to have a major impact on clinical practice, as these technologies are expected to accelerate the translation of basic discoveries to the clinical practice. In particular, proteomic technologies are likely to play a key role in the study and treatment of cancer, as they provide invaluable resources to define and characterize regulatory and functional networks, investigate the precise molecular defect in diseased tissues and biological fluids, and for developing specific reagents to precisely pinpoint a particular disease or stage of a disease.
Today, the application of novel technologies from proteomics and functional genomics to the study of cancer is rapidly shifting to the analysis of clinically relevant samples such as fresh biopsy specimens and biofluids. Being a patient-oriented organisation, The Danish Cancer Society catalysed in 2002 the creation of a multidisciplinary research environment, The Danish Center for Translational Breast Cancer Research (DCTB), to fight breast cancer. The direct access to and use of fresh patient material, as well as the close collaboration between basic researchers, surgeons, clinicians and pathologists is one of the unique features of the Centre.
Here I will present the proteomics strategies that we are currently been used to search for biomarkers for the early detection of breast cancer in the blood. Particular emphasis will be given to problems associated with tumour heterogeneity, clinical relevance of samples as well as marker validation.

141 INVITED

Protein Kinase Activity and Therapy Response

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Of the human kinome, approximately half of the tyrosine kinase complement is implicated in cancer. Tyrosine kinases are thus important targets for therapeutic interventions and potential biomarkers for stratifying patients to individualized cancer therapy. To extract multiplex tyrosine kinase profiles, high-throughput methodologies are needed. One such method is based on simultaneous generation of phosphorylation signatures of 144 tyrosine kinase substrates by tissue samples using a 3D flow-through microarray technology (PamChip Arrays®). Examples on the use of this technology in the context of identification of functional biomarkers of disease aggressiveness and therapy response will be given.
First, a study characterizing tyrosine kinase signaling networks in prostate cancer is presented. In addition to their significant roles in tumour progression and therapy resistance, tyrosine kinases are major players in development of castration-resistant disease, still remaining the most apprehensive aspect in prostate cancer management, defying effective treatment. By analyzing samples from a preclinical model eliciting therapy-naïve, androgen-deprived, and castration-resistant disease, respective tyrosine kinases implicated in the different disease states were identified. Subsequently, clinical validation was achieved by analyzing paired normal and tumour tissue samples from prostatectomies of locally advanced disease or following androgen-deprivation.
Secondly, the method was used to assess the tyrosine kinase activity in 67 pre-treatment tumour biopsies from locally advanced rectal cancer, aiming to identify subsets of tyrosine kinases predicting the response to preoperative chemoradiotherapy (CRT). The tyrosine kinase activity profiles were shown to predict therapeutic response, as assessed by histomorphologic tumour regression grade of resected tumour specimens. Generally, baseline tyrosine kinase activities in tumours showing poor CRT response were significantly higher than in tumours with good CRT response. Specifically, many of the discriminating kinases represented signaling pathways implicated in radiation resistance.
In summary, novel analytic technologies enabling high-throughput tyrosine kinase profiling are imperative for providing further insights into the complex biology causing different cancers and their therapy responses. Future individualized cancer therapy may benefit from such technologies being developed into specific arrays containing biomarkers identifying aggressive disease and therapeutic response.

142 INVITED

Cancer Protein Biomarkers

Abstract not received

Keynote Lecture (Sun, 25 Sep, 11:30−12:15)
Do We Still Need to Understand the Cancer Genome?

143 INVITED

Evolution of the Cancer Genome

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All cancers carry somatically acquired changes in their genomes. Some, termed “driver” mutations, are causally implicated in cancer development. The remainder are “passengers”, and bear the imprints of mutational processes operative during cancer development. Following the advent of second generation sequencing technologies the provision of whole cancer genome sequences has become a reality. These sequences generate comprehensive catalogues of somatic mutations, including point mutations, rearrangements and copy number changes and provide insights into the evolutionary processes underlying the development of individual human cancers including the factors generating variation and the forces of selection. These insights will form the foundation of our understanding of cancer causation, prevention and treatment in the future.

Special Session (Sun, 25 Sep, 13:15−14:15)
Current Issues in the Management of Germ Cell Tumours

144 INVITED

Relapse and Prognostic Factors in Patients With Metastatic Germ-Cell Tumours

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In patients with metastatic germ-cell tumours (GCT) prognostic factors at initial diagnosis are universally accepted to guide treatment decisions *(IGCCCG, J Clin Oncol 1997)*. In patients who progress or relapse after first-line cisplatin-based chemotherapy, however, the issue of prognostic factors is far more complex. Salvage treatment can induce longterm remissions in a substantial proportion of patients using four cycles of conventional-dose chemotherapy (CDCT) with cisplatin, ifosfamide plus either etoposide, vinblastine or paclitaxel. In a recent large, international multicenter analysis, five clinical variables had been shown to strongly impact on the rate of longterm remissions: histology, extragonadal tumour location, response to first-line treatment, response duration, levels of serum tumour markers AFP and HCG as well as the presence of liver, bone or brain metastases at the time of salvage treatment. Depending on the presence or absence of these adverse prognostic factors, longterm remissions varied between near zero to close to 75% or more at two years using either CDCT or high-dose chemotherapy (HDCT). As a result, for the first time an universally accepted prognostic score could be established also for the first-salvage setting *(IPFSG J Clin Oncol 2010)*. Using the same database of 1594 patients the results after HDCT were compared to those after CDCT. With the limitations of a retrospective comparison, HDCT was superior to CDCT in all prognostic groups spuring once again the discussion about the optimal first-salvage treatment strategy *(Lorch, J Clin Oncol 2011)*. HDCT also represents a curative option for patients with second or subsequent relapses, although longterm remissions are less frequent compared to it’s ealier use *(Einhorn, N Engl J Med 2007; Lorch, Ann Oncol 2010)*. Options for third-line chemotherapy are oral etoposide, paclitaxel, gemcitabine, oxaliplatin or combinations of these agents usually given as palliative treatment. However, in individual patients even third-line combinations incorporating new agents and multimodality treatment can still result in longterm remissions or even cure *(Bokemeyer, Ann Oncol 2008)*. Surgical resecion of all residual lesions is an integral part of any salvage strategy. The rates of vital undifferentiated cancer or mature teratoma are higher in patients after salvage treatment as compared to patients after first-line chemotherapy *(Rick, J Clin Oncol 2004)*. Surgery should be scheduled as early as possible after completion of salvage chemotherapy. In patients with late relapse GCT more than two years after cisplatin-based first-line treatment, salvage surgery rather than salvage chemotherapy should be the initial approach, particularly in patients with a resectable single site and normal markers or elevations of AFP rather than HCG. In conclusion, salvage treatment may cure a substantial proportion of patients with GCT, but should be limited to centers exprienced in caring for this rare and complex patient cohort.