Under the guidance of Prof. Helmut Popper (new Chairperson of the Education Committee) and continuous support of Prof. Fred Bosman, the Education Committee is undertaking major steps in order to create a dynamic and attractive education portal, being expected that it will be opened to the ESP members along 2012.

In February, a meeting of the Executive Committee was held at the ESP Brussels headquarters, during which fruitful discussions led, among other decisions, to the approval of financial support for the activities of the Working Groups and the National Societies.

For the Working Groups, a sum of €1,500 will be made available to the Chairpersons of all Working Groups, to be used at their discretion (e.g. to support the travel costs of an overseas speaker or to provide a dinner for invited speakers at a congress). The following conditions should apply: i) An annual activity report should be provided to the Executive Committee; ii) The Chairperson or Secretary of each working group should provide an up to date list of members; iii) A proper invoice must be submitted for reimbursement.

For the National Societies, financial support may be provided to those National Societies whose collective membership comprises at least 30% of their clinically active pathologists. In this setting, only projects/proposals addressing the following general goals will be accepted: i) In support of educational activities and academic development of National Societies (e.g. offering high-level courses through the ESP, or sending ESP member/supported speakers to courses of National Societies with collective membership); ii) In support of initiatives contributing to integration of European Pathology. The annual total ESP budget for support of National Societies will be €100,000 and the maximum annual support for any National Society will be €10,000.

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Continues from p.1

A Memorandum of Understanding (MoU) was signed between the ESP 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 the key areas for future collaboration.

Proposals for collaboration with several International Organizations and Societies were approved, namely with the United European Gastroenterology Federation (UEGF), the European Society for Medical Oncology (ESMO) and the European Crohn’s and Colitis Organization (ECCO). In the frame of these collaborations, joint meetings will be organized between the ESP and the aforementioned Societies (UEGF and ESMO), and the ESP will support a consensus meeting (ESP/ECCO) to establish standards for the diagnosis and pathological procedures in inflammatory bowel diseases and other colitis.

The arrangements for the Prague Congress (September 8-12, 2012) are quite advanced due to the enthusiastic activity of Ales Ryska (Chairperson of the Local Organising Committee) and his colleagues of the Local and Scientific Committees. About 50 bursaries were attributed to residents and trainees. The Scientific programme is almost ready and its high quality reflects the active contributions of the Working Groups and local organizers. The social programme is also expected to be very good. You will, for instance, be given the opportunity to enjoy Mozart’s opera Don Giovanni during an exclusive ECP performance at the Estates Theatre. Registrations for the Congress are now open (fees for the ESP members are substantially lower than for non-members).

The ESP invites all of you to visit the Prague Congress website (www.esp-congress.org) and register before the deadline for early registration (April 2, 2012).

Fátima Carneiro

Dear fellow pathologists,

Members of the European Society of Pathology,

As you must certainly already know, Prague will be hosting the 24th European Congress of Pathology in September. It is exactly 25 years, since the largest gathering of pathologists in Europe took place in our “City of a hundred spires”. Much has changed over these 25 years, which represent the difference between one generation and another. The “Iron Curtain” has vanished and Prague has become one of the most frequently visited cities in Europe. While strolling in its historical centre, you will meet people from all over the world. Not only has the spirit of the city changed, but the people too - English as the “lingua franca” can be used virtually anywhere and everyone welcomes tourists. I have to admit, that I regret not being able to be a tourist in Prague myself.

The last quarter of a century has seen enormous changes in pathology; we have become equal partners of our clinical colleagues and essential members of the multidisciplinary team. Our diagnoses are now cornerstones of clinical decision-making. We are facing a boom in new and highly sophisticated technologies and we must be prepared to adapt to sometimes completely new approaches. Hand in hand with the importance of our diagnoses is the growing issue of quality assurance of our work. It is likely that soon the practice of pathology will not be, like it was even 10 years ago.

With the boom in new technology and continuing unanswered questions, the importance of sharing information, experience and knowledge has never been more important. Our congresses play an essential role in this regard and this is one of the reasons, why the ESP decided to change from biennial to annual congresses.
So, we are approaching the forthcoming European congress, which will begin in less than 6 months’ time. I can assure you that both the scientific committee and the Local organizing committee are doing their best to make this meeting as successful as possible. We have confirmed speakers from numerous countries and the topics which are to be discussed look very enticing. However, we know that it is not possible to live by science alone and a good congress must also offer something beyond its basic role. Therefore, we have prepared a very tasteful social programme - you will have the chance to visit a dedicated performance of Mozart’s opera Don Giovanni, presented in the very same Estate theatre, where it had its world premiere directed by the Maestro himself. The congress party on the last evening will be in one of Prague’s medieval jewels, the gothic St. Agnes monastery; can you even imagine missing it? Nevertheless, despite all the efforts of the organizers, the congress can only be successful with satisfied participants. Thus I would like to invite you from the depth of my heart to come to Prague and to help us to make the congress a real success!

I am looking forward to welcoming you in Prague,

Yours sincerely,
Ales Ryska
Chair of the Local Organizing committee

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**News from the FADO front**

We knew the European Society of Pathology was powerful but we must confess we did not know it was SO powerful.

After having decided that FADO would be the *leit-motiv* of the Opening Ceremony at the Lisbon Congress of Pathology (August 31, 2013) it was very nice to acknowledge that FADO had been nominated by UNESCO, in the Meeting held in BALI, in November 27, 2011, as Intangible Cultural Heritage of Humanity.

It is a pity FADO is not written PHADO because it would bring an additional P to the Seven *Ps* Congress. The Lisbon Congress would turn into the Eight *Ps* Congress:

- Pathology after Prague
- Prognosis
- Predictive
- Personalized
- Portugal, Pleasure and Phado

The performer of the Opening Ceremony will be one of the most famous portuguese “fadistas” – CARMINHO.
On the Scheduling of the First Prague Congress of the European Society of Pathology

The first proposal to schedule a Congress of the European Society of Pathology (ESP) for Prague was made by Prof. Hedinger, President of ESP, at the Executive Committee Meeting (EC Meeting) held in Paris in September 18, 1980. After “fully accepting Prof. Seifert’s proposal of Hamburg as the site of the 1983 Congress”, it was also decided that “the next Congresses should hopefully be held in Greece (1985) and in an Eastern European country (1987).”

At that time Europe was politically divided and the Statutes of ESP recommended that geographic considerations (North versus South and West versus East) should be taken into consideration whenever selecting the sites of the European Congresses. Prof. Hedinger as a Grand Patron of European Pathology and a first class ESP President had wisely proposed Greece and an Eastern country to host the forthcoming Congresses.

The invitation to hold the 1987 Congress in Prague/CCSR was acknowledged at the EC Meeting held in Helsinki in September 1, 1981, and a preliminary acceptance was made in the General Assembly of the Helsinki Congress (Sept 2, 1981).

The discussion was re-started in the EC Meeting held in Helsinki in Sept 3, 1981: “As for the further Congress, the President received an oral invitation to Prague by the Czechoslovakian Society of Pathology through Docent Josef Stejskal, Paediatric Pathology, Prague. As Dr. Stejskal mentions, the Czechoslovakian pathologists would be happy to have the congress in Prague already in 1985. However, as this date has been fixed for Athens, it seems possible to postpone the invitation to 1987.”

At the EC Meeting held in Ljubljana, Yugoslavia, in June 11, 1982, chaired by Prof. Ferluga, Prof. Plank who was the Representative of CCSR at the Advisory Council “informed the meeting that Czechoslovak pathologists have now received authority from their government to issue the official invitation for the Prague Congress in 1987.”

In the General Assembly of the Hamburg Congress (September 21, 1983), “Prof. Stejskal presented the official invitation for the 1987 Congress to be held in Prague and briefly summarised preliminary preparations.” The invitation was, at last, formally accepted.

The official language of the ESP was also discussed in the 1983 Hamburg Congress of ESP: “The question of official languages of the Society was raised. It was pointed out that according to the Statutes, French, English, German, Italian, Russian and Spanish are all official languages. In practice, English is normally used.”

Summing up: The ESP decided that after the Budapest Congress in 1973 there would be another European Congress in an Eastern European country in 1987 and intelligently selected Prague. We were there and it was indeed a very good Congress.

Prof. Fátima Carneiro

Prof. Manuel Sobrinho-Simões
Minutes of Meetings of the ESP Executive Committee: Paris, September 18, 1980

Meeting of the Executive Committee, Paris, September 18, 1980.
The E.C. met in Paris on September 18, 1980 at 2 p.m. at the Hotel R.I.M. St. Jacques. The following members were present: Hedinger, Giordano, David, Dolowy, Lemberg-Bosch, Neelof, Sorensen, Vanhaecke, and Feltuga.
The following members had justified their absence: Swahn, Thomas, Feltuga.
Also, the following persons attended the meeting by invitation: Neelof, Sorensen, Vanhaecke, and Feltuga.

It is also decided that the next Congresses should hopefully be held in Greece (1985) and in an Eastern country (1986).

The President

The Secretary

Hamburg, September 18, 1983

EUROPEAN SOCIETY OF PATHOLOGY - Executive Committee
Summary of discussions and decisions at the committee meeting
Tuesday, September 19, 1983, 14.00, Congress Center, Hamburg
Present: Committee Members: Feltuga, President; Johannessen, President-Elect; Hedinger, Past-President; Giordano - Secretary; Swahn - Treasurer; David; Lemberg-Bosch; Tapasharlampoos; Hans.
Apologies: Committee Members: Donno.

Feltuga presented the formal written invitation of the Czechoslovak Society of Pathology and informed the Committee of preparations to date so that the venue of Prague for the next Congress could be given formal approval to the General Assembly. The Committee agreed that the Congress should take place at the beginning of September.

The President

The Secretary

Hamburg, September 18, 1983
The scientific, educational and life-long learning programmes of the Society are mainly based on the activities of the SGs which are, in addition, responsible for protocols, guidelines and quality controls.

To increase the number of members and retain them, the Executive Council of the Society, as from this year, is planning to offer free web access to some journals of pathology, with the right to download papers of interest in PDF format and to attend, free of charge, region-based, scientific meetings, specifically planned by the RSs to satisfy CME annual activities that are mandatory in Italy in order to maintain a professional licence.

In addition to these "peripherally organized" congressional activities, the Society organizes 1 major, four-and-a-half-day meeting every 3 years, with 2 Annual Congresses each generally lasting 2 and a half days. At the triennial meeting, almost all topics are covered, while annual congresses are focalized on selected, pressing topics. Study Groups play a pivotal role both in the planning and the realization of the scientific meetings. In addition, every year there are national or international topical meetings. Three meetings are already planned for 2012; i) 11th European Congress on Telepathology and 5th International Congress on Virtual Microscopy, to be held in Venice, 6-9 June; ii) Cytopathology National Congress, to be held in Trieste, 28-30 June; and iii) SIAPeC-IAP National Congress, to be held in Florence, 25-28 October.

The SIAPeC-IAP considers that a major mission is to conduct and constantly improve relationships with other national and international Scientific Societies. At present, at the Italian level, very close cooperative activities are going on with the Italian Association of Medical Oncology, on quality controls in order to validate the activities of laboratories performing molecular tests for Her-2, c-Kit, KRAS, and B-Raf.

Continues on p.7
At the 23rd European Congress of Pathology held in Helsinki, the President of the SIAPeC-IAP presented a documentary on the professional figure and activities of pathologists, this in cooperation with APOF (Association Pathologists Beyond Borders). The CD containing the film was offered to all participants and has widely encountered approval, at an extra-European level, as well. So much so that the Brazilian Society of Pathology and the Latin American Society of Pathology have requested permission for the use and diffusion of this audio-visual material in South America.

The SIAPeC-IAP closely collaborates with APOF, a Private Voluntary Organization (PVO in English, ONG in Italian) involved in the realization of projects for the development of pathological anatomy and oncologic diagnostics in developing countries. This association, founded in Venice in 1999, emanating from an initiative of a group of pathologists members of the Executive Council of the SIAPeC-IAP. The SIAPeC-IAP every year donates part of its revenues to support the numerous projects of APOF. A representative of APOF sits on the Executive Council of the SIAPeC-IAP.

Presently, the SIAPeC-IAP is revising and updating its statute and bylaws so as persistently to keep up with the times. With the intent of meeting the basic needs of members, the SIAPeC-IAP promoted the production of the Italian version of the last issue of the SNOMED in order to introduce this nomenclator in all Italian laboratories of pathological anatomy. Moreover, the Society has been charged with negotiating a public-liability insurance specifically oriented to satisfy the needs of practicing pathologists.

Finally, the SIAPeC-IAP will renew and update the website (http://www.siapec.it/) during the present year with special reference to support educational programmes. Particularly, in collaboration with Juan Rosai M.D., the SIAPeC-IAP will attend to the construction of an area relating to FAQs in pathological anatomy.

The Spanish Society of Pathology (SEAP), with its approximately 1,500 members, is amongst the national pathology societies with larger memberships worldwide. Strengthening of international links to achieve its full potential has become one of SEAP’s paramount objectives. In this context, the European Society of Pathology (ESP) is the obvious hub in which to converge with other national societies to jointly make European pathology all the more vibrant and significant. The need for stronger cohesion of European countries, dramatically evinced by the current global crisis, has its reflection in the necessity for national pathology societies to further coalesce into the ESP sphere. The latter ought to be an enriched harmonising whole resulting from the sum of its distinctive national parts.

In addition to its European focus, SEAP is impelled by cultural and linguistic reasons towards a close relationship with the Latin American Society of Pathology, the Central American Pathology Association, and their component national societies. In a broader international perspective, SEAP completely melted with the Spanish Division of the International Academy of Pathology (IAP) years ago. Hence the recent introduction of the acronym “SEAP-IAP” to designate a single society with fused memberships, bylaws, governing bodies, and economic assets. Worth mentioning, as well, is the rapprochement between SEAP-IAP and the Spanish Society of Medical Oncologists (SEOM), in an attempt to develop consensual policies for the diagnostic, prognostic, and predictive workup of cancer patients nationwide.

SEAP-IAP members are grouped into 16 territorial divisions (corresponding to Spain’s autonomous regions) whose presidents sit in the advisory committee. The latter also includes a residents’ representative and ten members in charge of the following areas: residency training, continued medical education, scientific committee, quality assurance, private practice, Spanish pathology white paper (updated every two years), communication and social projection, pathology technicians, society’s journal (Revista Española de Patología), and working groups.
At the apex of the advisory committee is the executive committee, formed by the president, past-president or president-elect, secretary, and treasurer. Administrative and economic affairs are run by the SEAP Foundation, whose governing body essentially overlaps with the executive committee of SEAP-IAP.

The president (currently, Prof. Ricardo Gonzalez-Campona), secretary, and treasurer serve a four-year term. They are accompanied by the past-president during the first half of their term and by the president-elect during the second half. The national congress is held every two years, whereas the presidential election takes place every four years, in the setting of alternate congresses. In this way, a person will serve as president-elect for two years, as president for four years, and as past-president for two more years. This prolonged period of executive service, recently established, seeks to impart continuity and solidarity to the society’s main projects.

The recently renovated SEAP-IAP central office in Madrid, acquired some years ago by Prof. Antonio Cardesa, provides the premises to work on the various projects and keep the ever growing files in order. Besides, the central office is the meeting point of the quality assurance programme experts, who jointly review the immunohistochemistry module slides under a multi-headed microscope, select cases to generate virtual slides for the surgical pathology and cytopathology diagnostic module, or discuss issues pertaining to the molecular pathology module (includes HER2, KRAS, EGFR, and BRAF, amongst others). The central office is also used for activities of the working groups, talks with commercial agents, and meetings with other scientific societies’ representatives.

Particularly rewarding has been the successful SEAP-IAP effort at the central government level to avoid any reduction in the four-year period of unalloyed anatomic pathology residency training currently in force in Spain. Training in special competence areas after residency completion is now being planned. As for CME, free-for-members winter and springtime courses are held every year in Madrid. The winter course takes place in the context of business meetings. Every two years the springtime course is replaced with the national congress, which is directly organised by the president of SEAP-IAP, regardless of the town selected as venue. The latest national congress, held in Saragossa in May 2011, congregated approximately 1,000 delegates.

The SEAP-IAP scientific committee, whose main task is the review and organisation of proffered papers at annual meetings and national congresses, is also responsible for fostering the participation of pathologists in biomedical research activities and for granting our society’s auspices to other institutions’ events. As for the SEAP-IAP 20-plus working groups, they often are powerful propellers whose progressive articulation with their European counterparts is of considerable strategic import. On the other hand, competitive innovation in our specialty does need the cooperation of well-trained technical personnel fully identified with the goals of modern pathology. Consequently, SEAP-IAP now organises teaching activities specifically addressed to pathology technicians and welcomes them to its national congresses.

Finally, the executive committee member in charge of communication and social projection acts also as webmaster and has the difficult mission of improving pathology’s social visibility, mainly through frequent contact with the media and patients’ associations. Inspired by previous work of North American pathologists, the SEAP-IAP website (www.seap.es) is developing a FAQ Initiative providing clear and succinct answers (illustrated with animations) to the most frequent questions posed by patients and their relatives upon reading pathology reports.

As prospects for economic improvement remain bleak across Europe, the challenge to all of us in 2012 is to keep moving along the steep path forwards. Evolutionarily, we pathologists are better adapted to deprivation than most other medical specialists. Let us seize the opportunity to jointly make European pathology a visible leading player in the increasingly restrained new game of medicine.

Prof. Aurelio Ariza
Paediatric and Perinatal Pathology Working Group

Dr. Marta Cohen

The 23rd European Society of Pathology Meeting was held in Helsinki, Finland, from 27 August to 1 September 2011.

At this recent meeting, the Paediatric and Perinatal Working Group – Chaired by Dr Irene Scheimberg - hosted a symposium on The paediatric intestine: why are children different from adults?; a short course on cardiovascular disease in the young; a Slide Seminar on Hepatic pathology; a Business meeting where a conference on the Genetics of long QT and another on genetic of cystic renal disease were presented. In addition, there was an oral free paper session with 9 papers that were accepted for oral presentation and a poster session with 30 posters on display (out of 44 abstracts submitted).

Those of us who regularly participate in the ESP meetings have noted a steady increase in the numbers of participants in our sessions. This year some of our sessions had an audience that exceeded 70 pathologists from different European and non-European countries. A key piece for this achievement has been the hard work of our working group and the style used to choose the paediatric and perinatal subjects. Priority is given to those aspects of our specialty that can benefit those pathologist in general practice, as these represent a large proportion of the ESP members. In addition, we strictly adhere to the spirit of the ESP, which guarantees a valuable educational experience by encouraging innovation, friendship and professional collaborations.

The success achieved at the recent ESP meeting in Helsinki would not have been possible without the incredible support provided by our local organiser Dr Riitta Karikoski. We are all in debt to her, as she was instrumental in identifying excellent local speakers that increase the level of the scientific program.

We are also grateful to Dr Irene Scheimberg for her hard work as Chair of our working group during the last 4 years and her success in consolidating our speciality within the European Society of Pathology.

We are now immersed in the organisation of the 24th European Society of Pathology Meeting, which will be held in Prague between the 8-12 September 2012. We expect that the program will be very exciting and that many experts from different corners of the globe will participate in our sessions. In addition to the senior and well known European Paediatric and Perinatal Pathologists that will participate in our sessions, we have received confirmation of the attendance of Dr Beverly Rodgers who will address issues on Placental Pathology, Dr Maria Tsokos who will present an Up-date in Ewing Sarcoma, Dr Cheryl Coffin who has agreed to present An Update on Classification, Grading, and Morphologic-Genetic Correlations in Spindle Cell Tumors and Dr Pauline Chou who will give a lecture on Prognostication in neuroblastoma: a continuous saga?

Let me take this opportunity to invite you all to join us in Prague, the city of 100 spires considered a jewel at the heart of Europe.

Dr Marta C Cohen
Chair
Paediatric and Perinatal Pathology Working Group
European Society of Pathology
A whole-genome massively parallel sequencing analysis of BRCA1 mutant oestrogen receptor-negative and -positive breast cancers


Abstract

BRCA1 encodes a tumour suppressor protein that plays pivotal roles in homologous recombination (HR) DNA repair, cell-cycle checkpoints, and transcriptional regulation. BRCA1 germline mutations confer a high risk of early-onset breast and ovarian cancer. In more than 80% of cases, tumours arising in BRCA1 germline mutation carriers are oestrogen receptor (ER)-negative; however, up to 15% are ER-positive. It has been suggested that BRCA1 ER-positive breast cancers constitute sporadic cancers arising in the context of a BRCA1 germline mutation rather than being causally related to BRCA1 loss-of-function. Whole-genome massively parallel sequencing of ER-positive and ER-negative BRCA1 breast cancers, and their respective germline DNAs, was used to characterize the genetic landscape of BRCA1 cancers at base-pair resolution.

Only BRCA1 germline mutations, somatic loss of the wild-type allele, and TP53 somatic mutations were recurrently found in the index cases. BRCA1 breast cancers displayed a mutational signature consistent with that caused by lack of HR DNA repair in both ER-positive and ER-negative cases. Sequencing analysis of independent cohorts of hereditary BRCA1 and sporadic non-BRCA1 breast cancers for the presence of recurrent pathogenic mutations and/or homozygous deletions found in the index cases revealed that DAPK3, TMEM135, KIAA1797, PDE4D, and GATA4 are potential additional drivers of breast cancers. This study demonstrates that BRCA1 pathogenic germline mutations coupled with somatic loss of the wild-type allele are not sufficient for hereditary breast cancers to display an ER-negative phenotype, and has led to the identification of three potential novel breast cancer genes (ie DAPK3, TMEM135, and GATA4).

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Results

After a median follow-up of 11 years in the core age group, the relative reduction in the risk of death from prostate cancer in the screening group was 21% (rate ratio, 0.79; 95% confidence interval [CI], 0.68 to 0.91; \( P=0.001 \)), and 29% after adjustment for noncompliance. The absolute reduction in mortality in the screening group was 0.10 deaths per 1000 person-years or 1.07 deaths per 1000 men who underwent randomization. The rate ratio for death from prostate cancer during follow-up years 10 and 11 was 0.62 (95% CI, 0.45 to 0.85; \( P=0.003 \)). To prevent one death from prostate cancer at 11 years of follow-up, 1055 men would need to be invited for screening and 37 cancers would need to be detected. There was no significant between-group difference in all-cause mortality.

Conclusions

Analyses after 2 additional years of follow-up consolidated our previous finding that PSA-based screening significantly reduced mortality from prostate cancer but did not affect all-cause mortality. (Current Controlled Trials number, ISRCTN49127736.)

Intratumor Heterogeneity and Branched Evolution Revealed by Multiregion Sequencing


Background

Intratumor heterogeneity may foster tumor evolution and adaptation and hinder personalized-medicine strategies that depend on results from single tumor-biopsy samples.

Continues on p. 12
Methods

To examine intratumor heterogeneity, we performed exome sequencing, chromosome aberration analysis, and ploidy profiling on multiple spatially separated samples obtained from primary renal carcinomas and associated metastatic sites. We characterized the consequences of intratumor heterogeneity using immunohistochemical analysis, mutation functional analysis, and profiling of messenger RNA expression.

Results

Phylogenetic reconstruction revealed branched evolutionary tumor growth, with 63 to 69% of all somatic mutations not detectable across every tumor region. Intratumor heterogeneity was observed for a mutation within an autoinhibitory domain of the mammalian target of rapamycin (mTOR) kinase, correlating with S6 and 4EBP phosphorylation in vivo and constitutive activation of mTOR kinase activity in vitro. Mutational intratumor heterogeneity was seen for multiple tumor-suppressor genes converging on loss of function; SETD2, PTEN, and KDM5C underwent multiple distinct and spatially separated inactivating mutations within a single tumor, suggesting convergent phenotypic evolution. Gene-expression signatures of good and poor prognosis were detected in different regions of the same tumor. Allelic composition and ploidy profiling analysis revealed extensive intratumor heterogeneity, with 26 of 30 tumor samples from four tumors harboring divergent allelic-imbalance profiles and with ploidy heterogeneity in two of four tumors.

Conclusions

Intratumor heterogeneity can lead to underestimation of the tumor genomics landscape portrayed from single tumor-biopsy samples and may present major challenges to personalized-medicine and biomarker development. Intratumor heterogeneity, associated with heterogeneous protein function, may foster tumor adaptation and therapeutic failure through Darwinian selection. (Funded by the Medical Research Council and others.)
Methods

A 14-gene expression assay that uses quantitative PCR, runs on formalin-fixed paraffin-embedded tissue samples, and differentiates patients with heterogeneous statistical prognoses was developed in a cohort of 361 patients with non-squamous NSCLC resected at the University of California, San Francisco. The assay was then independently validated by the Kaiser Permanente Division of Research in a masked cohort of 433 patients with stage I non-squamous NSCLC resected at Kaiser Permanente Northern California hospitals, and on a cohort of 1006 patients with stage I—III non-squamous NSCLC resected in several leading Chinese cancer centres that are part of the China Clinical Trials Consortium (CCTC).

Findings

Kaplan-Meier analysis of the Kaiser validation cohort showed 5 year overall survival of 71.4% (95% CI 60.5—80.0) in low-risk, 58.3% (48.9—66.6) in intermediate-risk, and 49.2% (42.2—55.8) in high-risk patients (p trend=0.0003). Similar analysis of the CCTC cohort indicated 5 year overall survivals of 74.1% (66.0—80.6) in low-risk, 57.4% (48.3—65.5) in intermediate-risk, and 44.6% (40.2—48.9) in high-risk patients (ptrend<0.0001). Multivariate analysis in both cohorts indicated that no standard clinical risk factors could account for, or provide, the prognostic information derived from tumour gene expression. The assay improved prognostic accuracy beyond National Comprehensive Cancer Network criteria for stage I high-risk tumours (p<0.0001), and differentiated low-risk, intermediate-risk, and high-risk patients within all disease stages.

Interpretation

Our practical, quantitative-PCR-based assay reliably identified patients with early-stage non-squamous NSCLC at high risk for mortality after surgical resection.
What’s new?
The Decline of Coronary Heart Disease in Europe:

What is Behind that Fall?
Dr. Loukas Kaklamanis

People wait for ages to hear good news, but on 4th of February 2012, three major epidemiological studies from three different countries in Europe (England, Denmark and Poland), published at the BMJ,344:1-58 No7842,2012, spread out the sparkling message: Heart disease is declining.

Kate Smolina et al from the Dept. of Public Health and Cancer Epidemiology Unit in Oxford-UK, followed and analysed data of declining mortality from 840,175 residents of all ages between 2002-2010. Although there has been detectable fall of acute myocardial infarction (AMI) in England since 1970, the determinants of this fall were unknown. The study question was: how much of the recent decline in mortality from AMI is attributable to changes in the event rate of AMI and how much to changes in case fatality? In their analysis the age standardised total mortality rate for AMI decreased by half while the age standardised event and case fatality declined by one third. (54%) of the decline in mortality is attributed to a decline in rates of AMI and just under one half (46%) to a decline in case fatality.

Morten Schmidt et al from Aarhus University Hospital in Denmark questioned how much did incidence of mortality from AMI change from 1984 to 2008 and how did sex and comorbidity affect prognosis?

Continues on p.15
They found out that the rate of first time admission for AMI and subsequent short term mortality, both declined by almost half for all patients, independent of sex and comorbidity but comorbidity burden was a strong prognostic factor for short and long term mortality, whereas sex was not.

Finally in Poland Piotr Bandosz et al from the Medical School of the University of Gdansk and the Department of Epidemiology in Warsaw analysed the reasons for the rapid decline in mortality from cardiovascular disease after the political, social and economic transformation in the early 1990s.

They identified that over half of the fall in mortality from coronary heart disease in Poland between 1991 and 2005 can be attributable to reductions in major risk factors and a third to evidence based medical treatments.

Dr. Loukas Kaklamanis
Geheimrat Rudolf Virchow (1821-1902) and the “Cellularpathologie” by Virchow

M. Thiery 1,2
(published in “Tijdschrift voor Geneeskunde, 67, nr. 17, 2011” and translated from Dutch by M. Marichal and M. Wells)

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This German polymath - physiologist, hygienist, anthropologist, ethnologist, archaeologist, medical historian and politician - has been called “the man who changed the face of medicine”(1) and was one of the most important personalities of the 19th century. His book “Die Cellularpathologie” is considered to be one of the hundred most important works in medicine. His name is associated with diseases, physiological, pathological and anatomical discoveries.

Rudolf Ludwig Karl Virchow was born on October 13, 1821 in Schivelbein (East-Pommeren) to a family of humble farmers (fig 1). His father wanted little Rudolf to get a good education and become “un homme du monde accompli” (2). He therefore sent his son to the Köstlin gymnasium, where teachers noticed the boys’ exceptional talent and provided him with a bursary to study in Berlin. In 1839, he attended the Friedrich-Wilhelm IV institute, a military-medical school, also known as the “pépiniaire”, where numerous famous physicians have been educated. In 1843 Virchow received his medical diploma from the hands of its Dean, the pioneer physiologist Johannes Müller (1801-1858).

After his promotion Virchow worked as an assistant (“Unterarzt”) in the “Charité” hospital in Berlin, where he treated patients and carried out research in anatomy and pathology.

In 1845, he became a prosector with Robert Froriep (1804-1861), who he succeeded in 1847. In the same year he was appointed “Privatdocent” in Pathological Anatomy and founded the journal “Archiv für Pathologische Anatomie und Physiologie und für klinische Medizin” (later renamed “Virchow’s Archiv”), in which he announced his goal: “Die bewusste Entwicklung der anatomischen und klinischen Erfahrungen als die erste und wesentliche Forderung der Zeit; aus einer solchen Empirie resultiere dann allmählich die wahre Theorie der Medizin, die pathologische Physiologie” (3).

In 1848 the Prussian government sent him to Upper Silesia to report on a typhus epidemic, a deathly rickettsial infection, transmitted by lice and typical of populations living in poor and neglected conditions. In his report, he denounced the undemocratic government and with his plea for urgent reforms stirred up a political hornets’ nest: “Nur Wohlstand, Bildung, Freiheit können Besserung bringen, und diese sind einzig möglich auf dem Boden einer vollen und unumschränkten Democratie”.

Having barely returned from this inspection, he participated actively in the Berlin Revolution of 1846, an armed resistance of the bourgeoisie against the Prussian government. He helped to erect barricades, treated the wounded and joined the “Medizinalreformbewegung”, organized by the medical corps that claimed autonomy and pleaded for a Ministry of Health. Unfortunately, this revolution was suppressed by the government and ended in bloodshed.

Reaction was prompt: the rebel was evicted from Charité and dismissed from his academic functions. But he was lucky: progressive Beiern had no objection to his liberal ideas and, recommended by the Professor of Obstetrics, Friedrich Scanzoni (1821-1891), he was appointed ordinarius in Pathological Anatomy at Würzburger University in 1849, where he headed both a clinical service and a research unit. He temporarily relinquished political action to concentrate fully on pathophysiology and published some of his most important works.

Continues on p.17
In 1856 Berlin repented of its bad treatment given that its Privatdocent was now famous. With the support of the influential Edwin, Baron von Manteuffel (1809-1885), Virchow was offered the chair of Pathological Anatomy and was appointed director of the “Institut für Pathologie”, which had been created for him. Two years later he published his renowned book “Celpathologie” (7).

For the second time, and this time successfully, he became involved in health politics and joined the “Fortschrittspartei”, being elected a council member.

From 1861 on, he loudly proclaimed his social-democratic ideas and pursued his campaign to improve public health. When he accused Otto von Bismarck (1815-1898) of lying, he was challenged to a duel, which luckily was cancelled, because Virchow was the one to choose the weapon and he chose ... the scalpel! From 1880 until 1893, he joined the Reichstag and that same year became a member of the Geheimrat.

In 1896 he initiated the construction of a gigantic new hospital complex, in which, three years later, he inaugurated a pathology museum, that would house his complete collection: more than 23000 specimens, collected, prepared, documented and labelled by him. It is a unique institute, part of a hospital intended for research, teaching and education of the population in the field of hygiene and medicine. On his 80th birthday, he was honoured by an international gathering and received the golden “Reichmedaille” from the hands of Emperor Wilhelm II himself.

But, mercilessly, his end was near: a jump from a horse tram was fatal: on September 5th, 1902, the almost 81-year old Geheimrat died as a consequence of a fractured head of femur. Virchow was a hyperactive little fellow, but a scientific giant, critical and sarcastic, yet mildly disposed towards competent collaborators and colleagues. He was an honest fighter who frankly admitted his mistakes, an inspiring teacher who recruited a multitude of students to his institute and trained a number of famous collaborators. A convinced patriot, who equipped a whole ambulance unit during the French-Prussian war (1870-1871), but did not hesitate to condemn the bombardment of the Paris museum of natural history and to call the Prussian “Militär” a “barbaric and destructive horde”.

The city of Berlin has Virchow to thank for its modern irrigation system and his country has to thank him, among many other things, for improved school hygiene, the introduction of systematic medical surveys in schools and the renovation of the hospital system. As an anthropologist and ethnologist he destroyed the myth of the “pure blond and blue eyed” German race (8). In later years he concentrated mainly on comparative anthropometrics and craniology and founded the “Berliner Gesellschaft für Antropologie, Ethnologie und Urgeschichte”.

As an archaeologist he discovered the existence of prehistoric pole houses in Northern East-Germany, accompanied amateur archaeologist Heinrich Schliemann (1822-1890) to Troy in 1878 and later went on study trips to Egypt and the Caucasus.

As a medical historian he wrote essays about the life and work of (among others) the German clinician Johann Schönlein (1793-1864), the Italian anatomist Giovanni Battista Morgagni (1682-1771) and his mentor Johannes Müller. But his real expertise was pathology, for which he had laid down the fundamentals during his first Berlin period and which he further developed in Würzburg. Morgagni had considered the “organ” as the seat of pathological processes, while for Marie-François Xavier Bichet (1771-1802) it was the “tissue”. Inspired by the works of Matthias Jacob Schleiden (1804-1881) and Theodor Ambrose Schwann (1810-1882), who respectively had declared the cell to be the origin of all phenomena of life in plants and animals, Virchow suspected that the cell was also the motor in pathological processes and should be investigated as the origin of illness. For pathological phenomena, pathologists and therapists should therefore, in his opinion, the
cell, the basic element of physiology and physiopathology. This was also the reason Virchow named his institute in Berlin “pathologic” and not “anatomopathologic”. Every (pathological) structure consists of cells, which according to the axiom “omnis cellula e cellula” originate from previously existing cells. Life goes on “nur durch legitime Succession der Zellenbildungen... Krankheit ist nichts anderes als Leben, aber ein Leben unter abnormen Bedingungen. Die Pathologie ist Physiologie, aber eine Physiologie mit Hindernissen. Wie entsteht Krankheit? Dadurch, dass abnorme Reize auf den Organismus einwirken. Diese Reize treffen das lebende Element, die Zelle bevor” (7).

Two years after returning to Berlin, Virchow introduced this brainchild to his students in 20 lectures, which were recorded stenographically and published the same year as a book entitled “Die Cellularpathologie in ihrer Begründung auf physiologische und pathologische Gewebslehre” (fig 2) (7). Two years later, this masterpiece had already been translated in English and Dutch. “Virchow’s cellular theory was the principle of life as such”, was the elliptical comment of recent biographers (6).

As mentioned, his name remains linked to a long list of physiological, pathological and anatomical discoveries. He was the first to clearly describe thrombosis and embolus; he formulated the classic triad that lies at the basis of venous thrombosis: changes in blood flow, damage to the vessel wall and changes in the composition of blood: “Virchow’s trias”(9).

The mention of the increase in leucocytes during infection dates from 1858, a process Virchow called “leukocytosis”. Shortly thereafter, he discovered the clinical image of “weisses Blut” during an autopsy and coined it “Leukämie”(10).

Hypertrophy of facial bones, with a lionish facial expression, so called “leontiasis ossium” is to this day named Virchow’s disease.

Another prime description is the “elephantiasis nostras”, oedema caused by a congenital stenosis of large lymphatic vessels or “Lymphatisches ödem mit Missbildungen”, also described by the American physician Forsyth Milroy (1855-1942) and named after both: disease of Virchow-Milroy.

Early on Virchow was also interested in the study of cancer: his theories about this were published in his “Archiv” in 1847. In 1863-67 he described in detail the microscopy of benign and malignant tumours (11). Every medical student is familiar with Virchow’s gland, in the left supraclavicular fossa, a metastasis of a carcinoma, usually of gastric origin to which French authors added the name of a Frenchman: Charles Troisier: (1844-1919): the gland of Virchow-Troisier.

Further eponyms are among others: the cells of Virchow, foam cells containing vacuolated and destroyed lepra cells, discovered when he was invited by the Norwegian government to investigate the leprosy epidemic in 1859.

Granulations of Virchow are granules present in the ventricles of the brain in dementia paralytica and crystals of Virchow are the orange- yellow haematoidin crystals sometimes found in haemorrhages. Bodies of Virchow-Hassall are the concentric corpuscles present in the thymus and also described by Arthur Hill Hassall (1817-1894), an English physician and chemist.

References:
As a part of the Congress programme the European School of Nephropathology supported by the ERA-EDTA and the Nephropathology Working Group of the European Society of Pathology was held on October 14, 2011 attended by 60 participants. Professor Michael J. Mihatsch, the President of the Nephropathology Working Group, along with ten other faculty members offered up-to-date information on glomerular, tubulo-interstitial diseases and transplant pathology-rejection related topics (all the lectures could be downloaded at http://www.nephropathology-esp.org/). ERA-EDTA was also generous distributing 2 bursaries to young pathologists involved in nephropathology.

The social activities included the Opening Ceremony at Biljana Hall at hotel Metropol followed by a welcome reception cocktail, as well as the Gala Concert at St. Sofia Church, one of the most impressive medieval buildings in Ohrid with frescoes from the 11th, 12th and 13th century, well known by its wonderful acoustics, with the participation of the Trio Skopje orchestra. All participants and the faculty members enjoyed enormously the Gala Dinner with Macedonian cuisine, music and dance.

The excellence of the scientific sessions and the good facilities of the hotel Metropol, as well as the enchanting city of Ohrid full of historical attractions in a most beautiful scenery of Ohrid Lake helped to create a very stimulating environment to exchange knowledge and experience, and to build bridges for collaboration with colleagues from the neighboring countries, as well as other European countries and countries all around the world. The Macedonian Association of Pathology, along with the Congress Organizing Committee and the Scientific Programme Committee assured excellent conditions for successful realization of this historical 1st Macedonian Congress, organized as a part of the celebration of the 40th Anniversary of the foundation of the Association.

Altogether the Macedonian pathology demonstrated the capacity to organize a very successful event and to show that we are practicing an updated diagnostic pathology and trying to introduce the technologic advances that were emphasized in all sessions of the Congress in their scientific projects.

Finally, on behalf of the Macedonian Association of Pathology and the Congress Organizing Committee I would like to express our great gratitude to the presence of all participants, the speakers, the sponsors, the institutions, and to all who helped to make a congress which was scientifically very successful, instructive and stimulating and socially very pleasant.
Announcements:

Follow the ESP on the Facebook:


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Practical, clinical, radiological and pathological diagnosis of skeletal tumours

21, 22 and 23 May 2012
Leiden

www.boerhaavenascholing.nl
Announcements:

www.bierzoderm.com

1st Dermatopathology Course in El Bierzo
July 19-20, 2012
Ponferrada, Spain

“Controversies in Dermatopathology”

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Symposium and slide seminar of the Swiss Society of Pathology

Update in Gastrointestinal Pathology

SATURDAY, 28TH April, 2012

Venue: UniversitätsSpital Zurich, Schmelzerberstrasse 12, Institut f. klinische Pathologie, Grosser Hörsaal

PROGRAM

9:00 – 9:45 Coffee and registration
9:45 – 9:55 Presidential Welcome Mathias Gugger

Morning session chaired by Gieri Cathomas and Achim Weber

9:55 – 10.35 Challenges in the diagnosis of inflammatory bowel disease
Neil Shepherd, Cheltenham, UK

10:35 – 11.15 The surgical pathology of colorectal cancer
Iris Nagtegaal, Nijmegen, the Netherlands

11:15 – 11:55 Case 1 Neil Sheperd, Cheltenham, UK
Case 2 Iris Nagtegaal, Nijmegen, the Netherlands
Case 3 Luigi Tornillo, Basel, Switzerland

11.55 – 12.55 Lunch break

Midday session chaired by Alessandro Lugli and Muriel Genevay

13:00 – 13.40 Barrett mucosa and dysplasia: an update
Jean-François Fléjou, Paris, France

13:40 – 14.20 Pathology in gastric cancer secondary prevention
Massimo Rugge, Padova, Italy

14:20 – 15.00 Case 4 Jean-François Fléjou, Paris, France
Case 5 Massimo Rugge, Padova, Italy
Case 6 Muriel Genevay, Geneva, Switzerland

15:00 – 15.20 Break

Afternoon session chaired by Luigi Tornillo and Gieri Cathomas

15:20 – 16.00 Mucinous neoplasms of the appendix
Joseph Misdraji, Boston, USA

16:00 – 16.50 Case 7 Joseph Misdraji, Boston, USA
Case 8 Achim Weber, Zürich, Switzerland
Case 9 Alessandro Lugli, Bern, Switzerland
Case 10 Gieri Cathomas, Liestal, Switzerland

16:50 Closing remarks Mathias Gugger

For information and registration: http://www.sgpath.ch/
Website of the slide seminars: http://pathorama.ch/vcollections/
Deadline for submission of a list of diagnosis on the website of the slide seminar is: 24. April 2012, 7:00 pm
The handout is available on the website of the slide seminar on 25.04.2012
Thyroid Pathology for the Practicing Pathologist. June 7 and 8, 2012 in Paris, France

This 2-day course on the Pathology of Thyroid Tumours will take place in Paris under the auspices of the I.A.P. French Division. This course will be given in English by Prof. R. Heimann (Brussels), Prof. J. Rosai (Milano), Prof. M. Sobrinho-Simões (Porto) and Dr. Ph. Vielh (Villejuif). It will consist of lectures alternating with slide reviews of cases brought by the participants and a slide seminar. The virtual slides of the cases of the seminar may be web accessed before the course. The audience will be limited to 22 participants.

Thursday, June 7, 2012
10.00 – 10.15AM: Welcome & Introduction - Ph. Vielh and R. Heimann
10.15 – 11.00AM: Introduction to thyroid pathology: some edible appetizers (R. Heimann)
11.00 – 12.30AM: Adenoma, follicular carcinoma and well differentiated tumours of uncertain malignant potential (J. Rosai)
12.30 – 02.00PM: Lunch
02.00 – 03.30PM: Papillary carcinoma and variants (M. Sobrinho Simões)
03.30 – 04.30PM: Poorly differentiated and anaplastic carcinomas (J. Rosai)
04.30 – 05.00PM: Coffee break
05.00 – 05.30PM: Medullary carcinoma (M. Sobrinho Simões)
05.30 – 07.30PM: Slide Seminar (J. Rosai and Faculty)

Friday, June 8, 2012
09.00 – 10.30AM: ABC of thyroid cytopathology (Ph. Vielh)
10.30 – 11.00AM: Coffee break
11.00 – 12.30AM: Hürthle cell lesions and “rare flowers”. Value of immunocytochemistry and molecular pathology (M. Sobrinho Simões)
12.30 – 02.00PM: Lunch
02.00 – 03.00PM: The Bethesda proposal (Ph. Vielh)
03.00 – 04.00PM: Pitfalls in thyroid pathology (J. Rosai)
04.00 – 04.30PM: Coffee break
04.30 – 06.30PM: Presentation and discussion of cases brought by the participants (M. Sobrinho Simões and Faculty)
06.30 – 06.45 PM: Conclusions and end of the Course

Course fees
360 euros for members of any IAP Division
420 euros for non members of IAP
The fees include registration, hand-out, access to the slide seminar and coffee breaks.
Please click on the following link to get access to the web page of the Thyroid Pathology for further information: http://www.francepathol.org/aip_v3/epl/fiche.cfm?num=97
Below the page on right if you click on S’INSCRIRE you have the possibility to pay online.
Thank you to return to the IAP French Division the Registration Form in attachment.

Contact: Hélène Moulin. French Division of the International Academy of Pathology.
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