

EUROPEAN SOCIETY OF PATHOLOGY NEWSLETTER

Winter 2017



TAKE A
LOOK
INSIDE

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Message from the President of the ESP

By Prof. Pierre Bedossa



After a very successful **European Congress of Pathology in Cologne**, and while the 29th ECP in Amsterdam is on a good track, our Society has been very active during the last few months on several different issues. I would

like to take this opportunity to briefly summarize some of its most recent achievements.

Since January 2017, **Prof. Daniela Massi** is the new Editor-in-Chief of our Journal, *Virchows Archiv*. Many thanks go to **Prof. Fred Bosman** for his impressive efforts along the years to make *Virchows Archiv*, the European Journal of Pathology, a strong and visible publication. Fred gathered around him a very active and professional team that shaped the future of our Journal. Prof. Massi has now the challenge to make *Virchows Archiv* even more successful and we thus strongly encourage all of our members to participate in this effort by reviewing submitted manuscripts or/and sending articles for publication in the Journal.

Also, important for the visibility of ESP and after the renewal of our website, the education portal is now operational. You should have an access to it through our website by login with your membership. The education portal is a living database that will progressively be enriched and will constitute an important tool for teaching and learning. Any contribution is welcome.

ESP has also a strong commitment to training programs. In an attempt to contribute to harmonization of the training outcome in various countries, the former European Association of Pathology Chairs and Program Directors (EAPCP) created a progress test. The main purpose was to build a

continuous evaluation system during the training of medical specialists and to monitor the progress of the trainees. After several years of success, the progress test vanished for several reasons. The pathology board of the European Union of Medical Specialists (UEMS) has mandated the ESP to resurrect such a test and therefore ESP has designed a task force which is currently operational. The first proof of the progress test should be ready before the end of the year. The format corresponds to what UEMS Pathology has been doing for years but with a more dynamic approach. We will need also your participation since this will require the creation of a test item bank.

We are entering in an important and strategic period for the society. According to the Statutes of the ESP, a new President-Elect has to be nominated and presented at the next General Assembly. Also, **Prof. Ilmo Leivo** is ending his term as ESP Secretary. On behalf of ESP Councilors and members, I greatly thank him for his dedication and continuous support of the ESP. Prof. Leivo has been instrumental in building the new statutes and bylaws of ESP. A new President-elect (Prof. Holger Moch, CHE) and a new Secretary (Prof. Aurelio Ariza, ESP) have been recommended. Three Council members have also been recommended: Prof. Glenn McCluggage (UK), Prof. Maria Rosaria Raspollini (ITA) and Prof. Anastasia Konstantinidou (GRC).

On a completely different angle, ESP took seriously into consideration the issue of formalin banning in Europe. Indeed, with the reclassification of formalin in terms of carcinogenicity, EU intends to ban the use of formalin. In the considerations that have led to these decisions, medical use of formalin has been almost completely ignored. The ESP and UEMS Section of Pathology have been trying to convince the European Parliament and the Council that they should make an exception so that pathology laboratories may continue to use this indispensable fixative. Our advisory board and the national societies of pathology have also been active in lobbying. These joint efforts resulted in a proposal for an amend-

ment recently presented to the European Parliament by three Spanish MEPs. Unfortunately, the amendment has been rejected (by just one vote!) by the European Parliament Commission for Employment and Social Affairs, but will be dealt with again at a Plenary Session of the European Parliament soon. Many thanks to all those who invested time and efforts for this important initiative, especially **Prof. Fatima Carneiro** and **Prof. Aurelio Ariza**.



ESP-QA foundation (European Society of Pathology Quality Assurance Organization) is now settled. The foundation will manage all issues about external quality assessment previously managed under the umbrella of ESP. A program aiming to ensure optimal accuracy and proficiency in biomarker testing has been adopted with new set-up. Registrations for the different sub-schemes are now open.

As you can see from this short summary, ESP is alive and well!

I wish you a pleasant reading of the ESP newsletter.

Editor's Message

By Prof. Gordan Vujanić



Dear colleagues

Here is a new issue of the ESP Newsletter, with plenty of interesting details about Society's activities and other items of interest.

The issue traditionally starts with President's message. Prof. Pierre Bedossa is first informing us about the appointment of Prof. Daniela Massi as the new Editor-in-Chief of our Journal, *Virchows Archiv*, and about our work on introduction of a progress test in pathology which is expected to be ready later this year. Sadly, despite very hard work of some of our members, the European Parliament Commission did not accept our arguments that formalin should not be banned from pathology laboratories, but we continue this 'fight', hoping for a positive outcome. Finally, we learn that ESP-QA foundation (European Society of Pathology Quality Assurance Organization) is now open and operational.

Our Secretary, Prof. Ilmo Leivo is informing us about nominations for the ESP President Elect and Honorary Secretary, as well as three Council members who will be replacing the current officers after the Congress in Amsterdam.

From the ESP Headquarter, Dr. Raed Al Dieri, ESP Director General, is informing us about staff changes and the appointment of a new Project Management Associate, Ms Teodora Gârbovan, who has joined us only recently but very timely to help with the preparation of this issue of the Newsletter. We also meet Dr. Maria Urbanowicz who is a new ESP-EORTC pathology fellow.

Prof. Folkert van Kemenade is updating us on the preparations for the 29th ECP in the exciting city of Amsterdam, where we are going to have a great scientific, but also a social programme. And the bravest of us can even demonstrate their swimming skills by taking part in a 2km charity swim in the city centre's canals!

Prof. Gabriella Nesi, Chair of the History of Pathology Working Group is reporting on the progress in building a European Network of Pathology Collections and Museums, which should become an important source of material for studying valuable pathology collections from around Europe. The ESP members and all interested professionals

are also reminded and invited to the Group's annual meeting in Coimbra, Portugal, from 30 June to 1 July 2017.

A report from the German Society for Pathology includes information about a very interesting project called "Academy for young pathologists" which is aimed to promote and help talented young pathologists to set up and do research. There is also information about the first Global Congress on Molecular Pathology in Berlin (3-5 April 2017), and the 101st annual meeting of the Society in June.

Dr. Loukas Kaklamanis prepared another *Analecta Medica*, with a selection of recent and important scientific abstracts. Professor Metka Volavšek reviews most recently published books from different areas of pathology. She also provides a list of pathology meetings around the world, which might be of interest to our members.

So, another Newsletter is in front of you, we hope you'll find some time to read it and we would be very grateful for any suggestions, criticisms and comments which may help us improving it.

Secretary's Message

By Prof. Ilmo Leivo



Election of New Officers of the European Society of Pathology

At the General Assembly in Amsterdam in September 2017, the following officers will demit office:

President-elect Prof. Dina Tiniakos
(UK/Greece) (as from September 2017 the
ESP President)
Secretary Prof. Ilmo Leivo (Finland)

The ESP Council:

Prof. Peter Schirmacher (Germany)
Prof. Metka Volavsek (Slovenia)
Prof. Tibor Tot (Sweden)
Prof. Cord Langner (Austria)
Prof. Xavier Matias-Guiu (Spain)
Prof. Ales Ryska (Czech Republic)
Prof. Holger Moch (Switzerland) - *not participating in decision concerning the President-elect*
Prof. Gordan Vujanic (UK)

recommends the following individuals for the above positions:

President-elect (from September 2017):

- ✓ **Prof. Holger Moch** (Zurich, Switzerland)

Secretary (from September 2017):

- ✓ **Prof. Aurelio Ariza** (Barcelona, Spain)

Their brief CVs are available on request.

The membership is now invited to make other nominations within six weeks of this communication. Any nomination must be approved by the individuals themselves and each must be supported by at least 5% of members of the society and accompanied by an abbreviated CV of no more than one page.

Election of Three New Members of the Council of the ESP

At the General Assembly in Amsterdam in September 2017, the following three regular members of the Council will demit office:

Prof. Ales Ryska (Czech Republic)
Prof. Holger Moch (Switzerland)
Prof. Gordan Vujanic (UK)

The following individuals are recommended by the Council to fill these positions:

Prof. Glenn McCluggage (UK)
Prof. Maria Rosaria Raspollini (Italy)
Prof. Anastasia Konstantinidou (Greece)

Their brief CVs are available on request.

These recommended candidates will be presented for formal approval at the General Assembly in Amsterdam in September 2017.

ESP HQ's Message

By Dr. Raed Al Dieri ESP Director General



Dear ESP members,

Our organization would not exist without the enthusiasm and contribution of our members. So as we start our annual program, we want to remind you of the following opportunities to be

involved with ESP. As a member, we encourage you:

- ✓ To attend our annual **Congress in Amsterdam** this year (2-6 September) at a reduced, early-registration fee. Registration and abstract submissions are now open. For more information please visit www.esp-congress.org

We would like to draw your attention that the ECP Amsterdam is the only Congress organized and endorsed by the ESP in 2017.

- ✓ For our young pathologists, the 2018 call

for the ESP Giordano Fellowship (GF) bursary is open. The deadline for receiving the applications is **June 15th 2017** by 16.00 CET. Please visit the ESP website for more information www.esp-pathology.org.

In light of the fact that pathology and pathologists play an increasingly vital role in clinical trials, mainly in the field of medical oncology, the ESP and EORTC invited young pathologists to apply for a joint ESP-EORTC Fellowship. It is our pleasure to introduce the first ESP-EORTC Joint Fellowship Awardee (2017), Dr. Maria Urbanowicz. Under the supervision of Prof. J-F Flejou, the Chair of the ESP's workgroup on Digestive Diseases and other key experts at EORTC, Dr. Urbanowicz will consolidate her experience and expertise in European cancer clinical research at the EORTC HQ, in Brussels.

On the occasion of being awarded the Fellowship, we have asked Dr. Urbanowicz to introduce herself (see below).

As the plans to professionalize the ESP HQ are under way, we are glad to announce the latest addition to the ESP team, as of January 2017. Our new Project Management Associate, Ms. Teodora Garbovan, will work closely with Sarah to manage and coordinate several ESP projects. We asked Teodora to introduce herself to the members of the Society (see below).

Finally, your support and opinion help outline the future of ESP and the benefits ESP provides to you as an esteemed member.

We are very proud of where we are today and thrilled about where we are headed.

“My name is Maria Urbanowicz and I am the new ESP-EORTC pathology fellow. A medical specialist in Pathology, I graduated from the University of Medical Sciences in Poznan, Poland and did my specialization at the 12 de Octubre University Hospital in Madrid, Spain.

This is just the beginning of my Brussels adventure, at the EORTC and I look forward to contributing with my expertise to clinical research programs. I chose this fellowship program because I am open to new experience and I like challenges. As my routine work as an assistant consisted of reviewing biopsies, I believe that for a pathologist, being involved in clinical research is a totally new experience. This is a big change for me and I will be doing my best to put my knowledge and experience into practice to the EORTC projects.

This fellowship is a fantastic learning opportunity for which I am extremely grateful. I think it is important for a pathologist to get a broader vision concerning research activities and to grasp the role played by diagnosis in clinical trials and the importance of a detailed assessment and accurate diagnosis of samples for a successful clinical study. I hope to make the most of my stay in Brussels!”



“My name is Teodora Gârbovan and I am the newest member of the ESP team, in Brussels, where I will be working as Project Management Associate. As a young Communications and Project Management professional I benefit from multiannual experience in both the not-for-profit and European public administration sectors. I joined the ESP team in late January and I will contribute to the coordination and management of the forthcoming ESP projects.

Apart from my project management tasks, I am in charge of writing and editing content on the ESP website and of maintaining its social media presence. My future goal is to make the ESP’s voice better heard in the virtual world so please do not hesitate to contact me if you have any newsworthy achievements in your field, any milestones in research that have been reached etc. I will be happy to promote them on our channels and spread the word.

Looking forward to meeting you and to our fruitful collaboration.”

Preparing for Amsterdam 2017

By Prof. Folkert van Kemenade



The motto of the ESP congress in Amsterdam 2017 is "Pathology for Patient Care."

That should do the job and make you want to book your tickets right now. The venue will be the RAI, a little south of

the city centre (4.5 km from Dam Square). From Schiphol Airport you can take the train (the omnibus or 'sprinter') to Amsterdam-RAI station (11 minutes). Don't take the train to Amsterdam Central, unless your hotel is there.

If you want to include more considerations into your decision to book for your next ESP Congress (September 2nd-6th 2017), here are some additional motives. Four excellent keynote speakers agreed to come to Amsterdam in order to update you on scientific progress on stem cells, inflammation, new diseases and neoplasia. This is actually your chance to see two female keynote speakers in one congress: a clear indication that the science and medicine faculty in the Netherlands is well advanced in gender equality. Of course, all the Working Groups have submitted their programmes and brought some interesting

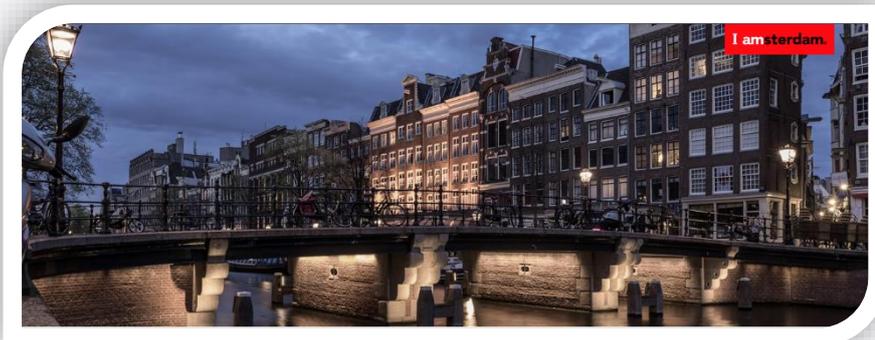
alliances as well. In addition, CPO Hanser calmly negotiates behind the scenes for the benefit of the congress. Knowing the locals in Amsterdam, the going will be tough.



Your next consideration for coming to Amsterdam may be the Dutch pathologists. Appraise some 'Netherlands Pathology' or the way they do things there. We have pre-emptively organized slots for drinks afterwards. Finally, the urban and metropolitan element should be on your pro/con list for visiting the ECP 2017 in the Netherlands. In other words: the true locals in Amsterdam.

More on that later.

Additional motives for coming to Amsterdam: the essence of our profession. Coming together, mingling, exchanging views on science and innovation, invigorating on daily practice and, above all, staying tuned on patient care are all vital for our profession. Free exchange of ideas and debate have always been Amsterdam's strengths. All this would be rather meaningless, if we do not include residents in our meeting.



They will hand down pathology to future generations. So, in Amsterdam, the residents will be organizing a part of the meeting by telling you who has best taught them. That is to say, whom they



(the residents) thought was best at teaching the tricks of the job by bringing their best teachers forward. Seize the opportunity to see their heroes. Certainly obligatory for all colleagues that are 40 and over (quite a stretch actually). Besides, haven't we all had our favourite teacher during our residencies? Ever thought of thanking them? New experts will be around as well: pathologists can take up the challenge against the machine. The consultant vs. deep learning!

Keep an eye on either the emerald or ruby room in the RAI.

The stakes are pretty high after the successful joint meeting in Cologne in 2016. In contrast with Cologne, Amsterdam will not be a joint meeting (no pun intended). As promised, more on the locals of the free city. They do their share, anticipating, so to speak, on this great event.

There will be a fundraising event for motor neuron disease: swimmers raise a minimum sponsorship before diving into the canals to swim a 2,000m course through the city centre. You can watch them on Sunday. Of course, you can also take a classic canal trip by boat (there are several points of departure). There is more in Amsterdam (or 'Mokum' in the old Yiddish vernacular) that is waiting for you: a theater festival, a fringe festival, a dance-, electro-, house-, dubstep-, hiphop- and punk fest (Amsterdam-North; on Saturday 2nd starting at 23.00).

The social programme will be in a more congruent vein than a dance festival. There will be some interesting venues on offer in - and outside of the city. Well, are you convinced? Have you already registered for the congress? Arranged your lodging?

We are looking forward to welcoming you.



29th European Congress of Pathology

Pathology for Patient Care

2 – 6 September 2017

Amsterdam RAI, The Netherlands

www.esp-congress.org

Building a European Network of Pathology Collections and Museums

By Prof. Gabriella Nesi

History Of Pathology Working Group



The History of Pathology Working Group is growing steadily through meetings, presentations and publications, thanks to the commitment of all its ESP members – of different ages and from different scientific fields – to publicize the values of

“historical discoveries, messages and material”. The ESP recognizes that such values can inspire new generations of undergraduate and postgraduate students.

The Anatomy and Pathology Museums are no exception to the gradual loss of interest in scientific museology and, not forgetting their conservative priorities, it is necessary to help them keep up with modern times if they are to maintain their original didactic role. In this regard, the same technical means and ways of communication that now rival traditional museums could contribute to their innovation and improve access to ancient collections, by digitally transferring them to photographs and documentaries, which could then be conveyed through appropriate appliances (CD-ROM, DVD) or shared via the World Wide Web. Starting with one particular anatomical specimen in the museum, a “route” can be hypothesized, which would cover patient clinical details, radiological images and histological findings, together with up-to-date bibliography on the subject. In order to provide scientific interpretation and historical contextual-

ization, this “route” would offer students an educational proposal and scholars a chance for deeper investigation. For all intents and purposes, anatomical collections are a “biological archive” amenable to research through modern radiological, pathological and biomolecular techniques.

The Pathology Museum of the University of Florence, founded in 1824, houses more than one hundred wax works and an ample number of osteological and anatomical preparations, both dried and fixed in formalin, including congenital malformations, genetic disorders and neoplasms. Furthermore, the Museum accommodates the original *Catalogo*, in which the anatomical preparations and wax works are listed and exhaustively described, and the *Registro delle Autopsie*, set up in 1839, with volumes concerning 1,469 clinical histories of autopsy cases performed between 1839 and 1881.



For the undergraduates of the Faculty of Medicine, visits to the Pathology Museum contribute significantly to their scientific, historical and cultural education. Besides, medical training was one of the main reasons behind the constitution of the Museum, intimately linked to the institu-

tion of the first Italian professorship of Pathological Anatomy at the University of Florence in 1840. The collections of the Pathology Museum have recently been restored to their original beauty and are now accessible both for didactic and research purposes. The Pathology Museum today, is part of the Museum of Natural History, under the auspices of the University of Florence.



To preserve the specimens and facilities is neither easy nor costless, and calls for patronage. In order for it to develop, a European Pathology Museum Network should aim to promote the study, access and divulgation of pathology collections. The History of Pathology Working Group intends to produce a comprehensive overview of all the multiple facets (i.e. history, diversity, location/geography, institutional status, existing networks and stakeholders, projects, professionals, audiences, policies, best practices and publications) of the European University museums.

Invitation to the Annual Meeting of the ESP History of Pathology Working Group

By Prof. Gabriella Nesi

Dear Colleagues, Dear Friends,

I have the pleasure to announce that The ESP History of Pathology Working Group (WG) is holding its Annual Meeting in **Coimbra, Portugal**, from June 30th – 1st July 2017. The conference will give the opportunity for WG members and all interested pathologists, to present their own data. Residents in pathology, PhD students and post-doctoral fellows are particularly encouraged to attend. The group is offering grants and waived registration fees for participants who are under 35.

For further details about the meeting do not hesitate to contact the local organizer, Prof. Rosa Henriques de Gouveia (rhgouveia@mail.telepac.pt), myself (gabriella.nesi@unifi.it) or the general mailbox:

wghp.esp.coimbra2017@gmail.com

We look forward to seeing you in Coimbra!

Best wishes,

Gabriella Nesi

Report from the German Society of Pathology

By Mrs. Nora Enzlberger
Assistant to the General Secretary
German Society of Pathology



In October 2016 the German Society of Pathologists hosted their third “Academy for young pathologists” in a German monastery. Twenty-six young scientists qualified for this significant instrument for promoting new talent and enjoyed

lectures and discussions with well-known German pathologists and representatives of professional organizations during a 5 day period. The three most promising participants received funding amounting to 2.000 Euros per person, for their current work. ESP and the German Society of Pathologists are considering to start a similar programme on a European level.

The upcoming 101st Annual Meeting of the German Society of Pathologists takes place between 22nd- 24th June 2017 in the Bavarian town Erlangen, Germany. Its focus lies on the pathology of head and neck, pathology and genetics, pathology and immunotherapy as well as neuropathology and neurodegeneration. Among the key-note speakers will be Prof. Mahul Amin (Cedars-Sinai Medical Center, California) on TNM-classification, Prof. Andreas von Daimling (Neuropathology Heidelberg, Germany), Prof. Hans-Georg Ramensee (Immunology Tübingen, Germany) as well as Prof. David Thomas (Darlinghurst Kinghorn Cancer Center, Australia).

More information at the link below:

<http://www.pathologie-kongress.com/kongressinformationen/informationen-in-english/>

From 3rd -5th April 2017 the Association for Molecular Pathology will host its first Global Congress on Molecular Pathology in Berlin, Germany. The German Society of Pathologists is giving the event organizational and content-related support as an Affiliate member. A multi-disciplinary scientific program showcases molecular technology with clinical applications in oncology (solid tumors, hematopathology), genetics (congenital, heritable) and infectious diseases.

We cordially invite interested pathologists and molecular biologists to join the launch of this great new series of conferences. Read more about this event here: <http://gcmp.amp.org/>

Analecta Medica

By Dr. Loukas Kaklamanis



GENETIC RISK, ADHERENCE TO A HEALTHY LIFESTYLE, AND CORONARY DISEASE

A.V. Khera, C.A. Emdin, I. Drake, et al.
NEJM 2016; 375: 2349-58

Background

Both genetic and lifestyle factors contribute to individual-level risk of coronary artery disease. The extent to which increased genetic risk can be offset by a healthy lifestyle is unknown.

Method

Using a polygenic score of DNA sequence polymorphisms, we quantified genetic risk for coronary artery disease in three prospective cohorts — 7814 participants in the Atherosclerosis Risk in Communities (ARIC) study, 21,222 in the

Women's Genome Health Study (WGHS), and 22,389 in the Malmö Diet and Cancer Study (MDCS) — and in 4260 participants in the cross-sectional BioImage Study for whom genotype and covariate data were available. We also determined adherence to a healthy lifestyle among the participants using a scoring system consisting of four factors: no current smoking, no obesity, regular physical activity, and a healthy diet.

Results

The relative risk of incident coronary events was 91% higher among participants at high genetic risk (top quintile of polygenic scores) than among those at low genetic risk (bottom quintile of polygenic scores) (hazard ratio, 1.91; 95% confidence interval [CI], 1.75 to 2.09). A favourable lifestyle (defined as at least three of the four healthy lifestyle factors) was associated with a substantially lower risk of coronary events than an unfavourable lifestyle (defined as no or only one healthy lifestyle factor), regardless of the genetic risk category. Among participants at high genetic risk, a favourable lifestyle was associated with a 46% lower relative risk of coronary events than an unfavourable lifestyle (hazard ratio, 0.54; 95% CI, 0.47 to 0.63). This finding corresponded to a reduction in the standardized 10-year incidence of coronary events from 10.7% for an unfavourable lifestyle to 5.1% for a favourable lifestyle in ARIC, from 4.6% to 2.0% in WGHS, and from 8.2% to 5.3% in MDCS. In the BioImage Study, a favourable lifestyle was associated with significantly less coronary-artery calcification within each genetic risk category.

Conclusions

One of these signatures, mainly found in cancers derived from tissues directly exposed to tobacco smoke, is attributable to misreplication of DNA damage caused by tobacco carcinogens. Others likely reflect indirect activation of DNA editing by APOBEC cytidine deaminases and of an endogenous clocklike mutational process. Smoking is associated with limited differences in methylation. The results are consistent with the proposition that smoking increases cancer risk by increasing

the somatic mutation load, although direct evidence for this mechanism is lacking in some smoking-related cancer types.

CLASSIFICATION AND CHARACTERIZATION OF MICROSATELLITE INSTABILITY ACROSS 18 CANCER TYPES

R.J. Hause, C.C. Pritchard, J. Shendure, et al.
Nature Medicine 2016; 22: 1342–50

Microsatellite instability (MSI), the spontaneous loss or gain of nucleotides from repetitive DNA tracts, is a diagnostic phenotype for gastrointestinal, endometrial, and colorectal tumours, yet the landscape of instability events across a wider variety of cancer types remains poorly understood. To explore MSI across malignancies, we examined 5,930 cancer exomes from 18 cancer types at more than 200,000 microsatellite loci and constructed a genomic classifier for MSI.

We identified MSI-positive tumours in 14 of the 18 cancer types. We also identified loci that were more likely to be unstable in particular cancer types, resulting in specific instability signatures that involved cancer-associated genes, suggesting that instability patterns reflect selective pressures and can potentially identify novel cancer drivers.

We also observed a correlation between survival outcomes and the overall burden of unstable microsatellites, suggesting that MSI may be a continuous, rather than discrete, phenotype that is informative across cancer types. These analyses offer insight into conserved and cancer-specific properties of MSI and reveal opportunities for improved methods of clinical MSI diagnosis and cancer gene discovery.

MUTATIONAL SIGNATURES ASSOCIATED WITH TOBACCO SMOKING IN HUMAN CANCER

L.B. Alexandrov, Y. Seok Ju, K. Haase, et al.
Science 2016 ; 354 :618-22

Tabacco smoking increases the risk of at least 17 classes of human cancer. We analysed somatic

mutations and DNA methylation in 5243 cancers of types for which tobacco smoking confers an elevated risk. Smoking is associated with increased mutation burdens of multiple distinct mutational signatures, which contribute to different extents in different cancers.

One of these signatures, mainly found in cancers derived from tissues directly exposed to tobacco smoke, is attributable to misreplication of DNA damage caused by tobacco carcinogens. Others likely reflect indirect activation of DNA editing by APOBEC cytidine deaminases and of an endogenous clocklike mutational process. Smoking is associated with limited differences in methylation.

The results are consistent with the proposition that smoking increases cancer risk by increasing the somatic mutation load, although direct evidence for this mechanism is lacking in some smoking-related cancer types.

MOLECULAR ANALYSIS OF CIRCULATING TUMOR CELLS IDENTIFIES DISTINCT COPY-NUMBER PROFILES IN PATIENTS WITH CHEMOSENSITIVE AND CHEMOREFRACTORY SMALL-CELL LUNG CANCER

L. Carter, D.G. Rothwell, B. Mesquita, et al.
Nature Medicine 2017; 23:114–9

In most patients with small-cell lung cancer (SCLC)—a metastatic, aggressive disease—the condition is initially chemosensitive but then relapses with acquired chemoresistance. In a minority of patients, however, relapse occurs within 3 months of initial treatment. In these cases, the disease is defined as chemorefractory. The molecular mechanisms that differentiate chemosensitive from chemorefractory disease are currently unknown.

To identify genetic features that distinguish chemosensitive from chemorefractory disease, we examined copy-number aberrations (CNAs) in circulating tumour cells (CTCs) from pretreatment SCLC blood samples. After analysis of 88 CTCs isolated from 13 patients (training set), we generated a CNA-based classifier that we validated in

18 additional patients (testing set, 112 CTC samples) and in six SCLC patient-derived CTC explant tumors¹. The classifier correctly assigned 83.3% of the cases as chemorefractory or chemosensitive.

Furthermore, a significant difference was observed in progression-free survival (PFS) (Kaplan–Meier P value = 0.0166) between patients designated as chemorefractory or chemosensitive by using the baseline CNA classifier. Notably, CTC CNA profiles obtained at relapse from five patients with initially chemosensitive disease did not switch to a chemorefractory CNA profile, which suggests that the genetic basis for initial chemoresistance differs from that underlying acquired chemoresistance.

THE GENOMIC LANDSCAPE OF SCHWANNOMA

S. Agnihotri, S. Jalali, M.R. Wilson, et al.
Nature Genetics 2016; 48:1339–48

Schwannomas are common peripheral nerve sheath tumours that can cause debilitating morbidities. We performed an integrative analysis to determine genomic aberrations common to sporadic schwannomas. Exome sequence analysis with validation by targeted DNA sequencing of 125 samples uncovered, in addition to expected NF2 disruption, recurrent mutations in ARID1A, ARID1B and DDR1.

RNA sequencing identified a recurrent in-frame SH3PXD2A-HTRA1 fusion in 12/125 (10%) cases, and genomic analysis demonstrated the mechanism as resulting from a balanced 19-Mb chromosomal inversion on chromosome 10q. The fusion was associated with male gender predominance, occurring in one out of every six men with schwannoma. Methylation profiling identified distinct molecular subgroups of schwannomas that were associated with anatomical location.

Expression of the SH3PXD2A-HTRA1 fusion resulted in elevated phosphorylated ERK, increased proliferation, increased invasion and in vivo tumorigenesis. Targeting of the MEK-ERK pathway

was effective in fusion-positive Schwann cells, suggesting a possible therapeutic approach for this subset of tumours.

CLINICOPATHOLOGICAL AND MOLECULAR FEATURES OF SESSILE SERRATED ADENOMAS WITH DYSPLASIA OR CARCINOMA

M. Bettington, N. Walker, C. Rosty, et al.
Gut. 2017; 66:97-106

Objective

Sessile serrated adenomas (SSAs) are the precursors of at least 15% of colorectal carcinomas, but their biology is incompletely understood. We performed a clinicopathological and molecular analysis of a large number of the rarely observed SSAs with dysplasia/carcinoma to better define their features and the pathways by which they progress to carcinoma.

Design

A cross-sectional analysis of 137 SSAs containing regions of dysplasia/carcinoma prospectively collected at a community GI pathology practice was conducted. Samples were examined for BRAF and KRAS mutations, the CpG island methylator phenotype (CIMP) and immunostained for MLH1, p53, p16, β -catenin and 0–6-methylguanine DNA methyltransferase (MGMT).

Results

The median polyp size was 9 mm and 86.5% were proximal. Most were BRAF mutated (92.7%) and 94.0% showed CIMP. Mismatch repair deficiency, evidenced by loss of MLH1 (74.5%) is associated with older age (76.7 versus 71.0; $p < 0.0029$), female gender (70% versus 36%; $p < 0.0008$), proximal location (91% versus 72%; $p < 0.02$), CIMP (98% versus 80%; $p < 0.02$) and lack of aberrant p53 (7% versus 34%; $p < 0.001$) when compared with the mismatch repair-proficient cases. Loss of p16 (43.1%) and gain of nuclear β -catenin (55.5%) were common in areas of dysplasia/cancer, irrespective of mismatch repair status.

Conclusions

SSAs containing dysplasia/carcinoma are predominantly small (<10 mm) and proximal. The mismatch repair status separates these lesions into distinct clinicopathological subgroups, although WNT activation and p16 silencing are common to both. Cases with dysplasia occur at a similar age to cases with carcinoma. This, together with the rarity of these 'caught in the act' lesions, suggests a rapid transition to malignancy following a long dwell time as an SSA without dysplasia.

Some recently published books

By Prof. Metka Volavšek



NOSE, PARANASAL SINUSES, AND NASOPHARYNX TEXTBOOK OF HEAD AND NECK PATHOLOGY, VOL 1

Margaret S. Brandwein-Gensler

168 pages, 120 illus, €65, Springer (2016)

The first of a multi-volume set, this textbook covers sinonasal and nasopharyngeal pathology. An ideal sign-out resource for head and neck pathology, it includes anatomy, staging, diagnostic, and prognostic information. Richly illustrated and well-structured, the easily accessible format includes glossaries, boxes of key points, and self-assessment questions at the end of each chapter.

DIFFERENTIAL DIAGNOSES IN SURGICAL PATHOLOGY: HEAD AND NECK

William H Westra, Justin Bishop

448 pages, 1084 illus, €165, Wolters Kluwer (2016)

Systematically solve tough diagnostic challenges in head and neck pathology with this new title in the Differential Diagnoses in Surgical Pathology series. This practical, full-color reference uses select images of clinical and pathological findings, together with succinct, expert instructions, to guide you through the decision-making process by distinguishing between commonly confused lesions of the head and neck. By presenting material according to the way pathologists actually work, this user-friendly volume helps you quickly differentiate entities that have overlapping morphologic features.

BIOPSY INTERPRETATION OF THE THYROID

Sylvia L Asa, Scott L Boerner

Series: Biopsy Interpretation

2nd ed, 300 pages, 400 illus, €160, Wolters Kluwer (2016)

Extensively revised to bring you up to date with new pathologic entities, new treatment methods, and much more, Biopsy Interpretation of the Thyroid, Second Edition is a highly practical guide to neck biopsies that involve thyroid tissue. Presented in a reader-friendly format, it uses a pattern-based approach to the accurate interpretation of thyroid lesions – from normal anatomy and histology to a wide range of both common and unusual findings. Clinical implications of each diagnosis are highlighted throughout the text to guide therapeutic decision making.

STATISTICS FOR PATHOLOGISTS

Danny A. Milner Jr., Rinda Soong, Emily E. K. Meserve, Douglas A. Mata

206 pages, €75, DemosMedical (2016)

This essential guide provides a clear, accessible review of the use of statistics in pathology studies. Spanning topics such as exploratory data analysis and descriptive statistics as well as the use of comparative statistics, concordance analysis, categorical and continuous data regression analyses, count data, survival analyses, decision point and clustering analysis, and more, this practical book comprehensively demystifies all the

statistical knowledge paramount to working in the field. Throughout the guide, the author team highlights common errors and pitfalls that occur while performing tests and interpreting data and they make suggestions on how to avoid mistakes. Chapters are uniformly structured for ease of use and each chapter concludes with review questions to facilitate self-assessment of the reader's skill in use of statistical methods.

HANDBOOK OF HEMATOLOGIC MALIGNANCIES

David A. Sallman, Alan F. List, Ateefa Chaudhury, Johnny Nguyen, Ling Zhang

402 pages, €80, DemosMedical (2016)

Handbook of Hematologic Malignancies provides a unique, practical, and concise guide focused on the must-know points of diagnosis, prognosis, therapeutic management, and cutting edge clinical trial opportunities for each hematologic malignancy. With an ever-increasing growth of evidence and a significant expansion of available treatment options for patients with hematologic disease, remaining current and up-to-date can be extremely challenging for practicing clinicians. This comprehensive subspecialty handbook is designed and organized for the busy haematologist, hematologic oncologist and trainee in mind.

PATHOLOGY OF OPPORTUNISTIC INFECTIONS AN ILLUSTRATIVE ATLAS

Ramesh K Gupta, Pallav Gupta, (Eds.)

175 pages, 105 illus, €180, Springer (2017)

This book presents the morphological details of various opportunistic pathogens for prompt identification, which is essential for the proper management of various bacterial, viral, fungal and parasitic infections encountered in immunocompromised patients.

PATHOLOGY OF LUNG DISEASE MORPHOLOGY – PATHOGENESIS – ETIOLOGY

Helmut Popper

699 pages, 632 illus, €230, Springer (2017)

This well-illustrated textbook covers the full range of lung and pleural diseases from the pathologic standpoint. Both diseases of adults and paediatric lung diseases are presented. The book will serve as an excellent guide to the diagnosis of these diseases, but in addition it explains the disease mechanisms and etiology. Genetics and molecular biology are also discussed whenever necessary for a full understanding. The author is an internationally recognized expert who runs courses on lung and pleural pathology attended by participants from all over the world. In compiling this book, he has drawn on more than 30 years' experience in the field.

**BREAST PATHOLOGY
PROBLEMATIC ISSUES**

Sami Shousha (Ed.)

283 pages, 173 illus, €170, Springer (2017)

This book covers practical diagnostic issues in breast pathology, with special emphasis on areas which pose diagnostic difficulties. These include dealing with the gross specimens derived from patients treated with conservative surgery and those who had neo-adjuvant therapy before surgery. It also discusses how to deal with axillary lymph nodes, proliferative breast lesions, including DCIS, and problematic core biopsies, as well as fibro-epithelial, spindle cell, lobular, mucinous, metaplastic and papillary lesions, molecular classification of breast cancers, breast lesions in male patients and breast immunohistochemistry. There is a focus on unusual benign and malignant breast lesions and a large number of high-quality images help the reader diagnose difficult cases.

DIFFERENTIAL DIAGNOSES IN SURGICAL PATHOLOGY: GYNECOLOGIC TRACT

Russell Vang, Anna Yemelyanova, Jeffrey D. Seidman

544 pages, 1600 illus, €165, Wolters Kluwer (2017)

Systematically solve tough diagnostic challenges in gynaecologic pathology with this new title in the Differential Diagnoses in Surgical Pathology

series. This practical, full-colour reference uses select images of clinical and pathological findings, together with succinct, expert instructions, to guide you through the decision-making process by distinguishing between commonly confused lesions of the gynaecologic tract. By presenting material according to the way pathologists actually work, this user-friendly volume helps you quickly differentiate entities that have overlapping morphologic features.

**ROSEN'S DIAGNOSIS OF BREAST PATHOLOGY BY
NEEDLE CORE BIOPSY**

Edi Brogi, Paul P Rosen, Syed A Hoda, Frederick C Koerner

4th ed, 544 pages, 1477 illus, €220, Wolters Kluwer (2017)

Accurately identify the full range of clinical and pathological entities with Rosen's Diagnosis of Breast Pathology by Needle Core Biopsy, Fourth Edition! With guidance from the same trusted authorities responsible for the esteemed clinical reference, Rosen's Breast Pathology, you'll gain masterful insights on how to confidently meet diagnostic challenges on needle core biopsy material. These challenges are summarized in the three maxims stated by Dr Paul Peter Rosen in the Preface to the First Edition of this book, and which continue to be relevant today: 1. Anything can turn up. 2. What you see is what you have. It may not be all there is. 3. What you see may be all there is. The pathologist must always keep these precepts in mind when offering a diagnosis based on limited material in needle core biopsy samples. This book will serve as a complete guide to interpreting this material.

WHO CLASSIFICATION OF HEAD AND NECK TUMOURS

WHO/IARC CLASSIFICATION OF TUMOURS, 4TH EDITION, VOLUME 9

El-Naggar AK, Chan JKC, Grandis JR, Takata T, Sloatweg PJ (Eds)

4th ed, 347 pages, 600 illus, IARC (2017)

The WHO Classification of Head and Neck Tumours is the ninth volume in the 4th Edition of the WHO series on histological and genetic typing of human tumours. This authoritative, concise reference book provides an international standard for oncologists and pathologists and will serve as an indispensable guide for use in the design of studies evaluating response to therapy and clinical outcome.

Diagnostic criteria, pathological features, and associated genetic alterations are described in a disease-oriented manner. Sections on all recognized neoplasms and their variants include new ICD-O codes, epidemiology, clinical features, macroscopy, pathology, genetics, and prognosis and predictive factors.

FROM MAGIC TO MOLECULES: AN ILLUSTRATED HISTORY OF DISEASE

Jan G. van den Tweel, Jiang Gu, Clive R. Taylor
670 pages, 600 illus, 80 €, Peking University Medical Press (2016)

The book is about the lives and times of those remarkable men and women whose work changes our understanding of the nature and cause of diseases that affected mankind over recorded history. It traces the earliest expressions of disease in prehistory on to the theories of the great Greek, Roman and Arabic practitioners of medicine, such as Hippocrates, Galen and Avicenna. In addition, it covers the rise of the Renaissance anatomists and the beginnings of a "scientific approach"; Morgagni, Da Vinci, Vesalius.

Next came the philosopher scientists of the 18th, 19th and 20th centuries; The Hunter Brothers, The Monros, Laennec, Dupuytren, Cruvelhier, Virchow, Paget, Harvey, Hodgkin, Osler, and a host of others in Western, Chinese and Japanese medicine. What makes the book unique, is the organ based approach of the 20th century when subspecialties were created by brilliant visionary men and women who gave the shape to medicine as we see it today.

Forthcoming Meetings in 2017

By Prof. Metka Volavšek



Diagnostic Methods in Pathology

March 22, 2017
Tromsø, Norway

1st Global Congress on Molecular Pathology

Association for Molecular Pathology
April 3-5 April 2017
Berlin, Germany

1st Cologne Conference on Lung Cancer

April 6-7, 2017
Cologne, Germany

2nd Meeting of the Pannonian Working Group of Gastrointestinal Pathology

"Pathology of the Anus and Rectum"
April 7-8, 2017
Ljubljana, Slovenia

4th IAP Pakistan Division AGM & 7th Annual HCSP Meeting

April 7-8, 2017
Karachi, Pakistan

Update in Hematopathology

April 8-9, 2017,
Palm Springs, California, USA

Gastrointestinal Lymphomas

April 12-14, 2017
Palm Springs, California USA

10th Asia Pacific International Academy of Pathology (APIAP)

April 24–27, 2017
Bali, Indonesia

The Pathology of Melanoma: An International Course

April 27-28, 2017
Paris, France

**BSOMP: Annual Scientific Meeting 2017
British Society of Oral & Maxillo-facial Pathologists (BSOMP)**

April 27-28, 2017
Cardiff, United Kingdom

**AAOMP: Annual Meeting 2017
American Academy of Oral and Maxillofacial Pathology (AAOMP)**

April 28 – May 3, 2017
Newport, USA

**BSCCP: 2017 Annual Scientific Meeting
British Society for Colposcopy and Cervical Pathology (BSCCP)**

May 3-5, 2017
Cardiff, United Kingdom

Recurring Problems in Breast Pathology and How to Resolve Them

May 5-7, 2017,
Palm Springs, California, USA

Genito-Urinary Tract Tumors Course

May 11-12, 2017,
Florence, Italy

Urologic Pathology in 2017: Emerging Concepts, WHO Classification and AJCC Updated

May 19-21, 2017
Palm Springs, California, USA

24th Baltic-German Symposium for Pathology of the German Division of IAP and 6th Symposium of the Baltic IAP Division

May 24–28, 2017
Riga, Latvia

The European Human Genetics Conference

May 27-30, 2017
Copenhagen, Denmark

**2017 Edinburgh Haematopathology Tutorial
"Phenotype and Genotype: Implications for Lymphoma Classification"**

June 1-2, 2017
Edinburgh, United Kingdom

2017 Australasian Division ASM

June 2–4, 2017
Sydney, Australia

Head and Neck Surgical/Cytopathology

June 3-4, 2017
Palm Springs, California, USA

**Basel Seminars in Pathology 2017
"Skin pathology"**

June 9-10, 2017
Basel, Switzerland

The 4th "Kidney Tumor Friends" Meeting

June 16-17, 2017
Plzen, Czech Republic

Belfast Pathology 2017

10th Joint Meeting of the British Division of the International Academy of Pathology and the Pathological Society of Great Britain & Ireland

June 20-23, 2017
Belfast, Northern Ireland

4th World Congress on Breast Pathology and Cancer Diagnosis

August 23-24, 2017
Toronto, Ontario, Canada

Head and Neck Pathology - Start to Finish

June 23-25, 2017
Palm Springs, California, USA

13th International Conference on Pathology

June 26-27, 2017
San Diego, USA

29th European Congress of Pathology
“Pathology for patient care”
September 2-6, 2017
Amsterdam, The Netherlands

63rd Annual Meeting of the Paediatric Pathology
Society (PPS)
September 7-9, 2017
Lisbon, Portugal

Mayo Clinic Pulmonary Pathology Workshop
2017
September 8-9, 2017
Budapest, Hungary

