Primary Cancer Prevention in the Post-Genome Era

Our health and diseases, including cancer, are determined by both host and environmental factors and their interactions. Carcinogenesis proceeds via multiple steps with a long latency period. Host factors include gender, ageing and the genetic background. Sex hormones play important roles which explain to a large extent the variation between male and female incidence rates. Cancer risk is correlated with the power function of age to the 5-6th (Doll, 1978). With regard to genetic factors, the functions of oncogenes and suppressor genes are important, as well as genetic instability. Retinoblastoma, for example, a genetically determined cancer, generally arises through inactivation of the suppressor gene Rb. Genetic polymorphisms, for example in genes encoding drug metabolising enzymes or factors necessary for DNA repair, may also have a crucial impact on health and disease, especially in individuals exposed to high levels of carcinogens, like smokers.

In this issue, Hamajima et al (2002b) provide an informative review of allele frequencies of 25 polymorphisms of 21 genes in Japanese, Koreans and Chinese, in comparison with Caucasians. They describe that variation of allele frequencies is rather limited among the three Mongoloid ethnic populations but widely discrepant from those of Caucasians, concluding that the differences might cause inconsistencies of epidemiologic studies due to variation in gene-gene and/or gene-environment interactions. However, there are obvious differences in cancer incidences in the three Mongoloid populations (Parkin et al., 1998) and it has long been clear that there is greater variation within racial groups than between them (Lewontin, 1972). Furthermore, according to conventional migration studies, the risk of stomach cancer in Japanese decreases in Issei migrants into the US (born in Japan) and apparently in Nisei (the second generation born in the US) (Shimizu et al., 1987). For cancers of the colon, breast and prostate, the trends are vice versa, indicating that most cancers are clearly dependent on environmental/lifestyle factors, environment-environment interactions and gene-environment interactions rather than genetic factors or gene-gene interactions.

As stressed by Brennan in a recent commentary review (Brennan, 2002), it is essential that we are very clear about the purpose of studies aimed at elucidating gene-environment interactions and what conclusions can be drawn. Furthermore we can not lose sight of the ethical considerations, as well as the legal and psychosociological ramifications (Austin, 2002; Holtzman and Andrews, 1997). Clearly genetic factors, particularly genetic polymorphisms, may help to establish evidence-based cancer prevention and prediction as well as tailor-made diagnosis and treatment. Genetic factors and gene-gene interactions are of interest in terms of pathogenesis, but by their very nature they cannot be modified. Unless we are in a position to offer concrete programs to assist those at high risk because of their genetic inheritance, a simple focus on deciphering which polymorphisms have a negative influence may face moral difficulties. There are of course many environmental factors, and environment-environment interactions, which can be modified, in terms of improvement of lifestyle but this is notoriously difficult to achieve in practice. While individuals at elevated risk might undoubtedly gain more from interventions, this may have to wait until we have more information on how best to encourage the general populace to adopt healthy practices. Accordingly, from the standpoint of primary cancer prevention (WCRF/AICR, 1997), avoiding risk factors, including smoking, and increasing exposure to preventive factors, including physical exercise, vegetables and fruit, are thus crucial, independent of the genotype of an individual, even in the post-genome era. As stressed by Rose (2001), modest behavioural changes at the general population level are likely to have a greater influence on public health than those which are restricted to specific groups. As argued earlier in this journal (Tajima and Moore, 2001), we are unlikely to ever be in the position of being able to predict with certainty whether any particular individual will or will not develop a cancer, no matter how much information is available regarding his or her genotype and environment, because of the major role played by chance.

Distinction must obviously be made between alterations in genes which pose high risk, as for example with familial polyposis, and the large number of low-risk genes. With the latter, Brennan has argued that there is a need for a more coordinated approach, with cooperation between laboratories to ensure that sample sizes are adequate for consistent results to be obtained (Brennan, 2002). The concerns raised by Vainio (2002) and Moore and Tajima (2002) in articles in this issue regarding the role of IARC are clearly of interest in this context. Studies of genetic polymorphisms will no doubt continue to attract a great deal of attention and should provide important insights into mechanistic aspects of carcinogenesis, and also the biochemistry of tobacco addiction, for example (Pianezza et al., 1998; Hamajima et al., 2002a). Whether screening for particular polymorphisms, singly or in groups, can be recommended in the foreseeable future will depend on how research progresses with regard to the social environment,
including economic factors. Regarding practical guidance for implementation of ethical principles, sources are limited although the Centers for Disease Control and Prevention in the USA did convene a multidisciplinary group to develop an appropriate informed consent approach (Bleskow et al., 2001). Whether something similar needs to be set up to guide workers faced with the particular needs of societies in the Asian Pacific is an open question. In decision-making for this area it may well be that involvement of community-based groups should be sought to complement ideas generated by scientists and public health officials. To paraphrase Austin (2002), any promise of genomics for improvement of public health requires respect for persons, beneficence and justice as a fundamental basis.

References


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