Opinion

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The Scope of Perspectives for Research in Oncodevelopmental Biology and Medicine

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The International Research Group for Car-cinoembryonic Proteins was founded by the late Professor H. Hirai, Department of Biochemistry, Hokkaido University School of Medicine, Sapporo, Japan, in 1972. At that time he emphasized, in the preamble of the Group's Newsletter, that 'It is the purpose of this gathering to improve and enhance the mutual exchange of information among researchers in the world who are studying cancer from the point of view of the reappearance of embryonic and/or fetal substances when normal cells become cancerous' [1].

The Group prospered, grew and changed its name to 'International Society for Oncodevelopmental Biology and Medicine' (ISOBM) in 1980. It was registered as one of the international organizations in Geneva, indicating much broader aims, namely that 'the objective of this Society is to promote interdisciplinary research from the point of recognizing phenomena and characterizing markers of ontogeny and differentiation so as to provide a basis for the advancement of methods for the diagnosis and management of cancer'.

Professor Sabine von Kleist, the immediate past President of the Society has described in 1994, in the preface of 'Twenty Years of ISOBM', the special issue devoted to the memory of the late Professor H. Hirai, that 'the scope and vision of the Society remained the same ... the research of human tumor antigens, especially carcino-fetal antigens in the very cradle of the Society and still plays a central and increasingly important role' [2].

It is, therefore, not surprising that the majority of the research in this Society relates to utilizing embryonic and/or fetal tissue. Accordingly, it must be remembered, and not overlooked, that researchers in this field have been obliged to heed, even though indirectly, regulations on the use and availability of such materials. Ethical and legislative considerations have gradually arisen on embryo and/ or fetal researches since the latter half of the 1970s pari passu with the development of studies on in vitro fertilization and/or embryo transfer techniques. It is indisputable that these studies need to be strictly retulated by authorized organizations such as the American Fertility Society, the International Law Association, and the World Health Organization.

Although these organizations differ in the way they implement the guidelines, it was the recommendation of the European Council Parliamentary Assembly that any research on

dead preimplantation embryos for scientific, diagnostic, therapeutic or other purposes is permissible, but subject to prior authorization. The recent report on the bioethics of human fetal

tissue research points to some favourable decision-making steps together with attention being paid to the morality of abortion [3].

It is thus desirable that researchers have to be aware of the regulations and plan well ahead for such investigations to enable them to proceed legitimately and/or ethically.

Rapid progress has also been made recently in the realms of biology and medicine in general, and especially in the field of human genetics, where breathtaking advances have unearthed latent somatic changes responsible for the induction of neoplastic changes, including the identification of detrimental gene changes and carrier states. Ethical problems inherent in simple testing of blood specimens using DNA technology will now arise as this approach is capable of accurate predictive diagnoses for cancer-prone syndromes.

As the leading edge of studies on gene alterations in cancer-prone families, three major reports became available. One concerns the Li-Fraumeni familial cancer syndrome in which germline p53 mutations have been detected. The other two are familial adenomatous polyposis and hereditary non-polyposis colorectal cancer. Suspected as causes of these two lesions are germline mutations of the APC gene on chromosome 5 in the former [4] and mismatch of repair genes, such as hMSH2, hMLH1, PMS1 and PMS2 in the latter [5]. In regard to the concept of multistep carcinogenesis, correlative progressive participation of gene abnormalities has been suggested in colon cancer, where these APC gene mutations play a role in initiation by changing the normal epithelia into adenoma cells with the concurrent effects of a K-ras gene mutation, and then the adenoma cell changes into a cancer cell due to the promoting effect of the p53 mutation. DCC gene mutations may play a further role with respect to metastases [6].

A recent further topic in this regard is the BRCA1 gene on chromosome 17q21, which is not only a strong risk factor for hereditary breast and ovarian cancers [7], but also a potential factor in the evolution of sporadic ovarian cancer [8]. According to the high frequency of the allelic deletions of 17q in sporadic breast and ovarian cancers, the existence of an additional tumor suppressor gene BRCA2 has been postulated.

The results of basic studies concerning the BRCA1 gene have been reported together with the epidemiological investigations regarding genetic testing and surveillance of the gene carrier state. Among the reports, it has been suggested that sociomedical problems might ensue: when is the optimal time to inform gene carriers, when is an appropriate age to enable them to make their own informed decisions about the implication of this knowledge and how will this information be interpreted by these individuals [9]. It has, of course, been questioned whether such people will prefer to know of their cancer risk status, and to make intentionally thereby judgements relevant to the rest of their lives. Awareness of their own carrier state may provoke profound anxiety.

This variety of influences will cause similar problems for all candidate subjects submitted to genetic testing or surveillance of any kind. It is also very likely that the use of gene linkage findings for genetic counselling of cancer-prone families will have potential hazards that affect public health policy, employment screening, occupation and decision logic [10]. Researchers and physicians ought to bear in mind these profound potential effects and be adequately educated to be able to deal with them.

In conclusion, I should like to express my sincere hope that when planning studies on oncodevelopmental biology and medicine, researchers will have due regard to the rapid development in current technologies, especially in DNA analyses, and that discussions are, therefore, needed of each such result, viewing it from the clinical, epidemiologic, genetic, biologic and medicosocial angles [11], and where possible, from medical ethical and philosophical standpoints.

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Research in Oncodevelopmental Biology and Medicine
Tumor Biol 1996;17:193-195
195