in a primary breast carcinoma is highly preserved in its distant metastasis. These findings suggest that metastatic capability in breast cancer is an inherent feature, and is not based on clonal selections. The results further imply that neo-adjuvant treatment given to patients based on (yet to be established) response expression profiles of their primary breast tumor might indeed prevent the outgrowth of micrometastases.

349 INVITED

Pharmacogenetics and genomics – prognostication and prediction: where is the future?

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Development of analytical methods as cDNA micro arrays and proteomics provides new opportunities with respect to studying cancer biology and development, early detection as well as prognostication and prediction of treatment sensitivity. Interesting findings are emerging from studies applying cDNA micro arrays to different tumour forms. Despite a substantial heterogeneity in gene expression between individual tumours [1], differences between tumours forms have been revealed [2]. Studies on breast cancer [1] and other tumours have shown that within each cancer form, individual tumours may be grouped into classes based on their gene expression profile. The identification of a subgroup of tumours expressing "basal-cell"-like characteristics, in contrast to the more common "luminal-cell" profile, has suggested a different cellular origin for tumours of the different classes [1]. Moreover, classifications based on gene expression profiles have been shown to be of prognostic value in a diversity of cancer forms [3–8]. Further, micro-array techniques have been successfully applied to in vitro experiments, exploring multiple gene activation in relation to events like restoration of p53 function [9], but also exploring mechanisms of drug resistance [10]. Contrary, only a few studies have so far evaluated use of micro arrays as tools exploring chemoresistance in vivo. These studies have involved a limited number of patients only [11,12]. While correlations between gene expression profiling and therapy response has been found, clearly the predictive value of these gene profiles need to be confirmed in larger studies. Further, these preliminary data do not suggest a predictive accurateness sufficient for therapeutic use. While the studies so far have applied different forms of global gene expression analysis, future studies may incorporate biological hypotheses, analysing expression of groups of genes known to be involved in a functional pathway.

References

[1] T. Sorlie *et al.*, *Proc Nat Acad Sci USA* **98**, 10869–10874 (2001).
[2] C. H. Chung, P. S. Bernhard, C. M. Perou, *Nature Gen* **32(Suppl)**, 533–540 (2002).
[3] D. Beer *et al.*, *Nature Med* **8**, 816–24 (2002).
[4] S. L. Pomeroy *et al.*, *Nature* **415**, 436–42 (2002).
[5] M. A. Shipp *et al.*, *Nature Med* **8**, 68–74 (2002).
[6] D. Singh *et al.*, *Cancer Cell* **1**, 203–9 (Mar, 2002).
[7] M. J. van de Vijver *et al.*, *N Engl J Med* **347**, 1999–2009 (Dec 19, 2002).
[8] E. Yeoh *et al.*, *Cancer Cell* **1**, 133–43 (2002).
[9] H. Yoon *et al.*, *PNAS* **99**, 15632–15637 (Nov 26, 2002).
[10] R. Wittig *et al.*, *Cancer Res* **62**, 6698–6705 (Nov 15, 2002).
[11] L. Pusztai *et al.*, *ASCO Proc* **22**, p1, Abstr 1 (2003).
[12] J. Chang *et al.*, *Lancet* **362**, 362–69 (2003).

350 INVITED

Combining proteomics and genomics for cancer analysis

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In the *Division of Functional Genome Analysis*, we are developing technologies for the identification, description and evaluation of cellular functions and their regulation by producing and processing biological information on a genomic scale. One emphasis in our efforts is work on DNA-, protein- and peptide-microarrays. Many chemical and biophysical issues are being addressed as part of this work in an attempt to understand the underlying procedural aspects, thereby eventually establishing superior analysis procedures. Based on the technical advances, the resulting methods are immediately put to the test in relevant, biologically driven studies on various organisms.

Concerning the analysis of human material, systems are being developed toward early diagnosis, prognosis and evaluation of the success of disease treatment with accentuation on cancer. Beside other applications, analyses are performed on the detection and use of disease-relevant polymorphisms in the area of molecular epidemiology. Also, comparative studies on epigenetic variations, transcript levels and actual protein expression by means of complex DNA- and antibody microarrays are under way. Early diagnosis from blood samples is being worked at that is based on the binding of serum components to peptide microarrays. Combining this data with clinical information permits the definition of sub-groups within an analysed cohort and eventually a means for diagnosis and prognosis as well as the identification of highly relevant targets.

(www.dkfz.de/funct_genome)

Friday, 19 March 2004 14:15–15:45

SYMPOSIUM

Late sequelae of breast cancer treatment, are they preventable?

351 INVITED

Cognitive functions after chemotherapy

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Currently, the interest in cognitive functioning following chemotherapy is rapidly expanding, as is reflected in a growing number of published articles on this topic. Although most studies are indicative of cognitive deficits after chemotherapy in at least a subset of patients, little is known about the pattern of cognitive deficits, the course of the deficits over time and the impact of deficits on daily-life situations. Moreover, a number of important confounding factors still exists and potential mechanisms by which chemotherapy can adversely affect the brain are insufficiently understood.

In 1998, a large prospective longitudinal neuropsychological study was started in the Netherlands Cancer Institute/Antoni van Leeuwenhoek hospital. In this study, several groups of breast cancer patients adjuvantly treated with cytotoxic agents (including high-dose CTC chemotherapy and standard dose FEC and CMF chemotherapy) were tested neuropsychologically at three points in time: at baseline (i.e. after surgery and prior to the start of chemotherapy) at 6 months and at 12 months after completion of treatment. Patients treated with chemotherapy were compared with stage I breast cancer patients not treated with chemotherapy and with healthy controls, tested at similar points in time. At each assessment point patients and controls were additionally interviewed with regard to cognitive problems experienced in daily life, psychological distress and fatigue. In co-operation with 15 hospitals in the Netherlands, approximately 400 breast cancer patients were tested.

We will present the first data of this study, and results will be related to the above-mentioned gaps in current knowledge.

352 INVITED

Surgery

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Since Halsted time, the surgical treatment of breast cancer has dramatically changed. The extent of demolitive operations has progressively reduced with a positive impact on the rate of complications and on the quality of patients life. Conservative surgery has allowed to achieve good cosmetic results with the same survival and without increase in local recurrence. Unfortunately a percentage of sequelae after surgery for breast cancer is still present. The most severe complication is lymphoedema of the operated arm. This is secondary to axillary dissection and normally causes functional impairment and psychological morbidity. The risk to develop lymphoedema is approximatively 25% with a great range in literature; the rate can raise if radiotherapy is associated. Once that lymphoedema is occurred, its treatment is very difficult with poor results and improvements. Manual lymphatic drainage is helpful for the initial phase and is pleasant for patients but requires specialized staff and high costs. Elastic bandage produces differentiated pressures on the arm decreasing from wrist towards shoulder. They have to be weared during activities or at rest. No importance was seen for treatment with drugs like anti-inflammatory, antihistamines and diuretics. 60–70% of patients with lymphoedema are overweight and maybe diet can play a role in the etiology of this complication. Neural "Stupor" of the brachial plexus is present in about 1% of cases and is due to an incorrect position during the operation. The patient has difficulty to move the arm in