Molecular Epidemiology, National Center for Toxicological Research, Jefferson, AR 72079 (E-mail address: cambrosone@nctr.fda.gov).
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