Number 9 – Autumn 2011

European Society of Pathology

Pathology newsletter

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Word from the President Prof. F. Carneiro

Two months after the last European Congress of Pathology held in Helsinki, I am addressing all of you in the quality of President of the European Society of Pathology.

In line with my predecessors, Michael Wells being the last, it is my pleasure to give an update on the ESP activities, aiming to keep members informed about the recent developments and future perspectives of our Society.

The analysis of the evaluation forms of Helsinki Congress is now finished. The results confirm the subjective impression that it was a very successful meeting, attended by more than 2,000 pathologists and accompanying persons. About 83% of the participants expressed an overall satisfaction rated as good/outstanding, and 85% of the participants considered the quality of the presentations as good/outstanding.

The high scientific quality, the warm and friendly atmosphere (members received a VIP treatment) and the social program contributed, altogether, to the success of the Congress. I would like to take this opportunity to express again the gratitude of the Society to the organizers, with a special reference to Veli-Pekka Lehto and Ilmo Leivo (Chair and Secretary, respectively, of the Local Organising Committee) for the excellent job they have done.

The two next European Congresses of Pathology will be held in Prague (September 2012) and in Lisbon (August/September 2013). Local organizers of the Prague Congress are working hard on the scientific program, based on the proposals received from the Working Groups, and the overall frame of the programme will be ready in the near future. I am sure Ales Ryska (Chair of the Local Organising Committee) and his colleagues will organize a great Congress.

A joint Congress of the European Society of Pathology and the International Academy of Pathology (IAP) is being organized for the year 2016. Representatives of both Societies met recently in Cologne (Germany), the ESP delegation being constituted by Michael Wells (Past President), Marco Santucci (Treasurer) and Krasi Serguieva (Administrator). A general agreement on the format of the joint Congress has been reached. Thanks Mike for your crucial role in this process.

A Memorandum of Understanding (MoU) is being prepared between the European Society of Pathology and the European Organization for Research and Treatment of Cancer (EORTC) describing the core principles in pathology that are mutually recognized as being important for clinical studies and identifying key areas for future collaboration.

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News from the ESP Working Groups :

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The ESP officers have been involved in their routine activities, participating in monthly teleconferences and have met face-to-face in Brussels headquarters on November 5th. The quality assurance programme in molecular pathology is moving ahead under the coordination of Han van Krieken, aiming to produce guidelines for a coordinated approach towards quality assurance for molecular testing in pathology. An EScoP course was held in Craiova (Romania) on "Thyroid and Parathyroid Pathology" (September 29 – October 2, 2011).

In the next Newsletter I will update ESP members on the forthcoming activities of the Society. In the meantime, efforts will be concentrated on providing support to the technical and scientific organization of Prague Congress. I am mentioning this point again because the recent evolution from biannual to annual ESP Congresses requires a big effort from the European Society, largely compensated by the opportunity to turn each Congress into an annual scientific forum (and a friendly "fiesta") for European Pathologists.

Fátima Carneiro

Head and Neck Working Group of the ESP.

Head-Neck WG chairs - Alena Skalova 2009, Ilmo Leivo 2005, Isabel Fonseca 2013, Roderick Simpson 2011, Silvana Di Palma 2007, Pieter Slootweg 2003,Antonio Cardesa 1993-01, Nina Gale 2001

The ESP working groups are an increasingly vital part of the Society and European pathology in general. It is an honour and a pleasure for me to follow my illustrious predecessors as chairman of the Head and Neck Working Group, and to have the opportunity in this newsletter to describe what we do.

Our Working Group, which was one of the earliest, was founded in 1993 at the European Congress of Pathology in Innsbruck. The initial driving forces were Antonio Cardesa of Barcelona and Henrik Hellquist then of Örebro, Sweden, who became our first chairman and secretary respectively.

The aim was to coordinate research and teaching activities among European pathologists interested in oral and otorhinolaryngeal pathology, as well as to promote knowledge in our speciality to general surgical pathologists throughout Europe, and ideally to clinicians as well. The anatomical areas to be covered were to include the oral cavity and salivary glands, upper aerodigestive tract and ear, together with the bone and soft tissues of the head and neck. Unlike the practice in North America, we decided largely to exclude diseases of the thyroid gland, which fell more into the remit of endocrine pathologists and their own separate working group.

I believe we have been highly successful in our aims: there have been major contributions at all subsequent biennial European congresses, as well as the six intercontinental and inter-congresses. These activities have comprised slide seminars and symposia/short courses, with a video masterclass at the recent Helsinki Congress.

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In addition, we held a day and a half pre-meeting with North American colleagues in Ljubljana in 2003, repeated at subsequent congresses, also including pathologists from Asia and elsewhere.

Initially in Berlin in 2001 and again more recently in Krakow and Helsinki, we have had joint sessions with the breast Working Group, particularly to cover salivary-like tumours of the breast and vice-versa, a subject that has long fascinated those working in both fields. In Prague in 2012, we are planning a similar joint session with the haematopathologists, to be followed by cooperation with other Working Groups at future congresses.

Since 1995, the Head and Neck Working Group has organised 4 day courses for the European School of Pathology (EScoP) in Torino (twice), Krakow, Ankara and Zagreb, as well as at EScoP sponsored courses in Ioannina and Belgrade. These have mainly (but by no means, exclusively) been for younger pathologists to receive a practical microscope-based grounding and update in surgical pathology of our subspeciality. We think they have been successful, and some attendees have subsequently joined our group and presented at congresses.

Members of the Working Group have published extensively in all major journals – see our annual reports on the website. Many of these have been collaborative inter-institutional projects, for example two recently described salivary neoplasms, mammary analogue secretory carcinoma (MASC) and cribriform adenocarcinoma of the tongue and other minor salivary glands (CATS). Through contacts made partly as a result of the Working Group, we have been able to pool our experience allowing a much larger series of cases than would have been otherwise. Similarly, the classification of pre-neoplastic laryngeal lesions originally developed by Nina Gale (a past chairman of the Working Group) has now been validated by a larger group of European pathologists, and was accepted by the WHO classification as one of its approved schemes.

We are also proud to have produced a textbook, “Pathology of the Head and Neck”, edited by Antonio Cardesa and Pieter Slootweg, to which many of us contributed chapters or sections. This was part of the long-established Remmele series of pathology textbooks and was published by Springer of Berlin in 2006, initially in English and subsequently translated into German. A second edition has just recently been commissioned.

By establishing a worldwide profile, we are the first port of call for those wishing a European contribution to head and neck pathology. Thus, we have been able to make substantial contributions to international congresses, such as those of the IAP, and we were very well represented in the 2005 WHO fascicle on head and neck pathology. We also have several members on the editorial board of *Head and Neck Pathology* journal.

This is what we have done, but I think our main achievement has been to be a recognisable body on the world map of head and neck pathology.

So far, so good – but we wish to develop even more in the future. We are always open to new members, and we try and involve as many as possible in presenting at congresses, particularly in slide seminars. So if anyone has a particularly instructive case, we try to invite that person to speak at the congresses. Obviously, a good command of the English language is an advantage, but not essential, as our subject is a particularly visual one.

In addition to academic activities, we try to have informal gatherings at congresses, often with a common dinner.

So for anyone interested in head and neck pathology, please contact the chairman (roderick.simpson@doctors.org.uk) or the secretary (franchi@unifi.it), and it will be our pleasure to welcome any member of the ESP to our group.

Roderick HW Simpson, Exeter, UK; chairman 2011-13.

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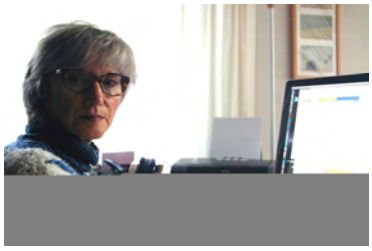
The Pathologist

Interview with Prof. F. Carneiro by Prof. M. Marichal

Prof. F. Carneiro



Prof. M. Marichal

In this column, we interview "special" ESP members: pathologists, young or old, who have something interesting to say, at least in the mind of the interviewer...

After Prof. Fatima Carneiro was elected president of the ESP, we were sure that our readers would want to know this great lady better, and asked and got our interview.

Prof. Fatima Carneiro was born in December 1954, in Sá da Bandeira, a small city in the South of Angola, by that time a Portuguese colony in West Africa. She studied in Angola, S. Tomé & Príncipe (small islands in the Atlantic ocean at the Equator line) and in Porto (in the North of Portugal). She lives in Porto since 1975 and got her MD at the Faculty of Medicine of the University of Porto. In 1989, Prof. Carneiro helped to create the Institute of Molecular Pathology and Immunology of the University of Porto (IPATIMUP), where she is now a Senior Researcher. Dr. Carneiro is also full Professor at the Faculty of Medicine, chairs the Discipline of Systemic Pathology – Oncological Pathology, and is head of the Department of Pathology of the University Medical Centre S. João, all in Porto. She is married to Alfredo Andrade and has two children, João and Marta.

Dr. Carneiro is a world authority on gastrointestinal pathology and has a special scientific and professional interest in (sporadic and hereditary) gastric cancer and its precursor lesions.

She was elected president of the ESP at the Helsinki Congress, in September 2011.

MM: As the head of a Department you are very much involved in diagnostic pathology, but you also find the time to teach, to perform world-class research and you have a close- knit family to care for. Since September you are the new president of the ESP. Women are generally good at multitasking, but this is more than just doing a few things at the same time. What is your secret?

FC: I guess it can be summarized in few words: having a marvellous family and feeling a strong professional motivation.

MM: Doing a job one loves is of course a big help. Have you always wanted to become a doctor and a pathologist?

FC: Becoming a medical doctor has been a dream since adolescence. At the end of the medical course, during which I had a teaching experience as monitor of Cell Biology, I was not sure about the specialty I would join. Along the general internship I had a clinical training experience that showed me the challenges of clinical activity. During that period I was also involved in the teaching of General Pathology at the Medical Faculty of the University of Porto. I thought that Paediatrics was an attractive specialty but soon I learned that I might lack the appropriate skills for becoming a clinical physician (I never learned to keep enough emotional distance from the patients' problems). The time arrived for a decision. By then, on the basis of my training during the medical course, teaching experiences and clinical activity, I knew that, whatever I would choose, it should give me the opportunity to put together teaching and research activity guided by clinical problems. All together, these "ambitions" led me to Pathology as the specialty that would allow me to practice in these three fields. The choice was clear, the experience most gratifying. Looking back, I think it was the right one.

MM: You were raised in Africa. Did this influence your life and your career?

FC: Being raised in Africa, where I spent childhood, adolescence and early adulthood, was the most delightful experience of my life. Growing up in an atmosphere of responsibility, freedom, and recognition of merit, I learned that success relies mostly on work. My family moved quite a lot among different places in Africa, with several intervening stays in "continental" Portugal, giving me the opportunity to face different challenges, to adapt to different environments, to create the feeling of "citizen of the world". Not everything was perfect, however. We experienced one year of civil war in Luanda (capital of Angola), after the democratic revolution in Portugal (1974). The day (June 5th, 1975) the University Hospital in Luanda was bombed (I was there for an exam in Pharmacology) showed that there are limits you cannot overcome. On that dreadful day my family decided to come back to Portugal and begin a new life. We left behind belongings, but we brought an experience of life that is the most valuable treasure one can have. I was not in Angola on the Independence Day, in November 1975, and I feel very sorry for that. All this gave me a kind of survivor resistance and the ability to face life with realism and the belief that one can always find renewed energy to build the future.

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MM: Africa has been very important during the first part of your life. Now you have your career in Porto and your family. Are any of your children following in your footsteps, career wise?

FC: My daughter, Marta, is a MD, now at the stage of choosing the specialty. She is very keen on clinical activity and Pathology is not in her plans. My son, João, followed a different path, after his father, in the engineering field. Both feel that an overcommitted professional life (as mine) is not what they want for them (wise, they are…).

MM: After Niki Agnantis, from Greece, we have now a second woman president, also from a Southern European Country; do you think this will make a difference in strategy, or management, compared to our two former presidents, who were male, from Northern Europe and approached the presidency more like managers do a company?

FC: I understand what you mean, but I am afraid that my experience of life gave me a kind of masculine ("go-for-it") approach to problems and challenges, in a professional way (maybe with a warmer, more feminine flavour). Let's see how efficient it will be. Anyhow, there is no way to avoid a management approach, though not in the sense of a company, since the deliverables of ESP activity are not "goods" but, otherwise, advances in science, achievements in basic and advanced education, and good quality diagnostic services for the benefit of patients.

MM: If management wise you will continue on the "élan" created by our former presidents, I am sure that you must have personal hopes and plans for the Society, other than applying a more feminine touch. Can you reveal some of them?

FC: Becoming the President of the European Society of Pathology is probably the most demanding challenge in my professional career. For the period of my Presidency, I decided to focus on the following areas − a kind of action plan for the next two years:

- Reinforcement of the role of ESP in the field of Education in Pathology**,** with the development of e-learning initiatives and maintenance/expansion of courses, for instance in the frame of European School of Pathology (EScoP). Along this line, the integration of the European Association of Pathology Chairs and Program Directors (EAPCP) in the European Society of Pathology will be strongly supported, aiming to consolidate the tools developed in the frame of EAPCP (such as Progress Tests at European level) for future harmonization of graduate education in Pathology.

- Reinforcement of the internationalization, with the establishment of solid links with International Organizations and Societies, namely IAP (International Academy of Pathology) and EORTC (European Organization for the Research and Treatment of Cancer). These actions are already on their way, led by Prof. M. Wells and F. Bosman, respectively, encompassing the ESP/IAP effort to organize a joint meeting and the initiatives for the development of a fruitful collaboration between ESP and EORTC.

- Reinforcement of the links with the National Societies of Pathology; in this setting, I think the collective membership may play a role, creating the basis for the ESP to act as a federation of the National Societies of Pathology.

MM: In your opinion, what will be the biggest challenges for the ESP and how do you plan to cope with them?

FC: Pathology is facing challenges that should be considered as opportunities. I think ESP will help to bridge the gap between the academic (research-driven) and the service-oriented pathology, if one is able to use appropriately the developments in several new fields, which are epitomized by molecular pathology. The Pathologist of the future should be able to understand the mechanisms of disease(s) and to translate new knowledge to patients' care. That is a question of education and learning, envisioning Pathology both as an integrative discipline and as a profession. I hope that the action plan I summarized above will help to cope with the current and future challenges.

MM: Thank you Fatima; I wish you all the luck with your presidency and of course, with the rest of your career and your family.

Prof. Mia Marichal

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Analecta Medica

Dr. Loukas Kaklamanis

1) Clinical Effect of Point Mutations in Myelodysplastic Syndromes

Rafael Bejar, M.D., Ph.D., Kristen Stevenson, M.S., Omar Abdel-Wahab, M.D., Naomi Galili, Ph.D., Björn Nilsson, M.D., Ph.D., Guillermo Garcia-Manero, M.D., Hagop Kantarjian, M.D., Azra Raza, M.D., Ross L. Levine, M.D., Donna Neuberg, Sc.D., and Benjamin L. Ebert, M.D., Ph.D.

N Engl J Med 2011; 364:2496-2506

BACKGROUND

Myelodysplastic syndromes are clinically heterogeneous disorders characterized by clonal hematopoiesis, impaired differentiation, peripheral-blood cytopenias, and a risk of progression to acute myeloid leukemia. Somatic mutations may influence the clinical phenotype but are not included in current prognostic scoring systems.

METHODS

We used a combination of genomic approaches, including next-generation sequencing and mass spectrometry–based genotyping, to identify mutations in samples of bone marrow aspirate from 439 patients with myelodysplastic syndromes. We then examined whether the mutation status for each gene was associated with clinical variables, including specific cytopenias, the proportion of blasts, and overall survival.

RESULTS

We identified somatic mutations in 18 genes, including two, *ETV6* and *GNAS,* that have not been reported to be mutated in patients with myelodysplastic syndromes. A total of 51% of all patients had at least one point mutation, including 52% of the patients with normal cytogenetics. Mutations in *RUNX1, TP53,* and *NRAS* were most strongly associated with severe thrombocytopenia (P<0.001 for all comparisons) and an increased proportion of bone marrow blasts (P<0.006 for all comparisons).

In a multivariable Cox regression model, the presence of mutations in five genes retained independent prognostic significance: *TP53* (hazard ratio for death from any cause, 2.48; 95% confidence interval [CI], 1.60 to 3.84), *EZH2* (hazard ratio, 2.13; 95% CI, 1.36 to 3.33), *ETV6* (hazard ratio, 2.04; 95% CI, 1.08 to 3.86), *RUNX1* (hazard ratio, 1.47; 95% CI, 1.01 to 2.15), and *ASXL1* (hazard ratio, 1.38; 95% CI, 1.00 to 1.89).

CONCLUSIONS

Somatic point mutations are common in myelodysplastic syndromes and are associated with specific clinical features. Mutations in *TP53, EZH2, ETV6, RUNX1,* and *ASXL1* are predictors of poor overall survival in patients with myelodysplastic syndromes, independently of established risk factors. (Funded by the National Institutes of Health and others.)

2) Regulation of cancer cell metabolism

Rob A. Cairns[1,2], Isaac S. Harris[1,2] & Tak W. Mak[1]

Nature Reviews Cancer *11,* 85-95 (February 2011)

Abstract

Interest in the topic of tumour metabolism has waxed and waned over the past century of cancer research. The early observations of Warburg and his contemporaries established that there are fundamental differences in the central metabolic pathways operating in malignant tissue. However, the initial hypotheses that were based on these observations proved inadequate to explain tumorigenesis, and the oncogene revolution pushed tumour metabolism to the margins of cancer research. In recent years, interest has been renewed as it has become clear that many of the signalling pathways that are affected by genetic mutations and the tumour microenvironment have a profound effect on core metabolism, making this topic once again one of the most intense areas of research in cancer biology.

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3) Genomic evidence of pre-invasive clonal expansion, dispersal and progression in bronchial dysplasia

Frank McCaughan[1,], Christodoulos P Pipinikas[2], Sam M Janes[2], P Jeremy George[2,3], Pamela H Rabbitts[4], Paul H Dear[1]*

The Journal of Pathology Vol. 224, Issue 2, pages 153–159, June 2011

Abstract

The term 'field cancerization' is used to describe an epithelial surface that has a propensity to develop cancerous lesions, and in the case of the aerodigestive tract this is often as a result of chronic exposure to carcinogens in cigarette smoke 1, 2. The clinical endpoint is the development of multiple tumours, either simultaneously or sequentially in the same epithelial surface. The mechanisms underlying this process remain unclear; one possible explanation is that the epithelium is colonized by a clonal population of cells that are at increased risk of progression to cancer. We now address this possibility in a short case series, using individual genomic events as molecular biomarkers of clonality. In squamous lung cancer the most common genomic aberration is 3q amplification.

We use a digital PCR technique to assess the clonal relationships between multiple biopsies in a longitudinal bronchoscopic study, using amplicon boundaries as markers of clonality. We demonstrate that clonality can readily be defined by these analyses and confirm that field cancerization occurs at a pre-invasive stage and that pre-invasive lesions and subsequent cancers are clonally related. We show that while the amplicon boundaries can be shared between different biopsies, the degree of 3q amplification and the internal structure of the 3q amplicon varies from lesion to lesion. Finally, in this small cohort, the degree of 3q amplification corresponds to clinical progression.

4) Objective assessment of lymphatic and blood vascular invasion in lymph node-negative breast carcinoma: findings from a large case series with long-term follow-up†

Rabab AA Mohammed[1,2,4,], Stewart G Martin[1], Ali M Mahmmod[1], R. Douglas Macmillan[3], Andrew R Green[2], Emma C Paish[2], Ian O Ellis[2]*

The Journal of Pathology Vol.223, Issue 3, pages 358–365, Febr. 2011

Abstract

In a previous study on a small series of breast cancers, we developed objective methods for the assessment of vascular invasion (VI), using immunohistochemical staining. We found that VI was predominantly lymphovascular invasion (LVI), with minimal contribution of blood vascular invasion (BVI). The aims of the current study were: (a) to assess the frequency, extent and prognostic role of LVI and BVI in a large, well-characterized series of LN-negative breast cancers; and (b) to assess the ability of VI to stratify early breast cancer into different prognostic groups. Paraffin-embedded sections from 1005 lymph-node (LN)-negative primary invasive breast cancers were stained for CD34, CD31 and podoplanin/D240 to detect BVI and LVI. VI lesions were assessed and the results were correlated with clinicopathological criteria and survival. VI was detected in 218 (22%); 211/218 (97%) were LVI, while BVI was detected in 7/218 (3%). The frequency of LVIs/section ranged from 1 to 79, with no significant difference between the frequency of LVI and outcome. The presence of LVI was significantly associated with adverse disease-free interval (DFI) and poor overall survival (OS) in both univariate and multivariate analyses.

The results from the study indicated that VI in early stage breast cancer is predominantly LVI and that its objective assessment is a powerful independent prognostic factor. Efforts to detect early metastatic activity, such as diligent pathological examination of sentinel LN biopsies would be complimented by the objective evaluation of VI status of the primary tumour. VI status should be included routinely in breast cancer staging systems.

5) Frequent mutations of *KRAS* in addition to *BRAF* in colorectal serrated adenocarcinoma

Karoliina Stefanius†, Laura Ylitalo†, Anne Tuomisto, Rami Kuivila, Tiina Kantola, Päivi Sirniö, Tuomo J Karttunen, Markus J Mäkinen

Histopathology Volume 58, Issue 5, pages 679–692, April 2011

Abstract

Aims: To define the occurrence of *KRAS* and *BRAF* mutations, microsatellite instability (MSI), and *MGMT* and h*MLH1* methylation and expression in colorectal serrated adenocarcinoma.

Methods and results:*KRAS* codon 12/13 and 59/61 and *BRAF* V600E mutations, MSI, and *MGMT* and h*MLH1* methylation and expression in 42 serrated adenocarcinomas and 17 serrated

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adenocarcinomas and in 27% and 0% of non-serrated CRCs ($P < 0.001$). The *KRAS* c12G→A transition was the predominant type of mutation in serrated adenocarcinomas. Forty-two per cent of *BRAF*-mutated serrated adenocarcinomas showed high-level MSI (MSI-H) ($P = 0.075$), 100% showed h*MLH1* methylation ($P = 0.001$) and 90.9% showed *MGMT* methylation ($P = 0.019$). Fifty-six per cent of serrated adenocarcinomas with microsatellite stability/low-level microsatellite instability harboured *KRAS* mutations. In non-serrated cancers, *KRAS* mutations were not associated with MSI status.

Conclusions: A high combined mutation rate (79–82%) of *KRAS* and *BRAF* in serrated adenomas and adenocarcinomas indicates that mitogen-activated protein kinase activation is a crucial part of the serrated pathway. *BRAF* mutations are specific for serrated adenocarcinoma and identify a subset of serrated adenocarcinomas with gene methylation and a tendency for MSI-H. A high frequency of *KRAS* mutations in serrated adenocarcinomas suggests that a significant proportion of *KRAS*-mutated CRCs originate from serrated precursors, thus challenging the traditional model of Vogelstein.

6) *NT5E* Mutations and Arterial Calcifications

Cynthia St. Hilaire, Ph.D., Shira G. Ziegler, B.A., Thomas C. Markello, M.D., Ph.D., Alfredo Brusco, Ph.D., Catherine Groden, M.S., Fred Gill, M.D., Hannah Carlson-Donohoe, B.A., Robert J. Lederman, M.D., Marcus Y. Chen, M.D., Dan Yang, M.D., Ph.D., Michael P. Siegenthaler, M.D., Carlo Arduino, M.D., Cecilia Mancini, M.Sc., Bernard Freudenthal, M.D., Horia C. Stanescu, M.D., Anselm A. Zdebik, M.D., Ph.D., R. Krishna Chaganti, M.D., Robert L. Nussbaum, M.D., Robert Kleta, M.D., Ph.D., William A. Gahl, M.D., Ph.D., and Manfred Boehm, M.D.

N Engl J Med 2011; 364:432-442February 3, 2011

BACKGROUND

Arterial calcifications are associated with increased cardiovascular risk, but the genetic basis of this association is unclear.

METHODS

We performed clinical, radiographic, and genetic studies in three families with symptomatic arterial calcifications. Single-nucleotide-polymorphism analysis, targeted gene sequencing, quantitative polymerase-chain-reaction assays, Western blotting, enzyme measurements, transduction rescue experiments, and in vitro calcification assays were performed.

RESULTS

We identified nine persons with calcifications of the lower-extremity arteries and hand and foot joint capsules: all five siblings in one family, three siblings in another, and one patient in a third family. Serum calcium, phosphate, and vitamin D levels were normal. Affected members of Family 1 shared a single 22.4-Mb region of homozygosity on chromosome 6 and had a homozygous nonsense mutation (c.662C→A, p.S221X) in *NT5E*, encoding CD73, which converts AMP to adenosine. Affected members of Family 2 had a homozygous missense mutation (c.1073G→A, p.C358Y) in *NT5E*. The proband of Family 3 was a compound heterozygote for c.662C→A and c.1609dupA (p.V537fsX7). All mutations found in the three families result in nonfunctional CD73. Cultured fibroblasts from affected members of Family 1 showed markedly reduced expression of *NT5E* messenger RNA, CD73 protein, and enzyme activity, as well as increased alkaline phosphatase levels and accumulated calcium phosphate crystals. Genetic rescue experiments normalized the CD73 and alkaline phosphatase activity in patients' cells, and adenosine treatment reduced the levels of alkaline phosphatase and calcification.

CONCLUSIONS

We identified mutations in *NT5E* in members of three families with symptomatic arterial and joint calcifications. This gene encodes CD73, which converts AMP to adenosine, supporting a role for this metabolic pathway in inhibiting ectopic tissue calcification.

(Funded by the National Human Genome Research Institute and the National Heart, Lung, and Blood Institute of the National Institutes of Health.)

7) Breast and cervical cancer in 187 countries between 1980 and 2010: a systematic analysis

Mohammad H Forouzanfar MD, Kyle J Foreman MPH ,Allyne M Delossantos BS, Prof Rafael Lozano MD, Prof Alan D Lopez PhD, Prof, Dr Christopher J L Murray MD, Mohsen Naghavi MD

Background

Breast and cervical cancer are important causes of mortality in women aged ≥15 years. We undertook annual age-specific assessments of breast and cervical cancer in 187 countries.

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Methods

We systematically collected cancer registry data on mortality and incidence, vital registration, and verbal autopsy data for the period 1980—2010. We modelled the mortality-to-incidence (MI) ratio using a hierarchical model. Vital registration and verbal autopsy were supplemented with incidence multiplied by the MI ratio to yield a comprehensive database of mortality rates. We used Gaussian process regression to develop estimates of mortality with uncertainty by age, sex, country, and year. We used out-of-sample predictive validity to select the final model. Estimates of incidence with uncertainty were also generated with mortality and MI ratios.

Findings

Global breast cancer incidence increased from 641 000 (95% uncertainty intervals 610 000—750 000) cases in 1980 to 1 643 000 (1 421 000—1 782 000) cases in 2010, an annual rate of increase of 3·1%. Global cervical cancer incidence increased from 378 000 (256 000—489 000) cases per year in 1980 to 454 000 (318 000—620 000) cases per year in 2010—a 0·6% annual rate of increase. Breast cancer killed 425 000 (359 000—453 000) women in 2010, of whom 68 000 (62 000—74 000) were aged 15—49 years in developing countries. Cervical cancer death rates have been decreasing but the disease still killed 200 000 (139 000—276 000) women in 2010, of whom 46 000 (33 000—64 000) were aged 15—49 years in developing countries. We recorded pronounced variation in the trend in breast cancer mortality across regions and countries.

Interpretation

More policy attention is needed to strengthen established health-system responses to reduce breast and cervical cancer, especially in developing countries.

Dr. Loukas Kaklamanis

Tips and Tops- News in Brief

Dr. Loukas Kaklamanis

Trial puts niacin—and cholesterol dogma—in the line of fire

- **Elie Dolgin**

  Nature MedicineVolume:17,756 (2011) 07 July 2011

The balance of 'good' and 'bad' cholesterol noted at routine checkups—and some of the drugs used to tip this balance—might not influence heart risk in the way widely thought.

It's already known that statins, which lower levels of low-density lipoprotein (LDL), do not work for everybody. As such, doctors have long sought to complement these agents that reduce 'bad' cholesterol with medicines such as niacins and fibrates that raise levels of the 'good' stuff—namely, high-density lipoprotein (HDL) cholesterol. New evidence, however, suggests that simply elevating HDL cholesterol levels in the blood does not necessarily translate into clinical benefit for patients.

“It's a beautiful hypothesis that HDL may be cardioprotective, and there are ample preclinical as well as observation data in support of that,” says Sanjay Kaul, a cardiologist at the Cedars-Sinai Medical Center in Los Angeles. “But when we put it to real test, which is the gold-standard randomized clinical trial, none of the treatments have passed muster.”

The most recent failure came in May when the US National Heart, Lung and Blood Institute (NHLBI) prematurely halted the AIM-HIGH study. The 3,400-person trial, which examined high-dose extended-release niacin given together with statin therapy, was cut short after a preliminary data analysis found no additional benefits of the vitamin B–based drug in this patient population. “Maybe we've been too simplistic in thinking that raising HDL any way confers the same benefit as when it happens physiologically, and that's what we're grappling with,” says the NHLBI's Patrice Desvigne-Nickens, a project officer for the trial.

“AIM-HIGH poses the most substantial challenge yet to the HDL cholesterol hypothesis,” says Dan Rader, a cardiologist at the University of Pennsylvania School of Medicine in Philadelphia who was not involved in the study.

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Pathology newsletter

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Michael Davidson, director of preventive cardiology at the University of Chicago and another trial onlooker, adds, “To those of us in the field, we thought it was the right kind of study—the right patient population to test the effect of niacin—and when the trial didn't work, it was both a disappointment and a surprise.”

Biomarker bias

Researchers routinely exaggerate the links between medical conditions and disease-related biomarkers by predominantly citing only those papers that report the strongest associations, according to a study published last month in *JAMA* (**305**, 2200–2210, 2011). Researchers from the University of Ioannina School of Medicine in Greece surveyed 35 highly cited papers with subsequent meta-analyses reporting on the same disease-associated genes, proteins or other biomarkers. For 29 of these pairings, the authors found the corresponding meta-analysis reported a smaller effect estimate than the widely referenced paper.

“Just because something is heavily cited doesn't mean it's necessarily correct,” warns Ian Blair, a biomarker expert at the University of Pennsylvania School of Medicine in Philadelphia.

Nature Medicine (2011) 17,763

TB or not TB

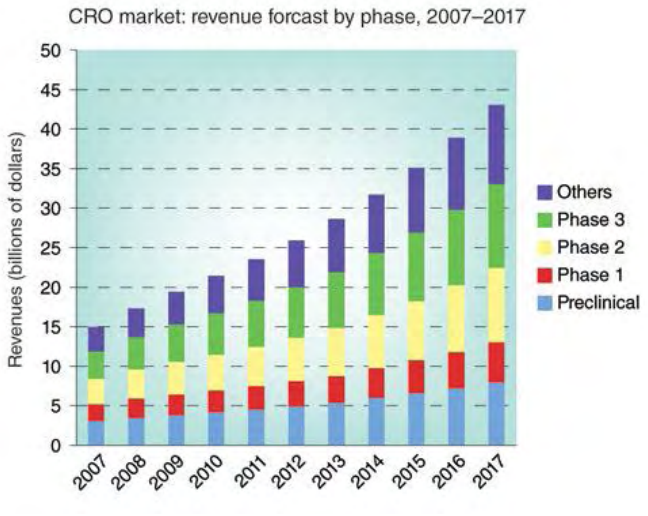
On 20 July, the World Health Organization (WHO) issued an urgent warning against the use of blood tests to detect active tuberculosis. In its first-ever explicit 'negative' policy recommendation, the Geneva-based health body emphasized that sputum smears and lab cultures remain the gold standard for active disease and that most serological assays sold by private clinics throughout the developing world suffer from both low sensitivity and low specificity, leading to high rates of false diagnoses.

“It's a case of inappropriate marketing,” says Mario Raviglione, director of the WHO's Stop TB department. Three weeks later, a WHO-commissioned literature review that analyzed close to 100 studies involving the commercial blood tests reported extremely wide variability in results (*PLoS Med.* **8**, e1001062, 2011).

Research outsourcing on the rise

As big pharmaceutical firms whittle down their in-house research operations, drugmakers are increasingly relying on for-hire service companies to perform the heavy lifting of drug development. In fact, last year about 21 cents of every dollar spent worldwide on drug research and development went to such contract research organizations—and the number is only expected to grow, according to a recent report by the consulting firm Frost and Sullivan.

“In the past, everyone wanted to work for pharmaceutical companies because that was where the money was, but that's not longer the case,” says Wei Garofolo, coordinator of the Toronto-based Global CRO Council, a group of 55 member companies involved in bioanalysis. “CROs are now booming.” See page 1036 for an opinion piece from the head of the Association of Clinical Research Organizations. (Nature Medicine 2011:17,9,1031)



Frost and Sullivan

B-RAF blocker

On 17 August, the FDA approved the first of a new class of skin cancer drugs targeted at a specific mutation found in about half of all people with metastatic melanoma. “The new age of cancer therapeutics has been ushered into melanoma with this drug,” says Levi Garraway, a cancer geneticist at the Dana-Farber Cancer Institute in Boston. The oral small-molecule drug, marketed as Zelboraf (vemurafenib) by Genentech of South San Francisco and Daiichi Sankyo of Japan, works by inhibiting the mutant B-RAF oncoprotein associated with driving tumor growth.

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UK biomedical boost

In the largest ever single cash injection into translational research in Britain, the UK government in August announced five-year funding totaling £800 million ($1.2 billion) to develop partnerships between National Health Service (NHS) hospitals, universities, industry and charities. “This sends out a very positive message and reflects a cultural shift for the NHS, showing that it has a critical role in innovative translational research,” says Mark Downs, chief executive of the London-based Society of Biology. The money, which comes in the shape of 31 awards, will be coordinated by the National Institute of Health Research, the research arm of the NHS.

Lasker luminaries

Two protein-folding pioneers have won 2011 Lasker prizes along with the first ever Chinese awardee. Yale University's Arthur Horwich and the Max Planck Institute of Biochemistry's Franz-Ulrich Hartl took home the Albert Lasker Basic Medical Research Award for uncovering the action of chaperonins, protein complexes that assist the folding of other proteins. This year's Lasker~DeBakey Clinical Medical Research Award went to Youyou Tu of the China Academy of Chinese Medical Sciences for discovering artemisinin, now a staple of malaria therapy, from the leaves of the wormwood plant. And, in an unusual twist, an institution—the US National Institutes of Health Clinical Center—rather than any single person won the Lasker~Bloomberg Public Service Award.

On thirtieth anniversary, calls for HIV cure research intensify

- Lucas Laursen Nature Medicine 2011,17,643

Thirty years ago this month, scientists first reported the existence of AIDS, and in the intervening decades researchers have focused steady efforts on prevention, long-term treatments such as antiretroviral drugs, and patient care. What has fallen in and out of fashion during that time is seeking a 'cure' for HIV. That changed when scientists reported that they had cured one man of the virus through a bone marrow transplant (*Blood* **117**, 2791–2799, 2011). But the circumstances of that 2007 transplant were unique, and researchers say they are uncertain about how to fund additional cure-directed research without cannibalizing other components of the global HIV/AIDS research machine.

“That's the tricky part,” says Bertrand Audoin, executive director of the International AIDS Society (IAS), a Geneva-based HIV research and education association. “Actually, to be honest, I'm glad it's not for me to decide.”

To address the issue, the IAS has invited a working group to its biennial research meeting in Rome this July to hash out ideas about how to include cure research within the existing framework of HIV/AIDS studies. “Our goal after the Rome meeting is to have enough scientific ideas to reach out to new donors,” Audoin says, though they will only ask for pledges this year. Funding requests for specific avenues of cure research will have to wait until the working group releases a more formal scientific strategy at the July 2012 meeting in Washington, DC…..

Dr. Loukas Kaklamanis

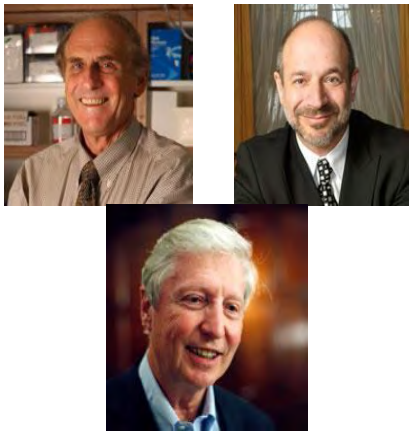
European Society of Pathology

Pathology newsletter

What's new?

Nobel award in Medicine for 2011 goes to Immunology Pioneers

Dr. Loukas Kaklamanis



R.Steinman, B.Beutler, J.Hoffmann

On the 3rd of October the Swedish Acadeny announced the Nobel Prize for Medicine, which was awarded to **Ralph Steinman** from Rockefeller University in New York, **Bruce Beutler** from the Scripps Research Institite in La Jolla, California and **Jules Hoffmann** from the French National Centre for Scientific Recearch (CNRS) in Strasbourg.

The award was overshadowed by sadness when it was realised, that R.Steinman, had died on Friday the 30th of September. The Nobel committee was not aware of his berievement but confirmed that the award still stands. Steinman suffering from pancreatic cancer, was being treated with immunotherapy which was based on his original discovery. Steinman was the first to discover a type of immune cell, known as a dendritic cell, that is of paramount importance to the 'adaptive' immune system. It identifies which pathogen has invaded the body in order to trigger a targeted response. Hoffmann and Beutler identified the molecular "bells" that first sound the alarm by recognizing features shared by numerous pathogens.

Ewen Callaway reports in Nature,478,13 (2011)

" Steinman's efforts to understand the immune system began in the early 1970s, when he joined the laboratory of Zanvil Cohn at Rockefeller as a postdoc. Cohn's group was studying an immune cell called the macrophage, which engulfs pathogens and other debris. Most researchers thought that macrophages then alerted adaptive immune cells called T cells to the presence of a specific pathogen.

Once activated, T cells multiply and combat infection, either by killing pathogen-infected cells or by steering another type of immune cell, the B cell, to produce pathogen-blocking antibodies.

In Cohn's lab, Steinman identified another type of immune cell, which he named the dendritic cell because of its long, tree-like arms (R. M. Steinman and Z. A. Cohn *J. Exp. Med.* **137,** 1142–1162; 1973). Cohn and Steinman showed that these cells are much more important than macrophages in activating T cells.

At first, dendritic cells "were a minor cell and everybody was loath to accept them", recalls Siamon Gordon, an immunologist at the University of Oxford, UK, who worked with Cohn and Steinman. "It was a bit like having two Popes — it was the dendritic cells versus the macrophages." Steinman continued doggedly collecting data, and eventually won over his critics.

Two decades after the discovery of dendritic cells' crucial role, a team led by Hoffmann was investigating why fruitflies, which lack an adaptive immune system, don't succumb to fungal infection. In 1996, they reported that the *Toll* gene, previously linked to embryo development, was also important for battling infections (B. Lemaitre *et al. Cell* **86,** 973–983; 1996). Flies with mutations in *Toll* died when exposed to bacteria or fungi.

At around the same time, a team led by Beutler, then at the University of Texas Southwestern Medical Center in Dallas, had spent six years looking for an immune-system gene in mice that produces a protein to recognize lipopolysaccharide (LPS), a molecule produced by certain bacteria that can cause septic shock. "We were obsessed," says Alexander Poltorak, an immunologist now at Tufts University in Boston, Massachusetts, who worked on the project. "We always thought we would find the gene tomorrow."

The team eventually found its LPS-sensing gene, and it looked remarkably like Hoffmann's *Toll* (A. Poltorak *et. al. Science* **282,** 2085–2088; 1998). Linking the two findings paved the way for the discovery of other Toll-like receptors that sense molecules made by pathogens but not their hosts, and form a critical part of the innate immune system.

The discoveries of dendritic cells and innate immune receptors have already had an impact on medicine. Vaccines are typically administered with an adjuvant, such as a metal, to prompt a rapid immune response. Drug companies such as GlaxoSmithKline are now developing adjuvants that activate Toll-like receptors.

"By doing this we are mimicking what actually happens during an infection without having an infection," says Vincenzo Cerundolo, associate director of Meanwhile, Provenge (made by the biotechnology company Dendreon of Seattle, Washington), the only cellular immune therapy against cancer to be approved by the US Food and Drug Administration, exploits dendritic cells that recognize a molecule produced by prostate tumours. Culturing and reinjecting the cells back into the patient fortifies the immune response against the tumour. "The reason why the field has progressed so much and is now in the clinic is because we understand how to activate the immune system," says Cerundolo. "

Dr. Loukas Kaklamanis

European Society of Pathology
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The 28th postgraduate IUCP held in Ioannina May 31st and June 3rd, 2011

Prof. Niki Agnantis

Prof. N. Agnantis in front

Prof. M. Wells

The 28th postgraduate IUCP on GYN Pathology-Oncology: Uterus (Part I) and Ovaries (Part II) was held in Ioannina, Hellas, between May 31st and June 3rd, 2011.

The Course has been very successful, according to the evaluation of the questionnaire, and the 31 students along with the 20 Faculty members enjoyed this fruitful Scientific Event.
Since the Course belongs to the third series of IUCP (the first one was held on May 1996 and the second on May 2004), we honored the members of the Faculty who contributed immensely to the success of the 1st and the 2nd Course, which were dedicated exclusively to GYN Pathology-Oncology. Our Honorary Guests were the following on alphabetical order: Arvaniti H., Bairaktari E., Karaiosifidou H., Paraskevaidis E., Pavlaki K., Sivridis E., Vakiani M. and Wells M.

Besides Science, everybody enjoyed the every-evening social events and especially the farewell dinner, which was held at the gorgeous “Hotel du Lac” with music and dance until early morning!!

The 28th IUCP belongs to history and now I am very pleased to announce to the ESP members the forthcoming 29th IUCP on Liver Pathology-Oncology, which will be held in Ioannina, Hotel “Palladion”, between the 24th and the 27th of April, 2012. For further information our ESP members can visit the IUCP website (http://www.**iucp**.gr) after January 20th, 2012.

Emeritus Professor Niki J. Agnantis
Director and Co-ordinator of IUCP

European Society of Pathology

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"IN ILLO TEMPORE"

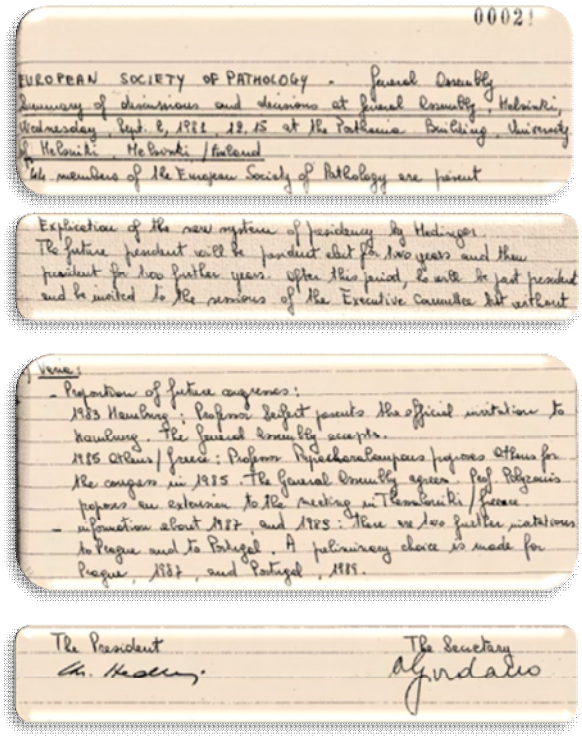
We have just held the European Congress of Pathology (ECP) in Helsinki (September 2011) and we are preparing the forthcoming Congresses for Prague (2012) and Lisbon (2013).

Curiously, the previous ECPs held in Prague (1987) and in Porto, Portugal (1989) – at that time the Congress were biannual – were decided in the General Assembly held In Helsinki, in September 1981, during the ECP (see below).

The 30-year interval between Helsinki ECP has led Veli-Pekka to "honour" the pathologists who visit Helsinki every thirty years (some of us even got a gift at the Congress Dinner).

So that young members can have an idea how the European Society of Pathology (ESP) was in the early eighties we decided to transcribe part of the minutes of the 1981 General Assembly.

Fátima Carneiro and Manuel Sobrinho-Simões



0002!

EUROPEAN SOCIETY OF PATHOLOGY - General Assembly
Summary of discussions and decisions at General Assembly, Helsinki, Wednesday, Sept. 2, 1981, 12.15 at the Porthania Building, University of Helsinki, Helsinki/Finland
44 members of the European Society of Pathology are present

Explication of the new system of presidency by Hedinger.
The future president will be president elect for two years and then president for two further years. After this period, he will be past president and be invited to the sessions of the Executive Committee but without being an official member of it.

Varia:
- Proposition of future congresses:
1983 Hamburg: Professor Seifert presents the official invitation to Hamburg. The General Assembly accepts.
1985 Athens/Greece: Professor Papachristophoros proposes Athens for the congress in 1985. The General Assembly agrees. Prof. Papaioannou proposes an extension to the meeting in Thessaloniki/Greece.
- information about 1987, and 1985: there are two further invitations to Prague and to Portugal. A preliminary choice is made for Prague, 1987, and Portugal, 1985.

The President Chr. Hedinger. The Secretary A. Giordano

Minutes of General Assembly of the EUROPEAN SOCIETY OF PATHOLOGY

Summary of discussions and decisions at General Assembly, Helsinki, Wednesday, Sept 2, 1981, 12:15 at Porthania Building, University of Helsinki, Helsinki/Finland
44 members of the European Society of Pathology are present

1. Report of the President
2. Report of the Secretary
3. Report of the Treasurer:

Approbation of accounts of the past financial year and budget of the next financial term. Assets Aug 1, 1981: hfl. 36.822,97. Election of Betz, Liège and Dustin, Brussels, as financial accountants.

4. New memberships: 69 applications. Accepted
5. Proposal of modification of article 9 of the statutes
   (2/3 majority of attending members):
   a) Extension of the validation of the Executive Committee from 3 to 4 years.

…

The modification of article 9 is accepted by all 44 members present.
No opposition, no abstention from voting.

…

   e) The extension of the validity of the present Council from 3 to 4 years is accepted. No opposition.

Explication of the new system of presidency by Hedinger.

The future president will be president elect for two years and then president for two further years. After this period, he will be past president and be invited to the sessions of the Executive Committee but without being an official member of it. To introduce this system, resignation of Hedinger as president in favour of Ferluga, who will be president from 1981 to 1983, and designation of Johannessen as president elect from 1981 to 1983 and as president from 1983 to 1985.

…

8. Varia:
   - Information about 1987 and 1989: there are two further invitations to Prague and to Portugal. A preliminary choice is made for Prague, 1987 and Portugal, 1989.

…

The President	The Secretary
Chr. Hedinger	A. Giordano

Announcements:

Berzelius symposium 86
***The Fifth* Arkadi M. Rywlin**
International Pathology Slide Seminar
Symposium in Anatomic Pathology
14–16 June 2012 in Stockholm · Sweden

Course Directors
Saul Suster, M.D. and Göran Elmberger, M.D., PhD

More information Symposium website:

http://www.sls.se/Forskning--utbildning/Berzeliussymposier/Anatomic-Pathology/

Symposium secretariat: annie.melin@sls.se · phone +46 8 440 88 78

1st EDINBURGH HAEMATOPATHOLOGY TUTORIAL:
"INTEGRATING TECHNOLOGICAL ADVANCES INTO DIAGNOSTIC PRACTICE"
JUNE 7-8, 2012
at
The Roxburghe Hotel, Edinburgh
offered by the
The University of Edinburgh & NHS Lothian University Hospitals Trust

Course Directors
John Goodlad, MD, FRCPath, Consultant Pathologist, Honorary Senior Lecturer

Thomas Brenn, MD, PhD, FRCPath
Consultant Dermatopathologist
Honorary Senior Lecturer

TUITION: £375.00 (£350 for Pathologists in training)

CONTACT: John Goodlad, Pathology, Western General Hospital, Crewe Road, Edinburgh, EH4 2XU, UK;
Tel: +441315371969; Fax: +445373618; Email: john.goodlad@nhs.net

ONLINE REGISTRATION: available from early October via our website at www.edinburgh-haematopathology.org.uk
or directly at

https://www.epay.ed.ac.uk/browse/extra_info.asp?compid=1&catid=75&modid=2&prodid=584&deptid=75&prodvarid=0

European Society of Pathology

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Announcements:

INTERNATIONAL PATHOLOGY COURSE ALONG THE HOLY LAND

DATE: October 6-13, 2013

LOCATIONS: Amman, Petra, Jerusalem, Ramallah

COURSE DIRECTORS:
- J.Rosai, MD (Italy)
- J.Forteza, MD (Spain)
- R.Young, MD (USA)

COURSE CO-DIRECTORS:
- J.Antunez, MD (Spain)
- L.Kahn, MD (USA)

FACULTY:
- J.Antunez, MD (Spain)
- J.Chan, MD (Hong Kong)
- J.Epstein, MD (USA)
- F.Facchetti, MD (Italy)
- J.Ferry, MD (USA)
- J.Forteza, MD (Spain)
- L.Kahn, MD (USA)
- R.Kurman, MD (USA)
- E.Montgomery, MD (USA)
- J.Rosai, MD (Italy)
- M.Sobrinho, MD (Portugal)
- R.Young, MD (USA)

SUBJECTS: Gynecologic pathology, Urogenital pathology, Endocrine pathology, Bone and Soft Tissue pathology, Hematopathology, Special techniques in Surgical Pathology

EDINBURGH PATHOLOGY

3rd EDINBURGH DERMATOPATHOLOGY TUTORIAL:
"PRACTICAL APPROACH TO THE DIAGNOSIS OF SKIN ADNEXAL TUMOURS"
JUNE 14-15, 2012
at the
The Roxburghe Hotel, Edinburgh, UK

offered by the
The University of Edinburgh & NHS Lothian University Hospitals Trust

Course Directors

Thomas Brenn, MD, PhD, FRCPath
Consultant Dermatopathologist
Honorary Senior Lecturer

John Goodlad, MD, FRCPath, Consultant Pathologist, Honorary Senior Lecturer

TUITION: £375.00 (£350.00 for members of the BSD)

CONTACT: Thomas Brenn, Pathology, Western General Hospital, Crewe Road, Edinburgh, EH4 2XU, UK; Tel: +44 131 537 1957; Fax: +44 131 537 3618; Email: t_brenn@yahoo.com

ONLINE REGISTRATION: Available from mid September on our website at:

www.edinburgh-dermatopathology.org.uk

European Society of Pathology

Pathology newsletter

Announcements:

Follow the ESP on the Facebook:

facebook http://www.facebook.com/pages/ESP-European-Society-of-Pathology/162320570501831?sk=info

www.esp-congress.org

Dear Colleagues,

From November 18-30 we offer the 6th EUROPALS pathology test for trainees (and pathologists). The test consists of 89 questions, partly straight multiple choice questions, partly still image based and partly virtual slide based, and extended matching questions. The chosen level is that of a trainee at the end of a residency programme. The test comprises of questions with a purely diagnostic orientation, molecular pathology test items and mechanism of disease oriented questions. After finishing the test you will immediately receive a test score. The test is purely formative: a tool for self assessment. The results are kept anonymously.

You can take the test by logging on to the website:

www.pathxl.co.uk/europals with your own password. If you have no login/password yet you can obtain one on the website.

The test takes approximately 2 hours. The best way to do the test is in one run but you can do the test in parts if you do not have time to do it in one effort.

The test is offered by the European Association of Pathology Chairs & Program Directors (EAPCP).

With best regards,

Fred T Bosman

Past- President EAPCP

A new **Medical School in Nepal** plans to set up a decent department of pathology. They have good young pathologists but there is a lack of equipment. Their request is for used, abandoned but in good working condition pieces of equipment:

1. ***rotating microtomes***
2. ***embedding machines (histokinettes)***
3. ***embedding station (paraffin dispenser and cold plate)***
4. ***staining machine***

The funds to get this by airfreight to Kathmandu are available.

Transportation to a central point (either Rotterdam or Lausanne) will be taken care of.

Please contact Prof. Fred Bosman if you wish to become part of this initiative: Fred.Bosman@chuv.ch

European Society of Pathology

Pathology newsletter

Announcements:

The European Society of Pathology is happy to announce a further benefit of the membership as from 2011: Members can purchase an annual subscription to the online version of the Journal of Hematopathology for **EUR 10.00 or for EUR 38.00** members can subscribe to both the print and online version. This Journal is the only specialized one for pathologists with an interest in Hematopathology.

You can find further information on the Journal at: www.springer.com/medicine/pathology/journal/12308.

The Journal was open access and online only in the first two years of its publication. Now, it is available both in print and online.

To apply for this service you can use the online member renewal or check the box on the letter you have received recently.

EuroClonality

Workshop
Nijmegen, the Netherlands, February 2012

www.EuroClonality.org

EuroClonality Board

Dr. Liz Hodges, Chair
Prof. Jacques J.M. van Dongen, past-chair
Dr. Ton Langerak, Treasurer
Dr. Monika Brüggemann, Secretary
Dr. Patricia Groenen, member
Dr. Frederic Davi, member
Dr. Jose Cabeçadas, member

Agenda

Educational Workshop

EuroClonality/BIOMED-2:

"Clonality assessment in Pathology"

February 2012

Nijmegen, the Netherlands