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Word from the President Prof. F. Carneiro

Herein, I will briefly summarize the initiatives recently undertaken by our Society.

Last months have been dominated by the organization of future Congresses of the ESP, namely the 24th ECP to be held in Prague, 8-12 September 2012, twenty-five years after the 11th ECP, held also in Prague, in September 1987. The enthusiastic and professional attitude of Ales Ryska and the other members of the Local Organising and Scientific Committees contributed decisively for the building of a superb scientific and social programme. As per 20 July 2012, more than 1,600 participants have registered for the Congress. Forty two bursaries were awarded to residents and trainees. Abstract submission exceeded the expectations of the organizers: 259 abstracts for oral presentations and 1,059 abstracts for posters have been submitted. Out of those, 173 abstracts for oral presentations and 887 for posters have been selected for presentation by the ESP Working Groups. The organizers are eager to welcoming you in Prague. If you have not registered yet, you can still do it (Please visit the Congress website: http://www.esp-congress.org/). I hope the scientific programme and social activities will constitute an irrecusable stimulus for your participation in the Prague Congress.

Together with the organizers of the 25th ECP to be held in Lisbon, from 31 August to 4 September 2013, we have already prepared a very attractive social programme and we will focus now on the building of the scientific programme, guided by the motto of the Congress – Pathology: A gate to the future.

Further, the ESP began to prepare the 26th ECP to be held in London, from 30 August to 3 September 2014. This Congress will be jointly organized by the ESP and the Pathological Society of Great Britain & Ireland. Officers of both Societies participated recently in a planning meeting in Sheffield, and have agreed on the most important financial and organizational issues.

In the frame of the strategy of our Society to support education initiatives of National Societies of Pathology, the ESP President and Past-President participated in the 2nd Pannonia Congress of Pathology, held in Siófok, Hungary, in May 2012, organized by the Pathology Societies and IAP Divisions of Austria, Croatia, Czech Republic, Hungary, Slovakia and Slovenia. Janina Kulka, the chairperson of the Congress, who is also a member of the ESP Executive Committee, and the members of the Organising Committee, managed to create a superb atmosphere within a high level scientific meeting. The ESP supported also the 14th Congress of Serbian Association of Pathologists and Cytologists, held in Belgrade, Republic of Serbia, in June 2012, under the auspices of the ESP.

Under the guidance of Helmut Poppen-
Chair of the Education Committee – efforts are being made to create a dynamic and attractive Education Portal, being expected that it will be opened to the ESP members along 2012. In the last month, the ESP members were invited to participate in an evaluation test of two companies in order to find a convenient Internet based system for managing digital slide collections. Hopefully, this process will allow, besides the development of the Education Portal, the maintenance of Proficiency Progress Tests organized by the European Association of Pathology Chairs and Program Directors (EAPCP).

Within the Molecular Pathology Program of the EScPoP, directed by Generoso Bevilacqua and Fred Bosman, the following courses were organized: Molecular Biology for Pathologists (Pisa, March 2012) and Molecular Pathology of the Breast (Pisa, May 2012). A Tutorial Course on Cytology for Pathologists took place in June 2012, in the ESP office in Brussels, organized by Fernando Schmitt, Philippe Vielh and Pio Zeppa.

The ESP continued fostering the cooperation with other International Organizations and Societies: 1) In 27 June 2012 I participated, as the President of the ESP, in the 1st investigator meeting of the Screening Platform of the EORTC for Clinical Trials in Advanced Colorectal cancer ("SPECTAColor"), an EORTC prospective screening initiative for the determination of molecular parameters for advanced colorectal cancer. Moreover, the ESP is involved in a direct collaboration with the EORTC and the Sanger Institute, addressing next generation sequencing issues on FFPE tissues; 2) For the collaboration with the European Society for Medical Oncology (ESMO), Paolo dei Tos was nominated as the ESP liaison officer. Fred Bosman organized the ESMO-ESP Joint Symposium on Molecular Diagnostics for Personalized Cancer Treatment, for the ESMO 2012 Congress that will be held in Vienna, in September/October 2012; 3) The Collaboration with the United Gastroenterology (UEG) has also been very fruitful, mainly due to the joint initiatives of Dina Tiniakos, member of both the ESP and the UEG Scientific Committee, and the ESP Working Group of Digestive Diseases Pathology, chaired by Cord Langner; 4) The ESP supported a consensus meeting with the European Crohn’s and Colitis Organization (ECCO) to establish standards for the diagnosis and pathological procedures in inflammatory bowel diseases and other colitis.

The quality assurance programme in molecular pathology is moving ahead under the coordination of Han van Krieken, and a meeting devoted to the creation of common European EQA database took place at the ESP office in June 2012, coordinated by Erik Thunnissen.

Overall, I think important steps have been taken in several fronts, aiming at the consolidation of the ESP as a leading Society in the field of modern Pathology, now moving in the direction of Personalized Pathology.

Fátima Carneiro
The 23rd European Congress of Pathology (ECP) was held at the Helsinki Convention and Exhibition Center in Finland from 27 August to 01 September 2011. Prof. Veli-Pekka Lehto was chairman and prof. Ilmo Leivo secretary of the congress. The scientific programme was arranged by 22 Working Groups and associated societies of the ESP in 9-11 parallel sessions. This was the first congress of the ESP where the new professional congress organiser of the Society CPO Hanser was responsible for the non-professional arrangements including the finances.

In the Opening ceremony prof. Veli-Pekka Lehto greeted the participants, and the audience was entertained by the Finnish male choir "Huutajat". Prof. Carlo Croce gave an opening lecture on micro-RNA dysregulation and cancer. Keynote speakers of the congress included prof. Susan Lindquist (Boston) on protein folding in health and disease, prof. Erkki Ruoslahti (Santa Barbara) on targeting of drugs and nanoparticles to tumours, prof. Markku Miettinen (Washington) on gastrointestinal stromal tumour, and prof. J.Han J.M. van Krieken (Nijmegen) on pathology today: progression, differentiation and transformation. Special session topics included comprehensive cancer centers, biobanks, cancer stem cells, tumor pathology in translation, pathology training in Europe, reverse translational research, micro-RNA in pathology, and animal models in pathology. Awards for best oral free paper and best posters were given. For the first time in ESP congresses, free admission to all slide seminars was included in the registration fee of the congress. All slide seminar cases were digitized and made freely available in the internet after congress.

The congress dinner was served at Hilton Kalastajatorppa restaurant. The congress concert featured contemporary and traditional Finnish music played by Tapiola Sinfonietta chamber orchestra. In addition, the new Guital Concerto by prof. George Kontogeorgos, a member of the ESP, was premiered at the concert. The gala dinner was held at Finlandia Hall to 450 participants entertained by the Riku Niemi Big Band.

The congress was attended by ca. 1800 pathologists, 200 accompanying persons and 400 exhibitors from 76 countries. A trade exhibition of 884m² was arranged by 57 exhibitors. The 23rd ECP was a scientifically and socially successful congress at the interphase of the previously biennial ECPs and the new professionally organised annual congresses. Prof. Michael Wells completed his term as the President of the ESP, and prof. Fatima Carneiro was elected as the new President.

Immediately after the congress, four educational courses of the ESP were arranged in St.Petersburg by the Working Groups of Hematopathology, Cytopathology, Infectious Diseases, and Head and Neck. Approximately 50 pathologists from the ECP in Helsinki travelled to St.Petersburg to participate in the courses together with 50 Russian pathologists. Speakers of the educational programme were both ESP and Russian participants. The courses were a successful get-together of Russian and European pathologists giving opportunities for new scientific contacts and social interaction.
Activities of the Education Committee in 2012

In February 11th, 2012 a meeting of the Education Committee took place in Brussels. The SOP for application for an EScOP branch was updated and accepted by the members. It can be found on the ESP website.

A report on ongoing courses was presented and new proposals were discussed. Due to an unacceptable format the application for an Uropathology course in Belgrade was rejected. This course proposal was based on lectures and had no interactive learning and microscopy sessions included.

The new Molecular Pathology branch in Pisa had it’s first course and was well attended. This part focused on general genetic and molecular pathology methods and applications thereof. The next courses are planned and will take place soon. A new EScOP tutorial on Cytopathology was accepted and took place in the Brussels office. The tutorial was well attended and it is planned to have another tutorial in 2013.

A new course on Uropathology has been accepted for the Krakow EScOP branch and will be conducted in September 2012.

Ankara applied for an extension as an official branch of ESCOP, which was accepted. The Zagreb branch of EScOP applied for a new course on Dermatopathology. After having sent the program proposal this course was approved.

A new logo was created for EScOP and should be used on all upcoming courses.

New Education Portal (EduPort):

A first discussion about creating an EduPort was held during the Helsinki Congress with Globit and CPO Hanser. Several meetings and phone conferences followed. This EduPort should integrate all information about Pathology, courses, conferences, etc. To become effective we will need a syllabus with almost all terms used in pathology, a wide variety of presentations, digital slides, video documents, and also links to PubMed and Virchows Archiv. Globit can provide 3 modules to integrate all this information into such an EduPort. Since we presently have not much content to integrate in such an EduPort, it would rather withdraw visitors instead of attracting them to such a portal.

ESP has however an urgent need for a web portal for digital microscopy, which is also an integral part of any EduPort. Therefore we proposed a stepwise action: First to install a digital slide portal and further on work on a syllabus as the basis for an EduPort.

Two companies for digital slide management (PathXL and Aurora) were chosen and a contest was prepared. 19 cases were selected from Dr. Popper’s collection and prepared for this test. In a mail ESP members were invited to join this test. 93 did respond positively and were grouped into group A and B (46 and 47 members). Both groups performed test 1 with one of the two companies and test 2 with the respective other company. Approximately two thirds of the users did participate in both tests. Ulrike Gruber-Moesenbacher prepared a survey. This survey will be a basis for a decision. We will next ask for bids from both companies and than make a decision, which platform will be contracted for the next 3 years.

This decision will be made before the Prague Congress. For the next ESP Congress in Lisbon everybody will be able to upload his/her slides directly to the digital slide box and place it into the right session. Both systems accept almost every scanner, so there is no need for any changes of your slide.

Following the Prague Congress the next work will be the syllabus of pathological terms, and discussion, which further steps, can be managed into the EduPort.
“IN ILLO TEMPORE”

The ESP diplomas and the Prague Congresses of 1987 and 2012

When Ales Ryska and his Colleagues of the Organizing Committee of the 2012 Prague Congress receive the ESP Diploma, the ceremony will be, for the less young members of our Society, a sort of déjà vu movie, after having witnessed, 25 years ago, the awarding of an identical diploma to Prof. Joseph Stejskal, the Organizer of the 1987 Prague Congress.

As you may have noticed the diplomas that our Society awards to Honorary Members and other distinguished personalities are true art pieces. The need for having an ESP diploma had been frequently addressed until Prof. Dusan Ferluga was asked to use his authority as Past-President and his knowledge of Latin to order from a Slovenian graphic artist the beautiful diplomas we have today. At the same time, Prof. Ferluga also ordered the ESP seal we are nowadays using and proposed a new letterhead for the ESP.

In the Executive Committee (EC) meeting immediately held after of the Hamburg Congress, on September 19, 1983, it was decided: “4. The diplomas, and proposed new letterhead and seal were accepted by the Committee. It was agreed that the unused diplomas should be kept by Ferluga for future use. The proposed letterhead and seal will be passed to the new President”.

It was decided, one year later, in the EC meeting held in Oslo, on March 10, 1984, that Prof. Ferluga should arrange additional diplomas “to be used to acknowledge the work for the Society by Congress organizers and Council and Committee members on retirement”.

On this occasion, Jan Vincents Johannessen, ESP President, suggested that Honorary Memberships should be conferred upon three founders of the Society, i.e., Profs Alexandra Piringer-Kuchinka (Austria), Janusz A. Groniowski (Poland) and Christian Nezelof (France). The President’s proposal was unanimously approved. It was also decided that the three Honorary Memberships would be given at the X Congress to be held in September 1985 in Athens.

In the EC meeting held in Hamburg, in April 1986, there was the following point on the preparation of the Prague Congress: “No financial support could be expected to be obtained from the Czechoslovak State or from any commercial firms or scientific societies. Participants below the age of 35 years should pay a congress fee corresponding to USD 120, whereas all others should pay USD 200. The fees for slide seminars should be paid directly to the Treasurer in Maastricht, however, for participants from Eastern Countries the slide seminar fees should be put on a separate account in Prague”.

In the XI European Congress of Pathology held in September 1987, in Prague, Prof. Christoph Hedinger was awarded the Honorary Membership and received the respective diploma brought to Prague by Dusan Ferluga.

Porto, July 20, 2013

Fátima Carneiro
Manuel Sobrinho Simões
“IN ILLO TEMPORE”

Minutes of Meetings of the ESP Executive Committee:

Hamburg, September 1983:

EUROPEAN SOCIETY OF PATHOLOGY - Executive Committee
Summary of discussions and decisions at the committee meeting
Monday, September 19, 1983, 14:00, Congress Center, Hamburg
Present: Committee members: Feilige, President; Johansson, President-Elect; Pedringer, Past-President; Giordano, Secretary; Swen, Treasurer; David; Lombard-Doel; Papaharakampou; Rank.

The diploma, with prepared letterhead and seal were accepted by the Committee.
It was agreed that the unused diploma should be kept by Feilige for future use. The prepared letterhead and seal will be passed to the new President.

The President
Feilige Dusan

The Secretary
Giordano

Hamburg, April 1986:

Financial support could be expected to be obtained from the European Union or from any commercial firms or scientific societies. Participants below the age of 35 years should pay a congress fee corresponding to USD 80, whereas all others should pay USD 200. The fees for slides presentation should be paid directly to the Treasurer in Maastricht; however, for participants from Eastern Europe, the slide material fees should be paid on a separate account in Russia.
The first meeting was organized by the IAP Hungarian Division, and as such it was already the 7th Technology Transfer in Diagnostic Pathology congress series of the IAP HD. We had the pleasure to have Dr. Kristin Henry, president of the IAP with us for that event.

The 2nd Pannonia Congress of Pathology, organized by 6 Central European countries, was supported by the ESP. The main topics covered were thyroid pathology, lymph nodes non-hematopathological diseases, selected topics in uterus pathology and quality control in pathology. Each countries’ pathological societies suggested speakers for each topic, and the organizers tried to cover the cytological diagnostic- and molecular pathological aspects as well. Two outstanding slide seminars were held on the last day of the conference: altogether 17 cases were presented by experts. Cases presented at one of the slide seminars were related to the main topics, the other – organised by Dr. Michal Michal from Plzen (Czech Republic) – covered rare diseases and new entities in pathology. Since this year the Hungarian Society of Pathology celebrates its 80th anniversary, this occasion was an excellent opportunity to remember the ancestors of contemporary pathology and also to celebrate with parties both on Thursday and Friday. Dako Central Europe brought authentic Czech beer for the Welcome Party, which made this evening even more special. The president of the Congress, Dr. Janina Kulka presented a historical slide seminar during the Congress Dinner, remembering the great Hungarian pathologist, Krompecher.

Both conferences during the week were honoured by the participation of world known experts, but the participation of the past- and the acting presidents of the ESP had a symbolic meaning too apart from the experience provided by the excellent keynote lectures Dr. Michael Wells and Dr. Fatima Carneiro held.

As an intercongress session, a very interesting discussion was initiated about the „brain drain” of pathologists from Eastern to Western Europe, moderated by Dr. Fredrik Bosman and Dr. József Timár. Prof. Bosman suggested to write a position paper about the problem in one of the upcoming issues of Virchows Archiv.

The official congress bureau of both conferences was K&M Congress, who did a great job much to the satisfaction of the participants. There were 321 participants from 25 countries and 4 continents at the congress.

The website of the conference (www.pannonia-pathology.com) was constructed by Mind Forum Ltd.
The genomic and transcriptomic architecture of 2,000 breast tumours reveals novel subgroups

The elucidation of breast cancer subgroups and their molecular drivers requires integrated views of the genome and transcriptome from representative numbers of patients. We present an integrated analysis of copy number and gene expression in a discovery and validation set of 997 and 995 primary breast tumours, respectively, with long-term clinical follow-up. Inherited variants (copy number variants and single nucleotide polymorphisms) and acquired somatic copy number aberrations (CNAs) were associated with expression in 40% of genes, with the landscape dominated by cis and trans-acting CNAs. By delineating expression outlier genes driven in cis by CNAs, we identified putative cancer genes, including deletions in PPP2R2A, MTAP and MAP2K4. Unsupervised analysis of paired DNA–RNA profiles revealed novel subgroups with distinct clinical outcomes, which reproduced in the validation cohort.

These include a high-risk, oestrogen-receptor-positive 11q13/14 cis-acting subgroup and a favourable prognosis subgroup devoid of CNAs. Trans-acting aberration hotspots were found to modulate subgroup-specific gene networks, including a TCR deletion-mediated adaptive immune response in the 'CNA-devoid' subgroup and a basal-specific chromosome 5 deletion-associated mitotic network.

Our results provide a novel molecular stratification of the breast cancer population, derived from the impact of somatic CNAs on the transcriptome.

2) APMIS 2012; 120: 298–304

Utility of whole slide imaging and virtual microscopy in prostate pathology

Whole slide imaging (WSI) has been used in conjunction with virtual microscopy (VM) for training or proficiency testing purposes, multicentre research, remote frozen section diagnosis and to seek specialist second opinion in a number of organ systems. The feasibility of using WSI/VM for routine surgical pathology reporting has also been explored. In this review, we discuss the utility and limitations of WSI/VM technology in the histological assessment of specimens from the prostate. Features of WSI/VM that are particularly well suited to assessment of prostate pathology include the ability to examine images at different magnifications as well as to view histology and immunohistochemistry side-by-side on the screen.

Use of WSI/VM would also solve the difficulty in obtaining multiple identical copies of small lesions in prostate biopsies for teaching and proficiency testing. It would also permit annotation of the virtual slides, and has been used in a study of inter-observer variation of Gleason grading to facilitate precise identification of the foci on which grading decisions had been based. However, the large number of sections examined from each set of prostate biopsies would greatly increase time required for scanning as well as the size of the digital file, and would also be an issue if digital archiving of prostate biopsies is contemplated. Z-scanning of glass slides, a process that increases scanning time and the size of the virtual slide up and down to assess subtle nuclear features such as nucleolar prominence.

The common use of large blocks to process prostatectomy specimens would also be an issue, as few currently available scanners can scan such blocks.
Continues from p.8

A major component of proficiency testing of prostate biopsy assessment involves screening of the cores to detect small atypical foci. However, screening virtual slides of wavy fragmented prostate cores using a computer mouse aided by an overview image is very different from screening glass slides using a microscope stage. Hence, it may be more appropriate in this setting to mark the lesional area and focus only on the interpretation component of competency testing.

Other issues limiting the use of digital pathology in prostate pathology include the cost of high quality slide scanners for WSI and high resolution monitors for VM as well as the requirement for fast Internet connection as even a subtle delay in presentation of images on the screen may be very disturbing for a pathologist used to the rapid viewing of glass slides under a microscope. However, these problems are likely to be overcome by technological advances in the future.


Comparison of Clinical and Pathological Characteristics of Isolated Aortitis and Takayasu Arteritis With Ascending Aorta Involvement

Hongyue Wang; Li Li; Linlin Wang; Qian Chang; Jielin Pu

Aims: Isolated aortitis (IA) is a newly recognized condition, but its differentiation from Takayasu arteritis (TA) is still a challenge. This study aims to explore the characteristics of IA.

Methods: The clinical and pathological data of 965 cases with excised ascending aortas were obtained by chart and slide review. IA cases were compared with TA cases and examined for CD3, CD4, CD8, CD20, CD68, CD138 and IgG4 of the infiltrates using immunohistochemistry.

Results: 24 cases of IA and eight cases of TA were identified. IA cases tended to be older than TA cases (mean 46.3 vs 33.9 years). Both groups had the same male/female ratio (1.0). IA cases tended to have a bigger aortic diameter (mean 59.7 vs 47.6 mm), statistically less intimal thickening (mean 678 vs 1101 μm), fewer lesions outside the ascending aorta (8% vs 100%), a lower erythrocyte sedimentation rate (mean 14.6 vs 27.0 mm/h) and more active aortitis (75.0% vs 62.5%) than TA cases. The number of CD3+ cells was equal to CD20+ cells in the media but fewer than CD20+ cells in the adventitia of IA cases. Their CD4/CD8+ ratio ranged from 1.0 to 1.8 while the number of CD68+ macrophages varied largely. IgG4+ cells ranged from 0 to 40 (mean 4) cells/HPF and the IgG4+/CD138+ ratio ranged from 0 to 0.36 (mean 0.06) in IA cases.

Conclusions: Cases of IA tend to have more histologically active inflammation except for a relatively normal erythrocyte sedimentation rate, localised lesions and milder intimal fibrosis than cases of TA. IgG4 abnormality may not be the main cause of IA.

4) Annals of Oncology 2012; 23(3):618-624

High Independent Prognostic and Predictive Value of Circulating Tumor Cells Compared With Serum Tumor Markers in a Large Prospective Trial in First-line Chemotherapy for Metastatic Breast Cancer Patients

J.-Y. Pierga; D. Hajage; T. Bachelot; S. Delaloge; E. Brain; M. Campone; V. Dieras; E. Rolland; L. Mignot; C. Mathiot; F.-C. Bidard

Background: Circulating tumor cells (CTCs) are a prognostic marker in metastatic breast cancer, but comparisons with serum tumor markers (CA 15-3, carcinoembryonic antigen and lactate dehydrogenase) variations are needed.

Patients and methods: CTCs were counted with CellSearch® at baseline, before cycle 2 (C2) and cycle 3 or 4 (C3/4) in 267 metastatic breast cancer patients on first-line chemotherapy with/without targeted therapy.

Results: Baseline CTC detection rate was 65% with ≥1 CTC/7.5 ml threshold and 44% with ≥5 CTC/7.5 ml and was independent of subtypes (luminal, triple negative, human epithelial growth factor receptor 2 (HER2)+). CTCs were associated with tumor markers, bone/liver involvement, tumor burden and performance status. CTC detection ≥1 CTC/7.5 ml was a strong prognostic factor for progression-free survival (PFS), P < 0.0001. Threshold of CTC ≥5 was statistically significant for PFS and overall survival (OS), P = 0.03 on multivariate analysis. Among patients with ≥5 CTC/7.5 ml at baseline, 50% had <5 CTC/7.5 ml at C2. Changes were correlated with both PFS and OS (P < 0.0001).

Continues on p.10
Primary tumor conventional dendritic cells and regression were protective against sentinel lymph node metastasis (odds ratio=0.714, 0.067; \( P=0.0099, 0.0816 \), respectively). Antitumor immunity was downregulated in the positive sentinel lymph node with an increase in regulatory T cells compared with the negative non-sentinel node from the same nodal basin (\( P=0.0005 \)) and matched negative sentinel lymph node (\( P=0.0002 \)). The positive sentinel lymph node also had decreased numbers of conventional dendritic cells compared with the negative sentinel lymph node (\( P<0.0001 \)). Adding sentinel lymph node regulatory T cell expression improved the discriminative power of a recurrence risk assessment model using clinical stage. Primary tumor regression was associated with prolonged disease-free (\( P=0.025 \)) and melanoma-specific (\( P=0.014 \)) survival. Our results support an assessment of local immune profiles in both the primary tumor and sentinel lymph node to help guide therapeutic decisions.

6) Laboratory Investigation 2012; 92: 1013–1019

**LARP7 is a potential tumor suppressor gene in gastric cancer**

Yulan Cheng, Zhe Jin, Rachana Agarwal, Ke Ma, Jian Yang, Soibrahim Ibrahim, Alexandru V Olar, Stefan David, Hassan Ashktorab, Duane T Smoot, Mark D Duncan, David F Hutchison, John M Abraham, Stephen J Metzler and Yuriko Mori

**Abstract:** We previously reported frequent truncating mutations of the RNA-binding protein gene, La ribonucleoprotein domain family, member-7 (LARP7) in gastric cancers (GCs) with frequent microsatellite instability. LARP7 negatively regulates positive transcription elongation factor-b (p-TEFb) by binding to and stabilizing 7sk RNA. p-TEFb has been linked to proliferation and de-differentiation in various tissues. Therefore, we reasoned that loss of LARP7 may contribute to gastric tumorigenesis. In this study, we evaluated LARP7 mRNA expression in 18 GCs, their corresponding non-neoplastic gastric tissues (N\(_{GC}\)), and 18 normal gastric tissues from healthy individuals (N\(_{H}\)). We also assessed the effects of transient small interfering (siRNA)-mediated LARP7 knockdown in immortalized non-neoplastic gastric epithelial cells. LARP7 mRNA was significantly decreased in GCs (median 2.5) relative to N\(_{H}\)s (median 14.9, \( P<0.01 \)) as well as relative to their corresponding N\(_{GC}\)s (median 8.1, \( P<0.01 \)).

Transfection of an siRNA directed against LARP7 (anti-LARP7 siRNA) into non-neoplastic gastric epithelial cells decreased 7sk levels by 72% relative to a control siRNA (\( P<0.01 \)). Furthermore, anti-LARP7 siRNA transfection increased cell proliferation by 23% (\( P<0.01 \)) and cell migration by 22% (\( P<0.001 \)) relative to control siRNA transfection. Taken together, these findings suggest that LARP7 downregulation occurs early during gastric tumorigenesis and may promote gastric tumorigenesis via p-TEFb dysregulation.

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**Immune response in melanoma: an in-depth analysis of the primary tumor and corresponding sentinel lymph node**

Michelle W Ma, Ratna C Medicherla, Meng Qian, Eleazar Vega-Saenz de Miera, Erica B Friedman, Russell S Berman, Richard L Shapiro, Anna C Pavlick, Patrick A Ott, Nina Bhardwaj, Yongzhao Shao, Imran Osman and Farbod Darvishian

The sentinel lymph node is the initial site of metastasis. Downregulation of antitumor immunity has a role in nodal progression. Our objective was to investigate the relationship between immune modulation and sentinel lymph node positivity, correlating it with outcome in melanoma patients. Lymph node-primary tissues from melanoma patients prospectively accrued and followed at New York University Medical Center were evaluated for the presence of regulatory T cells (Foxp3\(^+\)) and dendritic cells (conventional: CD11c\(^+\), mature: CD86\(^+\)) using immunohistochemistry. Primary melanoma immune cell profiles from sentinel lymph node-positive/-negative patients were compared. Logistic regression models inclusive of standard-of-care/immunological primary tumor characteristics were constructed to predict the risk of sentinel lymph node positivity. Immunological responses in the positive sentinel lymph node were also compared with those in the negative non-sentinel node from the same nodal basin and matched negative sentinel lymph node. Decreased immune response was defined as increased regulatory T cells or decreased dendritic cells. Associations between the expression of these immune modulators, clinicopathological variables, and clinical outcome were evaluated using univariate/multivariate analyses.

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All patients receiving anti-HER2 therapy had <5 CTC/7.5 ml after three cycles of treatment.

**Conclusion:** This is the largest prospective series validating the prognostic value of CTC independently from serum tumor marker. Elevated CTCs before C2 are an early predictive marker of poor PFS and OS, which could be used to monitor treatment benefit. CTC decrease under treatment seems stronger with targeted therapy.

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5) Modern Pathology 2012; 25: 1000–1010

Continues from p.9
An important study was published recently in the July 30 issue of the Journal of Clinical Oncology by Castle PE et al. under the title “Clinical human papillomavirus detection forecasts cervical cancer risk women over 18 years of follow up”. The authors tested 19,512 women attending a health maintenance program at Kaiser Permanente Hospital in Portland, Oregon, for both HPV 16,18 research test and Pap smear and the long term benefits (>10 years) were analysed.

In their results they showed that a baseline negative HPV test provided greater reassurance against CIN+3 over the 18-year follow up than a normal PAP. Both PAP and HPV tests predicted who would show CIN3+ within the first 2 years. However only HPV test predicted who would be positive for similar lesions in 10-18 years.

They concluded that “HPV testing to rule out cervical disease followed by Pap testing and possibly combined with the detection of HPV16 and HPV18 among HPV positives to identify those at immediate risk of CIN3+ would be an efficient algorithm for cervical cancer screening, especially in women age 30 years or older”.

One of the co-authors, Dr. A.Lorincz, Professor of molecular epidemiology at Queen Mary Hospital in London, said that “HPV DNA testing detects more cervical precancers than the PAP test, and women who are negative for high-risk HPV-DNA have improved protection from the risk of cervical cancer.

He emphasized however that “the research does not suggest that one test should replace the other but confirms the importance of both screenings”. He underlined that “the main aims of the study were to see how many extra cases of precancer lesions can be discovered by the additional use of HPV DNA testing as compared to routine testing”.

In their discussion the authors revealed that: “As previously reported, separate HPV16 and HPV18 detection adds further risk stratification beyond what can be achieved by cytology alone among HPV positives; we also found that CIN3 after HPV16 detection developed sooner after baseline than after other HPV genotype detection, consistent with reports that HPV16-related CIN and cervical cancer develop at younger ages than other HPV genotypes. Among HPV-positive women with normal cytology, HPV16 and HPV18 detection can identify a group of women who have substantial risk of CIN3+. Using a more conservative approach to estimating the risks, we observed a lower risk after HPV18 than we previously observed. Our previous estimates used 1 year as the unit of time, leading to a larger absolute risk than justified by the number of events because of compounded unstable estimates. Yet the risk of CIN3+ after one-time detection of HPV18 was substantially higher than for the other HR-HPV genotypes in aggregate. HPV18 is strongly associated with adenocarcinoma and AIS, which is on the rise in Western countries and is preferentially missed by cytologic HPV16 separately in screening.

Despite the limitations of the study, the data presented provide additional support for the use of HPV testing in routine screening in women age 30 or older. Importantly, an HPV test provides greater reassurance against CIN3 and cervical cancer than Pap testing and thus might be used as the screen to rule out disease in healthy women, whereas Pap is useful as a secondary diagnostic test to identify HPV positive women at immediate risk of CIN3+. There is also evidence from other studies suggesting that HPV testing might help to identify women at risk for AIS and invasive adenocarcinoma, which are poorly detected by cytology-based screening alone.”

Are we approaching the era where Histopathologists could acquire a new tool to diagnose more safely precancer lesions? If this new technology proves feasible, would provide Pathologists and medical laboratories a different, and possibly less complex, methodology to use when assessing a case of cervical lesions?

Is this the rising combined molecular and classical pathology type of our future everyday work? Should Pathologists include it in their diagnostic procedures?

I have the feeling that more and more Pathologists believe that it is becoming more and more convincing that although morphology (Pap smear for instance) could never be replaced in detecting phenotypic lesions, the molecular technologies could provide an additional solid diagnostic approach hand in hand with morphology.

Dr. Loukas Kaklamanis
Rare Cancers – A Pathological Challenge to be Addressed

Co-authors:

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More than 500,000 people in the European Union are diagnosed with a rare cancer every year. Accounting for more than 20% of all cancers, a total of 186 cancers have been defined as rare by the Surveillance of Rare Cancers in Europe (RARECARE) project. They affect more than 4 million people in the European Union.¹ Evidence also suggests that survival rates for rare cancers are lower than for common cancers.¹

Pathology reports set the foundation for successful cancer care. However, many pathologists may be confronted with a specific rare cancer perhaps once or twice in their entire professional career. This is why diagnosing rare cancers accurately can present a real challenge for a pathologist. At the same time, it is extremely important, especially in the field of rare cancers, to combine information from biology, pathology and clinical practice to set up an appropriate treatment plan.

Pathologists need to be aware of the potential diagnostic pitfalls in rare cancer pathology, especially when taking into account that some of these difficulties may lead to different treatment plans or prognoses. For example, a study on the pitfalls in neuroendocrine tumour (NET) diagnosis revealed that “neither laboratory tests nor octreoscans are completely reliable diagnostic tools because other clinical disorders or atypical radiological findings may mimic a carcinoid, hence leading to an erroneous NET diagnosis.”¹

To assess the concordance between primary diagnosis and second opinion, a recent study looked at sarcomas, another group of rare malignant tumours, which has numerous histological subtypes and accounts for around 5% of all rare cancers.

After collecting the histological data of 448 patients diagnosed with sarcoma in the French Rhône-Alpes region between March 2005 and February 2006, the study found that “full concordance was reported for only 54% of cases included” and “more than 45% of first diagnoses were declared invalid by the panel of experts conducting the centralized pathological review.”¹

The high rate of partial concordance or discordance between initial sarcoma diagnosis and centralized expert review was also confirmed in a more recent population-based study of more than 2,000 sarcoma patients in three European regions: Aquitaine and Rhône-Alpes (France) and Veneto (Italy). The study systematically compared initial diagnoses with second opinions from regional and national experts and found that “more than 40% of first histological diagnoses were modified at second reading, possibly resulting in different treatment decisions.”¹

In order to better address the diagnostic challenges posed by rare cancers, the European Society of Pathology (ESP) has recently joined Rare Cancers Europe (RCE), a multi-stakeholder initiative, which is led by the European Society for Medical Oncology (ESMO) and aims to address issues of particular relevance in rare cancers, also including late or incorrect diagnosis. Together with RCE, we have developed a short survey to help us better understand rare cancer-related issues and challenges for pathologists and identify potential solutions.

We encourage all pathologists to take this survey by completing a short questionnaire, which will take no more than five minutes of your precious time to complete. To do so, please click on the following link: http://www.surveymonkey.com/s/pathologyrarecancers. The survey will close on 31 October 2012 and the results will be published in the following ESP Newsletter. Please be assured that the information you give in the survey is completely confidential. Also, if you decide to state your name and email address, they will never be linked with any of the information you provide. Thank you for your collaboration!

To learn more about the RCE partnership, please visit www.rarecancerseurope.org. Please also visit us at the ESP booth during our 24th European Congress of Pathology from 8 to 12 September 2012, where we will also distribute information on the RCE initiative.


¹ Bajetta E, Platania M. Pitfalls in neuroendocrine tumour diagnosis. Rare Tumors. 2009 Dec 1;1(2):e32. Available from: http://www.biomedcentral.com/1471-2407/10/150

The ESP WG Pathologists in Favour of Developing Countries and the Italian NGO Pathologists beyond Borders.

Dr. Davide Soldini

Most developing countries are trying to improve the functioning of their public healthcare systems in order to extend their impact beyond life-sustaining interventions, acknowledging the importance or health-related quality of life. In this respect, there is increasing awareness among healthcare professionals about the importance of medical specialties such as surgical pathology, which offer a solid scientific basis to guide surgical interventions and aid physicians to make better informed decisions in patient management.

The Italian NGO “Associazione Patologi Oltre Frontiera”:

(APOF, “Pathologists Beyond Borders”, http://www.patologioltrefrontiera.it) has initiated a variety of projects supporting the implementation of surgical pathology in low-resource settings (mainly in countries of sub-Saharan Africa) over the past 10 years (visit our short film at http://www.youtube.com/watch?v=gihpw7GzMEI). However, these projects, primarily aimed at creating and managing surgical pathology laboratories but also focusing on preventive medicine programs, cannot be supported solely by Italian volunteers. APOF has therefore supported the creation of the new Working Group “Pathologists in Favour of Developing Countries (http://esphumanitarian.wordpress.com/) within the European Society of Pathology (ESP), in direct collaboration with the Italian Society of Pathology (SIAPEC).

The collaboration of pathologists within the Working Group and with the ESP is deemed essential for the success of the project “Telepathology Project for sub-Saharan Africa”, aimed at creating more than 40 surgical pathology laboratories (microscope-free and telepathology platforms) according to European http://cargocollective.com/inunlampo and http://www.indiegogo.com/inunlampo. These will introduce you to a documentary film which we plan to make on the progress of ongoing and planned projects, also contributing to increase awareness of our work standards. A key aspect of the project will consist in providing adequate training for technicians, both onsite and online, with the help of the few local pathologists able to carry out online training and diagnostic activities. Among the challenges faced by the project are ensuring sufficient funding for equipment, in particular the satellite connection, finding pathologists ready to travel to the laboratories, connection with oncologists, as well as legal problems associated with telepathology.

Finally, we invite you to visit the links: http://cargocollective.com/inunlampo and http://www.indiegogo.com/inunlampo. These will introduce you to a documentary film which we plan to make on the progress of ongoing and planned projects, also contributing to increase awareness of our work.
Announcements

EScoP

European School of Pathology - Zagreb Edition 2012
Update in Dermatopathology

Dr Khadija Aljefri,
Newcastle, UK
Dr Nigel Kirkham,
Newcastle, UK
Dr Boštjan Luzar,
Ljubljana, Slovenia
Dr Bernhard Zelger,
Innsbruck, Austria

This course is created for younger pathologists and pathology residents. During three day course (October 22-24, 2012) the broad spectrum of dermatopathology will be covered. Participants will have opportunity to listen to few lectures and to take active part in slide seminars, followed by wrap-up sessions. It is designed for improvement and standardization of diagnostic abilities of participants.

The course is organized by the Institute of Pathology, University of Zagreb School of Medicine and Ljudevit Jurak University Department of Pathology, Sestre Milosrdnice University Hospital, and led by highly recognized European pathology experts. 

LIMITED NUMBER OF PARTICIPANTS!!!

Registration fee:
180 euro or 1300 kuna
(lunches and course dinner included)

Venue and contact:
Institute of Pathology,
University of Zagreb School of Medicine
Salata 16, Zagreb, Croatia
phone: +385 1 4921151
fax: +385 1 4921151
email: ilbreic@mef.hr

For information and registration course web site:
http://escop.umfcv.ro/2012/Welcome.html
Announcements:

Monday 18th – Friday 22nd March 2013 DIAGNOSTIC DERMATOPATHOLOGY COURSE
LENSBURY
CONFERENCE CENTRE TEDDINGTON ENGLAND

This annual 5 day course has been held for the past 25 years, since 1984, at the Hammersmith Hospital; hence known as the Hammersmith Diagnostic Dermatopathology Course. The course is run jointly by Thomas Brenn MD PhD FRCPath and Eduardo Calonje MD DipRCPath. As usual the quality of the course content and the expertise of its speakers will retain the same high standards it is known for. A major change is the new and formidable venue at the Lensbury Conference Centre in Teddington. The Lensbury Conference Centre is extremely well located on the banks of the River Thames, 20 minutes from Heathrow Airport, 25 minutes from Central London and with regular train services from Waterloo London (www.lensbury.com).

The course is designed for practising pathologists/trainees in pathology and dermatologists/trainee dermatologists with a special interest in Dermatopathology. Some knowledge of Dermatopathology is essential. Although the course covers most topics fairly thoroughly, this is not a basic course for beginners.

The course is divided into 10 topics covering a wide range of inflammatory and neoplastic pathology involving the skin. The course includes lectures on every topic followed by a microscopy session on each topic and ends with a “trouble shooting” demonstration session. The unique and superb slide collection contains more than 10000 cases and is annually revised and new cases are annually added by Dr Eduardo Calonje, Director of Dermatopathology at the St John’s Institute of Dermatology.

CPD points: 35 (The Royal College of Pathologists)

For further details and registration follow the link:
www.londondiagnosticdermatopathology.com

International Pathology Meeting towards the Holy Land.

6-13 October 2013

This 8-day course on Pathology will take place on Amman, Petra and Jerusalem organized by Prof. J. Forteza (Spain), Prof. J. Rosai (Italy) and Prof. R. Young (USA). The co-directors of the course are Dr. J. Antunez (Spain) and Dr. L. Kahn (USA). The course will be given in English by Dr J. Antunez (Spain), Dr. J. Chan (Hong Kong), Dr. J. Epstein (USA), Dr. F. Facchetti (Italy), Dr. J. Ferry (USA), Dr. J. Forteza (Spain), Dr. L. Kahn (USA), Dr. R. Kurman (USA), Dr. E. Montgomery (USA), Dr. J. Rosai (Italy), Dr. M. Sobrinho (Portugal) and Dr. R. Young (USA).

The course will alternate one day of scientific sessions and one day of cultural agenda and tourism.

Course fees: Euro 3,300 (double room, per person); Euro 3,900 (single room). The registration fee includes: Attendance to all the scientific sessions, course handout, full board and accommodation, sightseeing tours as detailed in the program, guides/interpreters, travel insurance and taxes.

Please click on the following link to get access to the web page of the meeting http://www.ipm-holyland.com

Contact: Congrega, S.L.; Calle Rosalía de Castro, 13 - 1º Izq. ; 15004 A Coruña (Spain); Phone +34 981 216 416.
Announcements:

Follow the ESP on the Facebook:


24th European Congress of Pathology
Pathology – Science for Patients
8 – 12 September 2012
Prague Congress Centre, Czech Republic

www.esp-congress.org

EuroClonality WORKSHOP: “Clonality assessment in Pathology”
February 11-12, 2013

Introduction
Clonality testing is at present an established tool in the diagnosis of malignant lymphomas. Between 5-15% of samples submitted to pathology laboratories which are suspected to be malignant lymphomas can benefit from clonality testing, provided that this is performed in laboratories with sufficient expertise. With the introduction of a new and complete set of primer sets for the full program of clonality testing by the Biomed-2 group in 2003, a major step in standardization and quality improvement was set. At the moment, many laboratories throughout the world are introducing the technology, resulting in questions on pitfalls in technique and the interpretation of the results.

EuroClonality/Biomed2 workshops
Therefore, the EuroClonality/Biomed2 consortium decided to organize annual workshops for laboratories that have introduced clonality testing using the new Biomed-2 primers sets in order to further improve the quality and reliability of the technique in routine practice. Since the vision of the EuroClonality/Biomed-2 consortium is that clonality testing can be performed only reliably when there is close interaction between the molecular biologist and the (hemato)pathologist, these workshops are organized for such partners.

The workshops are for a maximum number of 16 persons and uses cases from the Nijmegen group as well as cases from the participants on a hands-on basis, using multihued microscopy for pathology evaluation and raw data from clonality tests for interpretation.

We therefore invite persons to the workshop:
- who have started to use the Biomed-2 PCR technique
- who are able to bring cases for evaluation during the workshop
- who participate as combination of pathology and molecular biology: 2 persons per institute will be accepted for the workshop.

Participation
The registration fee for participation in the workshop is € 200. The registration form, including personal details and description of the cases to be presented, should be received by the Workshop Secretariat (workshop@euroclonality.org) no later than December 1, 2012. The registrants will be informed about the acceptance for the workshop no later than December 19, 2012. Information on the program, travel to Nijmegen and accommodation fees will be provided upon acceptance of the registrants.

With this background, we are convinced that the workshops are a very fruitful experience that will lead to improved diagnosis of malignant lymphomas and thereby better care for our patients.

On behalf of the EuroClonality/Biomed-2 consortium on Clonality testing,
Patricia Groenen, Han van Krieken, Tom Langerak and Jacques van Dongen
contact: workshop@euroclonality.org

www.EuroClonality.org
Dear Colleague,

We invite all European pathologists with an interest in gastrointestinal pathology to sign up to become members of The European Network of Gastrointestinal Pathology (ENGIP) by filling out the form below and sending it to the following address: engip@medunigraz.at.

To become a member you only need to be a practicing pathologist (M.D.). If you have colleagues in your hospital or in other institutions who might be interested, or if you have access to email lists of pathologists, do not hesitate to forward this information!

Please provide your contact data and give us some information on your experience and your special interest in gastrointestinal pathology.

Name:  
E-mail Address:  
Affiliation:  
Name of Hospital / Institution  
City  
Country  
Experience in Pathology:  
Resident  
Board Certified Pathologists  
Since  
Since  
Interest in Gastrointestinal Pathology:  
Diagnostic Histopathology  
Molecular Pathology  
Research  

ENGIP is a non-profit organization and works as a network for communication rather than a formal society. We do not take any membership fees. Perhaps you have heard about ENUP, the very successful European Network of Uropathology which was introduced by Lars Egevad from Karolinska / Stockholm. ENGIP aims at transferring the ideas and the spirit of ENUP into the field of gastrointestinal pathology and our special thanks go to Lars Egevad for his kind support.

Hence, the purpose of ENGIP is to get a route for dissemination of relevant information such as guidelines, consensus documents, society information (particularly from the European Society of Pathology), courses, research collaborations, grants etc. for gastrointestinal pathology.

We will regularly conduct web-based surveys on how gastrointestinal pathology is practiced in Europe. The results of these surveys are compiled and sent back to the network participants in order to give immediate feedback. Hopefully, the survey results may give a better picture of how gastrointestinal pathology is practiced in Europe and it is our hope that this will make it easier to issue formal guidelines and also be a support for you in your daily practice.

When we email to the members, we use email subjects (headings) such as: ENGIP/Information; ENGIP/Guidelines; ENGIP/Survey invitation; ENGIP/Survey results; etc. So the participants can quickly identify the emails as ENGIP information.

In addition, a homepage for the web-based presentation of ENGIP is available under the following address: www.medunigraz.at/ENGIP. We are aware of the concerns that people may have about privacy and the risk of spamming. Therefore, we will not spread the address list to others than the steering committee members listed below. The email addresses will always be suppressed in group emails. The email list will not be forwarded to congress secretariats, commercial interests or other societies. Whenever you change your address or wish to be removed from the list, please email to engip@medunigraz.at.

ENGIP is run by the members of the Steering Committee who are supported by the members of the Advisory Board, the members of which, respectively, are as follows:

Steering Committee:
Cord Langner / Graz, Austria; Alessandro Lugli / Bern, Switzerland; Iris Nagtegaal / Nijmegen, The Netherlands; An Rastimäki / Helsinki, Finland; Magali Svrcel / Paris, France; Michael Vieth / Bayreuth, Germany.

Advisory Board:
Fred Bosman / Lausanne, Switzerland; Fatma Carneiro / Porto, Portugal; Arzu Ensari / Ankara, Turkey; Jean-François Flejou / Paris, France; Karel Geboes / Leuven, Belgium; Robert Genta / Dallas, USA; Thomas Kirchner / Munich, Germany; Gunter Klappe / Munich, Germany; Gregory Lauwers / Boston, USA; Robert Reddell / Toronto, Canada; Neil Shepherd / Gloucester, UK.

We hope that you will find this service useful!

With kind regards,
Cord Langner (Coordinator of ENGIP)  
Graz / Austria  
cord.langner@medunigraz.at

Alessandro Lugli (Coordinator of ENGIP)  
Bern / Switzerland  
alessandro.lugli@pathology.unibe.ch
BIAL Award 2012

Once again and meeting its mission to support medical research, the BIAL Foundation will held the 15th edition of the BIAL Award.

The BIAL Award 2012 establishes two prizes:

- **BIAL Merit Award in Medical Sciences** (200,000 Euro) - designed to distinguish an intellectual work written specifically for this purpose, on any freely chosen medical topic. Only research of high quality and scientific relevance will be considered.

- **BIAL Award in Clinical Medicine** (100,000 Euro) - designed to distinguish an intellectual work written specifically for this purpose on any freely chosen medical topic on clinical practice. Only work of high quality and relevance will be considered. At least one of the authors must be a native physician of a Portuguese speaking country.

The BIAL Award 2012 Regulation is available at


The link for the BIAL Award Newsletter is the following: