Plenary Lectures

PL-1 Genetic Predisposition to Breast Cancer

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Epidemiological studies show that breast cancer tends to cluster in families. In principle, this familiar clustering might be due either to the effect of uncommon genes of strong effect, causing a small number of families with a high risk of breast cancer; or to much commoner genes of lesser effect, which could account for a substantial fraction of breast cancer in the general population, but lower risks to a given individual. The practical and public health implications of these two models are different.

The identification of two predisposing genes, BRCA1 and BRCA2, from multiple case families provides clear evidence for the existence of uncommon strongly predisposing genes. In the medium to long term understanding the normal function of these genes and its disruption in cancers may provide a basis for the design of rational approaches to therapy and prevention. More immediately, the identification of the genes provides the opportunity for genetic diagnosis of women at risk. This raises a number of practical, social and ethical issues.

The potential contribution of commoner but less highly predisposing genes is still uncertain and will be a major area of research in the coming decade.

PL-2 Selective Control of Oncogene Expression in Tumors. Therapeutical Developments

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The activation of proto-oncogenes and the inactivation of tumor-suppressor genes and DNA repair genes play key roles in the transformation of normal into malignant cells and the development of tumors. The restoration of the activity of tumor-suppressor genes, e.g., p. 53, can be achieved by gene transfer using gene therapy protocols. The inhibition of oncogene expression can make use of different approaches: antisense oligonucleotides and ribozymes to inhibit mRNA translation, antigene oligonucleotides to control transcription, oligonucleotide aptamers and single-chain antibody to block protein function. The lecture will focus on the use of antisense oligonucleotides to control oncogene expression (e.g., ras oncogenes) and growth factors (e.g., IGF1). Antigene oligonucleotides can also be used to control oncogenes and growth factors or their receptors. In both cases (antisense and antigene), pharmacological approaches and gene therapy protocol can be developed to control tumor growth and/or elicit an immune response against the tumor.

PL-3 Prognostic Factors in Treatment Planning: Use or Abuse?

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The review of the literature on prognostic factors in breast cancer is a tremendous task because many researches are in progress for finding new prognostic factors, especially hormone receptors, biological markers, expression of oncogenes, expression of proliferation-related antigens, etc. But if there are many papers describing new prognostic factors, very few papers indicate how these new factors are taken in account for treatment planning. If we want to use new factor in medical decision making, we have to ensure that: data were collected uniformly with very few missing data, statistical method was adequate, determination is reproducible and widely available with quality control, prognostic significance was assessed by two or more concordant large studies, new factor gives independent prognostic information, prediction has therapeutic implications.

Currently there are more than 75 putative breast cancer prognostic factors reported in human, but in practice in the FNCLCC SOR project establishing guidelines for breast cancer, very few factors are taken into account in treatment planning. There are:

- patient related factors: age, hormonal status;
- tumor related factors: TNM, tumor size, inflammatory signs, axillary node status, histologic type, hormone receptors, multifocality;
- treatment related factors: feasibility of conservative surgery.

Even if we want to individualise treatment according to prognostic factors of the patient, we have to be very careful because treatment efficacy is not always demonstrated in many small subsets of patients.