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Molecular Biomarkers for Environmental Epidemiology

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A new and evolving area of research termed molecular epidemiology attempts to merge sophisticated and highly sensitive laboratory methods with analytical epidemiologic methods. Molecular epidemiology bridges basic research in molecular biology and studies of human disease causation by combining laboratory measurement of internal dose, biologically effective dose, biologic effects, and the influence of individual susceptibility with epidemiologic methodologies (*1*). The most common view is that the approach represents a natural convergence of molecular biology and epidemiology (*2*).

The number of biomarkers available for evaluating disease risk in humans is quite large. Their utility for human biomonitoring is suggested by the well-known paradigm of environmentally induced cancer, which represents end points for assessing the entire spectrum of human-genotoxicant interactions (*3*). These biomarkers begin with exposure and include absorption, metabolism, distribution, critical target interaction (i.e., DNA damage and repair), genetic changes, and finally, disease, which is the area of traditional epidemiology. The development of biomarkers has given rise to the field of molecular epidemiology, which uses these biomarkers rather than disease to assess the risk of environmental exposure (*4,5*).

Environmental factors are implicated in the vast majority of human diseases. These include exposures due to lifestyle (smoking, diet, alcohol consumption), and chemicals in the workplace and general environment. In a complex interaction, risk from these environmental exposures is modulated by genetic and acquired susceptibility factors. Molecular epidemiology has the potential to clarify the contribution of environmental factors to disease causation and to identify high-risk groups and individuals for purposes of prevention.

A considerable number of toxic and carcinogenic chemicals are found routinely in the different environmental media. Tobacco smoke contains 4-aminobiphenyl (4-ABP), polycyclic aromatic hydrocarbon (PAH), 4(*N*-methylnitrosamino)-1-(3-pyridil)-1-butanone (NNK), and many other carcinogens. Diverse carcinogens are found in the food supply, including aflatoxin, dichlorodiphenyltrichloroethane (DDT), *N*-nitrosodimethylamine (DMN), PAH, and heterocyclic amines. An estimated 1,000 new chemicals are produced yearly and few of the more than 50,000 chemicals currently in commerce have been sufficiently tested (6). From the public health perspective, we need to know what effects these agents have at the environmental exposure levels, and we need early warning systems to detect those effects.

To prevent environmentally related disease including cancer, we must identify environmental risk factors in a more timely way and then determine which groups and individuals are at greatest risk. The next step is to design interventions targeted to those populations and individuals. Molecular epidemiology has potential in this regard. Molecular epidemiology fuses advances in the molecular biology and molecular genetics of cancer with epidemiology to understand the molecular dose of specific agents, their preclinical biological effects, and the biologic factors that modulate susceptibility to these exposures (7,8). Biomarkers can thereby mitigate the two problems that have plagued epidemiology--the long latency of cancer and fragmentary information on exposure.

Diverse biomarkers have been assayed in human peripheral blood and other tissues. They include internal dosimeters such as cotinine (a metabolite of nicotine), molecular dosimeters such as carcinogen-DNA and carcinogen-protein adducts formed by chemicals such as PAH and 4-ABP, and preclinical effects such as chromosomal aberrations, gene mutations, and changes in the structure or function of oncogenes and tumor-suppressor genes. The extent to which biomarkers are modulated by genetic susceptibility factors such as polymorphisms in the P450 or glutathione transferase genes or oxidative injury-related genes have also been studied.

In conclusion, biologic markers can be incorporated into a wide variety of epidemiologic studies of populations exposed to environmental toxicants. Molecular epidemiology ultimately may prove to be a useful tool in prevention of environmentally related disease.

Reference

1. Perera FP, Whyatt RM. Biomarkers and molecular epidemiology in mutation/cancer research. Mutat Res 313:117-129 (1994).

2. Perera FP, Whyatt RM, Jedrzychowski W, Raugh V, Manchester D, Santella RM, Ortman R. Recent developments in molecular epidemiology. A study of the effects of environmental polycyclic aromatic hydrocarbons on birth outcomes in Poland. Am J Epidemiol 147:309-314 (1998).

3. Committee on Biological Markers of the National Research Council. Biological markers in environmental health research. Environ Health Perspect 74:3-9 (1987).

4. Albertini RJ, Nicklas JA, O'Neill JP. Future research directions for evaluating human genetic and cancer risk from environmental exposures. Environ Health Perspect 104 (suppl 3):503-510.

5. Albertini RJ. The use and interpretation of biomarkers of environmental genotoxicity in humans. Biotherapy 11:155-167 (1998).

6. Perera FP. Prevention of environmental pollution: good for our health. Environ Health Perspect 101:562-563 (1993).

7. Perera FP. Molecular cancer epidemiology: a new tool in cancer prevention. J Natl Cancer Inst 78:887-898 (1987).

8. Hulka BS, Griffith JD, Wilcosky TC. Biologic Markers in Epidemiology. New York:Oxford University Press, 1990.