are well designed, the study group well defined and the treatments and assessment of long term outcome (including toxicity) are standardised.

Keynote Lecture (Wed, 23 Sep, 11:15−12:00)
Insights into the cancer cell, stem cell interface through systems biology

223 INVITED

From RNAi screens to molecular function: A systematic pipeline for gene function in mammalian cells

F. Buchholz[1], M. Theis[1], D. Krastev[1], M. Slabicki[1], L. Ding[1]. [1]*Max Planck Institute, Institute for Molecular Cell Biology, Dresden, Germany*

RNAi screens typically deliver a large number of candidate genes that play a role in a biological process. The validation of these candidates and the dissection of the molecular mechanism are often time consuming and cumbersome. Hence, RNAi libraries employed during the screening process should be of high quality to avoid tedious downstream work. We have developed endoribonuclease prepared (e)siRNAi libraries for efficient and specific RNAi screening. The advantages of esiRNAs will be discussed and example screens will be presented. We have also developed a pipeline using BAC recombineering technology and tissue culture transgenesis to streamline the analysis of hits identified in large scale RNAi screens. Together, these resources represent a seamless pipeline for the systematic analysis of mammalian genes.

Special Session (Wed, 23 Sep, 13:30−14:30)
What is new in the pathogenesis of urothelial cancer?

224 INVITED

Hereditary factors in bladder cancer

L. Kiemeney[1]. [1]*Radboud University Medical Centre Nijmegen, Department of Epidemiology and Biostatistics & HTA, Nijmegen, The Netherlands*

First degree relatives of patients with bladder cancer have a two-fold increased risk of bladder cancer but high-risk bladder cancer families are extremely rare. There is no clear Mendelian inheritance pattern that can explain the increased familial risk. This makes classical linkage studies for the mapping of susceptibility genes impossible. The disease is probably caused by a combination of exposure to exogenous carcinogens and a large number of susceptibility genes with modest effects.
Genome-wide association studies (GWAS) are better suited to identify these genes. Three of these studies are ongoing of which one reported the first results. In this presentation, an overview will be given of hereditary factors in bladder cancer and the relevance of the results of the GWAS will be discussed.

225 INVITED

Histopathological profile of bladder cancer

A. Lopez-Beltran[1]. [1]*Reina Sofia University Hospital, Department of Pathology, Cordoba, Spain*

Bladder tumors represent a heterogeneous group of cancers that include those that are:
1. Papillary in nature and limited to the mucosa (Non-invasive, stage Ta).
2. High grade and flat confined to the epithelium (Non-invasive, stage Tis)
3. Invasive into the lamina propria or submucosa (Early invasive, stage T1)
4. Invasive into the muscularis propria or beyond (Invasive, stage T2-T4).

The natural history of these bladder cancers is that of recurrence of disease and progression to higher grade and stage disease. Furthermore, recurrence and progression rates of superficial bladder cancer vary according to several tumor characteristics, mainly tumor grade and stage. The most recent World Health Organization (WHO) classification of tumors of the urinary system includes epithelial abnormalities and metaplasia as well as urothelial dysplasia and carcinomas in situ as flat lesions. The papillary lesions are broadly subdivided, following the current WHO classification, into benign (papilloma and inverted papilloma), papillary urothelial neoplasia of low malignant potential and non-invasive papillary carcinoma (low or high grade). Invasive papillary carcinoma and non-papillary (solid) carcinomas are subdivided into low and high grade neoplastic lesions. Each of these lesions is defined with strict morphological criteria to provide more accurate information to urologists and oncologists in managing patients. There is still debate in the literature as to whether the 2004WHO system should be the only one to be used in clinical practice. The key points of the latest World Health Organization (WHO) classification of non-invasive urothelial tumors are: a. The description of the categories has been expanded in the current version to improve their recognition, b. One group (papillary urothelial neoplasm of low malignant potential) with particularly good prognosis does not carry the label of 'cancer', c. It avoids use of ambiguous grading such as grade 1/2 or 2/3 (according to the WHO classification published in 1973, d. The group of non-invasive high grade carcinoma is large enough to contain virtually all those tumors that have biological properties (and a high level of genetic instability) similar to those seen in invasive urothelial carcinoma. e. This scheme is meant to replace the 1973 WHO classification. From the practical point of view, the use of both the 1973 and the latest WHO classifications is recommended until the latter is sufficiently validated. This presentation summarizes the recent literature concerning important issues in the pathology and the clinical management of the patients with bladder urothelial carcinoma. The initial proposal of the WHO has been achieved with most reports clearly recognizing that categories are better defined than in previous classifications. Questions such if PUNLMP remains as a clinically useful category or if this category should be expanded including all low grade Ta lesions (PUNLM and Low grade papillary carcinoma) as a wider low malignant potential neoplastic category not labelled as cancer needs to be discussed in the near future. In this presentation, emphasis is placed on macroscopic appearance, and synchronous or metachronous presentation (field disease vs. monoclonal disease with seeding), classification and microscopic variations of bladder cancer with clinical significance, TNM distribution and the pathologic grading according to the most recent WHO proposal.

226 INVITED

Genomic alterations in urothelial carcinoma subgroups

M. Knowles[1]. [1]*Cancer Research UK Clinical Centre, St James's University Hospital, Leeds, United Kingdom*

Bladder tumors are heterogeneous in their histopathology and clinical behaviour. Currently, assessment of risk for recurrence and progression to invasive disease is not precise and response to specific therapies cannot be predicted accurately. It is anticipated that a thorough knowledge of the molecular alterations that are involved in the development and progression of bladder cancer will lead to greater predictive power and the application of targeted therapies. The current state of knowledge of genomic alterations found in urothelial carcinoma will be summarised.

Special Session (Wed, 23 Sep, 13:30−14:30)
Immune system and ovarian cancers

228 INVITED

Antigen specific active immunotherapy for ovarian cancer

H. Nijman[1], C.J.M. Melief[1], C.A.H.H. Daemen[2], N. Leffers[3]. [1]*Groningen University Hospital, Department of Gynaecologic Oncology/CMCV4th floor, Groningen, The Netherlands;* [2]*Groningen University Hospital, Department of Microbiology, Groningen, The Netherlands;* [3]*Groningen University Hospital, Department of Gynaecologic Oncology/CMCV4ht floor, Groningen, The Netherlands*

Introduction: Epithelial ovarian cancer is the most frequently diagnosed malignancy of the ovaries. Standard therapy consists of cytoreductive surgery, an attempt to remove as much tumour bulk as possible, followed by platinum-containing chemotherapy. Although initial response rates to primary therapy are high, the majority of patients with advanced stage disease relapse. The observation that survival rates were higher in patients with certain intra-tumoral immune cells (i.e. T-lymphocytes), suggested that the stimulation of anti-tumour immune responses, i.e. immunotherapy, might be a useful approach to improve the prognosis of patients with ovarian cancer. In this survey, the feasibility of antigen-specific active immunotherapy is evaluated. As immunotherapy is a relatively novel treatment strategy for ovarian cancer, not only randomised controlled trials, but also early phase studies were included in this review.
Material and Methods: Thirty studies evaluating antigen-specific active immunotherapy in 1230 patients with ovarian cancer were identified with a systematic search of study reports published between 1966 and 2008. Information on clinical responses, survival, immunological responses, and adverse events was available for 18, 18, 29, and 22 studies respectively.
Results: the most frequently described strategy (1134 patients in 14 studies) was the administration of antibodies targeting CA-125, better known as a tumour marker for ovarian cancer. Most of these studies were