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ABSTRACTS

Keynote Lectures

Wednesday, 1 September 2010, 11.45–12.30, Aula Duża

KL-01 New trends in breast pathology
Chairperson: T. Tot, Sweden

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New trends in breast pathology
*M. van der Vijver**
*The Netherlands

Thursday, 2 September 2010, 11.45–12.30, Aula Duża

KL-02 Emerging mechanisms of tumor initiation and progression: lessons from the bladder cancer model
Chairperson: H. van Krieken, The Netherlands

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Emerging mechanisms of tumor initiation and progression: lessons from the bladder cancer model
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Bladder cancer has served as one of the most important sources of information about the events that underlie the development of human solid malignancies. Although "field effects" that alter the entire bladder mucosa appear to initiate disease, tumors develop along two distinct biological "tracks" referred to as papillary and non-papillary that present different challenges for clinical management. More recently, whole organ mapping combined with genomic platforms have identified a novel class of candidate tumor suppressors (forerunner genes) that localize near more familiar tumor suppressors but are disrupted at an earlier stage of cancer development. These studies suggested three steps for the involvement of the model tumor suppressor locus, RB1, in tumor development. In the first step, one allele of forerunner (FR) gene and RB1 is inactivated by deletions. In the second step, homozygous inactivation of the FR genes is accomplished by hypermethylation or mutations. The inactivation of FR genes is associated with the initial clonal expansion of preneoplastic urothelial cells. In the third step, the contiguous tumor suppressor, RB1, is inactivated by a mutation, which is associated with clonal evolution into carcinoma in situ progressing to invasive cancer. Furthermore, we have discovered that aggressive muscle-invasive tumors express molecular markers characteristic of a developmental process known as "epithelial-to-mesenchymal transition." Emerging evidence indicates that urothelial cancers contain subpopulations of tumor-initiating cells (cancer stem cells), but the phenotypes of these cells in different tumors may be heterogeneous, raising questions about whether or not the two major subtypes of cancer share a common precursor.

Friday, 3 September 2010, 11.45–12.30, Aula Duża

KL-03 Predictive pathology: fact or fancy?
Chairperson: F. Carneiro, Portugal

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Predictive pathology: fact or fancy?
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Pathology as a medical specialty has been around for about a century and a half, even though the interest in understanding disease, the focus of pathology as an academic discipline, has inspired physicians since the dawn of mankind. Understanding disease remains the primary focus of pathology. In the practice of diagnostic pathology, this knowledge, notably through its morphological expression, is applied to the diagnosis of disease through the examination of cells and tissues. Relatively new in this field is the notion of pathology as 'the science behind the cure'. This phrase, coined by the Pathological Society of Great Britain and Ireland, refers to a widening of the scope of pathology: 'Understanding disease' continues to be applied to diagnosis and classification, but now also to conceiving of new ways to treat and of new diagnostic tools assisting the physician in choosing the appropriate treatment. Targeted therapy, the target being a molecular pathway involved in the pathogenesis of the lesion, along with biomarkers that are predictive for response to treatment, are in the forefront of pathology. Targeted drugs that require 'companion' diagnostics, a combination also called 'theranostics', are reshaping the practice of pathology. It is this

considered as suspicious of malignancy. After a revision of these cases, two showed features of BCA, while in the remaining two, the suspicious of malignancy persisted because of minimal amount of stroma, predominant epithelioid cell morphology and cellular density.
Conclusion: BCA shows characteristic features that allow in many cases a precise diagnosis. It may be difficult to differentiate from epithelial-rich pleomorphic adenoma, and in these cases, a diagnosis including both possibilities seems preferable. In our series, the absence of stroma was responsible for the misdiagnosis with acinic cell carcinoma in two cases.

005

SDHB expression in paraganglioma–pheochromocytoma syndromes: advantages and limits

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Objective: Pheochromocytoma and paraganglioma are rare tumors arising from chromaffin cells. Almost 10% of them are part of typical familial syndromes: Von Hippel–Lindau disease (VHL), neurofibromatosis type 1 (NF1), multiple endocrine neoplasia type 2 (MEN2) and type 1 (MEN1), pheocromocytoma–paraganglioma syndromes (PGLs; SDHB, SDHC, and SDHD) and a newly described syndrome related to TMEM127 gene mutations. Recently, SDHB immunohistochemical analysis has been proposed as a promising molecular marker for succinate dehydrogenase mutation-related neoplasms (i.e. PGLs).
Method: All cases of reported pheochromocytomas (n=160) and paragangliomas (n=57) between 1988 and 2009 were retrieved from the archives of the Department of Pathology of Padova University. FFPE specimens were genetically characterized for familial syndromes. Syndromic cases and a control group were semiquantitatively (0, 1+, 2+) evaluated for SDHB immunohistochemical expression.
Results: Out of 217 cases, 21 cases showed SDHD (n=3), TMEM127 (n=3), RET (n=6), MEN1 (n=2), VHL (n=4), or NF1 (n=3) germline mutations. The other six sporadic cases were evaluated as control. The three SDHD-mutated cases showed either negative (n=1) or 1+ (n=2) SDHB immunostaining. Completely negative staining was also observed in a sporadic case. A strong SDHB immunoreaction was observed in 19 and a weak immunoreaction in four of the remaining cases.
Conclusion: SDHB immunohistochemical analysis, even not PGL-specific, can be used to triage genetic testing in pheochromocytoma/paraganglioma patients. Further multi-institutional studies should investigate the diagnostic power of this remarkable novel diagnostic tool.

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Biochemical and histological effects of sitagliptin on Zucker diabetic fatty rat pancreas

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Objective: Inhibition of dipeptidyl peptidase-4 (DPP-4) activity by sitagliptin has been shown to improve glycemic control in patients with type 2 diabetes mellitus (T2DM) by prolonging the actions of incretin hormones, but the real impact of low-dose sitagliptin treatment on pancreatic lesions is almost unknown. This study aimed to evaluate the effects of sitagliptin on the biochemical and histological (pancreatic) parameters of Zucker diabetic fatty (ZDF, fa/fa) rats, an animal model of T2DM.
Method: Diabetic (fa/fa) ZDF male rats were treated with vehicle or sitagliptin (10 mg/kg body weight per day) during 6 weeks (n=8 each). The following parameters were assessed: serum glycaemia, HbA1c, insulin and lipid profile; serum and pancreas oxidative stress (MDA) and endocrine and exocrine pancreas histology, estimating and rating inflammatory infiltrate, fibrosis, vacuolization and congestion in a semiquantitative score ranging from 0 (minimal) to 3 (severe and extensive damage).
Results: Sitagliptin in diabetic ZDF rats promoted beneficial effects on dysglycaemia, dyslipidaemia, inflammatory profile and pancreatic oxidative stress. Endocrine and exocrine pancreas presented a reduction/amelioration of fibrosis severity, inflammatory infiltrate, intra-islet vacuolation, and congestion vs the vehicle-treated diabetic rats.
Conclusion: The favourable biochemical profile promoted by sitagliptin in the diabetic rats, together with protection against endocrine and exocrine pancreatic lesions, might represent a further advantage of low doses of sitagliptin in the management of T2DM.

Thursday, 2 September 2010, 14.30–16.30, Aula Średnia B

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001

Defenders of the colon: comprehensive assessment of potential prognostic immunologic biomarkers in mismatch repair-proficient colorectal cancer

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