Word from the President Prof. F. Carneiro

Since the last Newsletter (Winter 2012) an intense activity has been developed by the ESP in different fronts.

One of the major actions was the revision of the ESP Statutes and Bylaws, in order to acknowledge the new management model and to fulfill the aims and current challenges of the Society. The ESP lawyer and accountant played a crucial role during this quite long process. The revised Statutes and Bylaws will be made available to the ESP members who will be invited to provide suggestions and comments for improvement. This is indeed a major issue and I would like to stress that we need your collaboration from now until September 4, 2013. This is the date of the General Assembly, the body that has the sole authority to change the Statutes and Bylaws. For that purpose a massive attendance of the next General Assembly (during the Lisbon Congress) is required and the ESP counts on the mobilization of its members to achieve this goal. The new version of the Statutes, translated to Dutch language, will be published in the Belgian Official Gazette (“Bijlagen bij het Belgisch Staatsblad”), to conform to provisions of Belgian law.

The Executive Committee has been engaged in the nomination and electoral process for the offices of President-elect and Secretary and the four new Executive Committee members. The procedure has followed the current Statutes and Bylaws. In this Newsletter you will find the recommendations of the Executive Committee for the aforementioned positions as well as an invitation for other nominations.

The initiative on International Collaboration on Cancer Reporting (ICCR) acknowledged the request of the ESP to work with the ICCR on common datasets, to be included in the expert groups and to have representation on the writing committees. In the future, when the ICCR embarks on a dataset of a new organ site, a member of the relevant ESP WG will be included in the expert group. European pathologists will now join those of the USA, Canada, Australia and the UK as partners in this international collaborative effort and the ESP will provide an ESP nominee on the ICCR organizing committee.

The preparation of the Lisbon Congress (August 31 – September 4) is quite advanced. The preliminary programme was published and distributed to all ESP members and is available at the Congress website (www.esp-congress.org). The scientific activities will be centered upon Diagnosis, Prognosis and Prediction, having Personalized Pathology as the ultimate goal. Following the motto of the Congress – “Pathology – A gate to the future” – a particular attention has been paid to the Residents who will organize, among other scientific and social activities, a Plenary Residents Seminar whose “Grande Finale” will take place at the closing events of the Congress. For the purpose of the Plenary Residents Seminar (PRS), 12 leading Departments of Pathology from Portugal were invited to submit 2 cases each, that will be available online every month from January to June 2013 (4 cases each month). From the 24 cases that were received, 12 cases were selected for the “Grande Finale”

Continues on p.2
Continues from p.1

cases, 4 will be selected by Prof. Ales Ryska to be presented at the Congress by the Residents. To make this initiative as lively as possible, all Pathologists and Residents are invited to observe and discuss the cases, make comments and propose diagnoses. To have access to the cases you just have to connect to http://prs.slidesci.org/ and follow the simple instructions displayed on screen.

The preparation of the 26th ECP is moving smoothly, in a joint organization of the ESP and the Pathological Society of Great Britain & Ireland. This Congress will be held in London, from 30 August to 3 September 2014. Future Congresses approved by the last General Assembly of the ESP will be held in Belgrade (2015) and Cologne (2016), the latter jointly organized by the ESP and the German Division of the IAP. Proposals from the ESP Executive Committee for the venues for ECP 2017 (Amsterdam) and ECP 2018 (Bilbao) will be presented in the next General Assembly (during the Lisbon Congress).

The Education Committee has been deeply involved in the process of building the Education Portal, to be opened (hopefully) before the Lisbon Congress.

A very fruitful meeting on external quality assurance (EQA) in molecular pathology was held in Naples, March 22-23, 2013. The action plan derived from this meeting encompasses several initiatives, including the proposal to create a European database for EQA schemes in molecular pathology.

Looking forward to the Lisbon Congress, the ESP invites all of you to visit the Congress website (www.esp-congress.org).

It will be a pleasure to welcome you in Lisbon!

Fátima Carneiro
LISBON CONGRESS

Concert at São Carlos National Theatre
performed by the Coro Gulbenkian (conducted by Jorge Matta)
Programme Summary
(for further details please visit the website of Lisbon Congress: http://www.esp-congress.org)

The program opens up a panoramic soundscape, even though still partial, onto the musical life ongoing in Portugal and Brazil between the middle of the 17th century and the early years of the 19th century and in two very particular contexts. The first is that of the official sacred music played at the great liturgical festivals of the Patriarchal Church of Lisbon and so very often in the presence of the royal court alongside other senior political and ecclesiastical dignitaries from the reign of King João V onwards. This model would naturally bear repercussions on the musical repertoire performed in the main cathedrals across Brazil throughout the colonial period by Portuguese and Brazilian chapel masters with prominent maestros including André da Silva Gomes, in São Paulo, and José Maurício Nunes Garcia, in Rio de Janeiro. These ostentatious religious ceremonies frequently had the royal court of King João VI in attendance after 1808 following its relocation to Brazil due to the vicissitudes of history.

The second specific context evoked is the sacred repertoire of the black or Creole Villancicos deriving from the Augustine monks of the Santa Cruz Monastery of Coimbra in the mid-17th century. Among the monastery’s residents, there were a number of highly talented musicians and composers with high levels of education given that the majority were from aristocratic backgrounds. They produced this interesting set of sacred musical works composed for the liturgical celebration of Christmas and distinctively theatrical in nature and with a strong festive dimension. One particularly curious facet of this repertoire is its incorporation of a series of linguistic characteristics, rhythms and lyrics from different ethnic backgrounds – especially from Portugal’s African colonies – that had been interweaving with the Portuguese social reality ever since the 16th century. This musical repertoire, with every indication that it was produced within the church context, very suggestively illustrates the cultural interchange that had gradually taken root in daily interactions and relationships ongoing between persons from different ethnic backgrounds within the context of the pluri-continental Portuguese monarchy towards the end of the Ancien Régime.

Mariana Portas
Election of Officers of the European Society of Pathology

At the General Assembly in Lisbon in September 2013, the following officers will demit office:

**President-elect** Prof. Han van Krieken (as from September 2013 **President of the ESP**)

**Secretary** Prof. Ilmo Leivo (Prof. Leivo has expressed his willingness to continue his work as Secretary for another four years)

The ESP Executive Committee:

Prof. Aurelio Ariza
Prof. Jean François Fléjou
Prof. Janina Kulka
Prof. Arzu Ensari
Prof. Generoso Bevilacqua
Prof. Silvana Di Palma
Prof. Laurence de Leval
Prof. Hans Kreipe

recommends these individuals for the following positions:

*President elect with effect from September 2013:

**Prof. Pierre Bedossa** (Paris, France)

*Secretary with effect from September 2013

**Prof. Ilmo Leivo** (Turku, Finland)

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 the members of the society and accompanied by an abbreviated CV of no more than one page.

Prof. Fatima Carneiro
ESP President

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Election of Four New Members of the Executive Committee of the ESP.

At the General Assembly in Lisbon in September 2013, the following four members of the Executive Committee will demit office:

Prof. Generoso Bevilacqua
Prof. Silvana Di Palma
Prof. Laurence de Leval
Prof. Hans Kreipe

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

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

Their brief CVs are available on request.

These recommended candidates will be presented for formal approval at the General Assembly in Lisbon in September 2013.

Prof. Fatima Carneiro
ESP President
This photo (Fig.1) was taken at the Norwegian Radium Hospital, Oslo, in March 1985, during the meeting of the Scientific Committee of the X European Congress of Pathology (ECP) that would be held in Athens, Sept 1-6, 1985.

This meeting was held one year after the Joint meeting of the Executive Committee of the European Society of Pathology (ESP) and the Scientific Committee of the X ECP (Fig. 2) also at the Norwegian Radium Hospital, Oslo, on March 10, 1984.

Prof. Jan Vincents Johannessen (1) was the President and Prof. Sture Falkmer the Secretary of the ESP.

The most important point of the agenda of the Joint meeting (1984) was the forthcoming Athens Congress: The President, the late Prof. N. Papacharalampous (2), the Chairman of the Local Organising Committee (LOC), the late Prof. George Tiniakos (3) and the General Secretary, Prof. Niki Agnantis (4) gave a detailed description of the on-going organization. It was decided that the early registration fee would be “USD 200 for members of the European Society of Pathology and USD 220 for non-members. After June 1, 1985, the fee will be USD 220 and USD 250, respectively”. It was also decided that “Because of the present difficult situation as regards the possibility to obtain foreign currency, the participants from the East-European countries may be exempted from paying the registration fee”.

The Executive Committee decided also that “At the X Congress in Athens, honorary membership will be given to Profs Groniowski, Nezelof and Piringer-Kuchinka. On the same occasion, Prof. Hedinger will be nominated for honorary membership at the XI Congress in Prague, 1987”.

The sequence of the ESP Presidents in this period was the following: Prof. J. V. Johannessen was the President of the Society in the Athens Congress (1985), Prof. G. Seifert (5) in the Prague Congress (1987) and Prof. A. Llombart-Bosch (6) in the Porto Congress (1989). Prof. D. Ferluga (7), who had been ESP President in the Hamburg Congress (1983), proposed Ljubljana as site for the 1991 ECP that was eventually cancelled due to the regional war. Prof. D. Ferluga organized later on, in 2003, a superb Congress in Ljubljana, Slovenia (XIX ECP).

The other gentlemen in the picture are Prof. D. Williams (8), Prof. G. Coggi (9), Prof. D. Serrão (10) and Prof. A. Hecht (11).

The links with the forthcoming Lisbon Congress – XXV ECP (August 31-Sept 4, 2013)

Professor Daniel Serrão had suggested Lisbon as the XII ECP (1989) but the Executive Committee decided it would be better to hold it in Porto, having Prof. Antonio Llombart-Bosch as ESP President, Prof. Daniel Serrão as Congress President and Manuel Sobrinho-Simões as Chairman of the LOC. Fátima Carneiro had just got her Specialist degree and has been one of the driving forces of the LOC of the XII ECP. One of the Plenary Sessions of the Lisbon Congress will commemorate the 150th anniversary of the creation of the Academic Chairs of Pathology in Coimbra, Lisbon and Porto, having Prof. Daniel Serrão as Guest Speaker and Prof. Antonio Llombart-Bosch as Chairperson.

Fifty years ago (March 30, 1963), Prof. Giordano chaired, in Brussels, the Foundation Meeting of the ESP. The meeting was attended by Prof. Scarff (UK), Prof. Mellgren (Sweden), Prof. Orcel (France), Prof. Krauspe (West Germany), Prof. Schornagel (The Netherlands) and, as representatives of the “Société Belge d’ Anatomie Pathologique”, Prof. Maisin, Prof. Dustin and Prof. Betz. At the Lisbon Congress we will commemorate the 50th anniversary of the ESP founding event in a Plenary Session chaired by Prof. D. Ferluga and having Prof. J.V. Johannessen as Guest Speaker.

Dina Tiniakos, daughter of Prof. George Tiniakos, will organise together with Anna Batiastatou an art exhibition – “Art Paths in Lisbon” – that will be held at the Lisbon Congress (for details, please visit the website: http://esp-pathology.org).

All the former Presidents and Officers of the ESP have been invited to attend the XXV ECP and it would be a privilege to host them in Lisbon. Besides the ESP personalities who have been in charge of the ESP activities in the XXI century, we hope to have in Lisbon Prof. C. Nezelof, Prof. S. Falkmer, Prof. G. Seifert, Prof. U. van Haelst and Christine van Haelst, Prof. C. Berry, Prof. G. Coggi, Prof. J.M. Nesland, Prof. R. Heimann and Prof. G. Klöppel.

Porto, March 25, 2013

Fátima Carneiro                                      Manuel Sobrinho-Simões
Continues from p. 5 *In Ilo Tempore*

Legends:

Fig. 1 – Members of the Scientific Committee of the X European Congress of Pathology (ECP), in the Norwegian Radium Hospital, Oslo, March 1985.

Fig. 2 – Minutes of the Joint meeting of the Executive Committee of the European Society of Pathology (ESP) and the Scientific Committee of the X European Congress of Pathology (ECP), Oslo, March 1984.
The Quality assurance program on KRAS testing of the ESP: ongoing progress.

The number of molecular tests, we as pathologists perform for treatment decisions increases rapidly. As we all know, these new tests need a different approach to validation and external quality assurance (EQA) and it is therefore that the ESP had decided to set up a European program for EQA for KRAS mutational analysis in colorectal cancer. This program was set up with emphasis on the close interaction of pathologists and molecular biologists under the guidance of Els Dequeker, who is very experienced in quality assurance for molecular tests. The set-up of the program was supported by Amgen. The outline and early results of this program has been described earlier in the newsletter, was published in Virchows Archive (and is well received: 123 citations within 4 years), and the Oncologist. More than 300 laboratories participated so far and those with a good result can be found via the ESP website. Next to KRAS mutation testing for patients with colorectal cancer, ALK and EGFR testing has become the topic of external quality assurance. This first round was completed in 2012 and the second is ongoing, with Eric Thunnissen as coordinator. Important developments have taken place and through the quality assurance program we learned a lot. We know now that each round about 10-15% laboratories have not a good enough result. We have learned that we are able to indicate laboratories that are not good enough, and also that then can improve based on our feedback. We know that for colorectal cancer and KRAS testing the primary tumor is reliable and there is no need to take a biopsy from a metastasis. The crucial issue of number of tumor cells in a sample, the problems with sensitivity in case there are few has become very apparent. The value and problems of artificial slides in quality assurance have become clear. Finally, recently a document was published in Virchows archive which gives a guideline for the organization of quality assurance program in molecular pathology.

There are nevertheless still quite some challenges. Next generation sequencing is rapidly replacing standard methods and the number of genes that need to be evaluated in a certain tumor is increasing. These two developments go along together very well, but it is extremely difficult to create reliable quality assurance for such approaches. In March 22nd-23rd, the 2nd meeting on quality assurance in molecular pathology took place in Naples, organized by Nicola Normanno, and this was one of the major topics.

It is the vision of the ESP that molecular pathology is now an integrated part of pathology and thus it is important high quality can be delivered. Where possible the ESP wishes to support this vision. Much more information can be found on the website.

Han van Krieken

References:


On 22nd-23rd March 2013 in Naples, the second meeting on quality assurance on molecular pathology took place. The event was sponsored by the ESP, AIOM and SIAPEC. Almost thirty people attended the meeting representing academia, pharma, and industries. The event was chaired by Prof. Van Krieken from the ESP and Prof. Normanno from the AIOM.

During the meeting many topics were discussed and series of actions were planned. Task forces were created to deal with the important points listed below:

- There is a need for formal recognition of the present group/initiative by European agencies and/or accreditation bodies.
- There is need for a guideline on reporting based on existing documents like the ISO norm, the CAP guideline and others.
- There is need for recognition of clinical molecular biologists in pathology/clinical scientist in molecular pathology by the ESP.
- The ESP is advised to create a label for EQA programs in molecular pathology.
- There is good progress in the creation of a database with results of EQA schemes. This project will move on with support of the ESP.
- EQA programs for FISH for ALK alterations and Her2 amplifications are already being developed/executed. For diagnostic tests for lymphoma and sarcoma there is an unmet need.
- The need for a guideline on criteria for laboratories that perform molecular tests was recognised and will be addressed.
- It is very clear that a need for EQA for platforms/NGS approaches is going to be needed soon. A group will create the first ideas.

The group will meet again in September this year during the European Congress of Pathology of the ESP in Lisbon in order to report on the developments of the above-described action points.

It was felt that more parties should be invited to participate in the future QA in molecular pathology meetings, such as: patients, statisticians, and regulators.

Next year 2014, the group will meet again in Naples as it is considered a perfect meeting location and the event was organized smoothly by AIOM represented locally by Prof. Nicola Normanno. Most important, the meeting was very successful with many decisions and actions derived of a great importance for the future of molecular pathology.

I am glad to summarize the recent activities of the Gynaecological Pathology Working Group in 2012 and to inform about the future activities of the Group.

During last year, major effort was given to prepare the guidelines on tumour sampling and reporting of ovarian surface epithelial/stromal tumours. After a systematic review of published studies, the analysis of WHO classification, and of FIGO staging, the guidelines, drafted by myself and Dr. Lynn Hirschowitz (Birmingham, UK), were revised by six distinguished experts of our group namely Harry Holлемa; Sigurd Lax; Glenn McCluggage; Francisco Nogales; Jaime Prat; and Michael Wells. These guidelines have been presented during the business meeting of our Group at the 24th European Congress of Pathology held in Prague on September 2012 and endorsed by the group members and ultimately presented to the ESP Executive Board. These guidelines represent a tentative to homogenize the pathologists’ referrals around Europe, since the attitudes are quite different among different areas and different regions.

The document can be freely downloaded from the ESP website (http://www.esp-pathology.org/pdf/GYN%20WG%20Recommendations%20PoPr.pdf).

We warmly invite you to diffuse the guidelines in your practice and in your country.

For this year, we are focusing on a questionnaire relative to the sampling and the reporting of cervical, vaginal, and vulvar pathology: the questionnaire will be sent soon to the Group Members. We would like to prepare a survey on the different ways of sampling and working in this area and we hope to be able to present and discuss the results at the next Lisbon ESP Congress.

Our Chair Harry Holлемa has worked hard to provide the Prague Congress with excellent sessions on Gynaecological Pathology. All were highly scientific and very well attended and we are also thankful to our members who have provided unusual cases discussed in a specific session. He has also finalised the program of the next Lisbon Congress: the leitmotiv this year will be the pathology of cervix. Again some of you have already submitted excellent difficult cases for discussion and I forecast a very lively session.

Looking forward to see you many in Lisbon in September.

Best personal regards,

Maria Rosaria Raspollini Secretary/Elected Chair
Gynaecological Pathology Working Group
No significant heterogeneity existed between studies. The population attributable risk fraction for the United States was estimated to be 8.2% for squamous cell carcinoma and 3.7% for basal cell carcinoma. This corresponds to more than 170,000 cases of non-melanoma skin cancer each year attributable to indoor tanning. On the basis of data from three studies, use of indoor tanning before age 25 was more strongly associated with both squamous cell carcinoma (relative risk 2.02, 0.70 to 5.86) and basal cell carcinoma (1.40, 1.29 to 1.52).

Conclusions Indoor tanning is associated with a significantly increased risk of both basal and squamous cell skin cancer. The risk is higher with use in early life (<25 years). This modifiable risk factor may account for hundreds of thousands of cases of non-melanoma skin cancer each year in the United States alone and many more worldwide. These findings contribute to the growing body of evidence on the harms of indoor tanning and support public health campaigns and regulation to reduce exposure to this carcinogen.

Abstract

Objective To synthesise the literature on indoor tanning and non-melanoma skin cancer.
Design Systematic review and meta-analysis.
Data sources PubMed (1966 to present), Embase (1974 to present), and Web of Science (1898 to present).

Study selection All articles that reported an original effect statistic for indoor tanning and non-melanoma skin cancer were included. Articles that presented no data, such as review articles and editorials, were excluded, as were articles in languages other than English.

Data extraction Two investigators independently extracted data. Random effects meta-analysis was used to summarise the relative risk of ever use versus never use of indoor tanning. Dose-response effects and exposure to indoor tanning during early life were also examined. The population attributable risk fraction for the United States population was calculated.

Results 12 studies with 9328 cases of non-melanoma skin cancer were included. Among people who reported ever using indoor tanning compared with those who never used indoor tanning, the summary relative risk for squamous cell carcinoma was 1.67 (95% confidence interval 1.29 to 2.17) and that for basal cell carcinoma was 1.29 (1.08 to 1.53).
Atherosclerosis is thought to be a disease of modern human beings and related to contemporary lifestyles. However, its prevalence before the modern era is unknown. We aimed to evaluate preindustrial populations for atherosclerosis.

Methods
We obtained whole body CT scans of 137 mummies from four different geographical regions or populations spanning more than 4000 years. Individuals from ancient Egypt, ancient Peru, the Ancestral Puebloans of southwest America, and the Unangan of the Aleutian Islands were imaged. Atherosclerosis was regarded as definite if a calcified plaque was seen in the wall of an artery and probable if calcifications were seen along the expected course of an artery.

Findings
Probable or definite atherosclerosis was noted in 47 (34%) of 137 mummies and in all four geographical populations: 29 (38%) of 76 ancient Egyptians, 13 (25%) of 51 ancient Peruvians, two (40%) of five Ancestral Puebloans, and three (60%) of five Unangan hunter gatherers (p=NS). Atherosclerosis was present in the aorta in 28 (20%) mummies, iliac or femoral arteries in 25 (18%), popliteal or tibial arteries in 25 (18%), carotid arteries in 17 (12%), and coronary arteries in six (4%). Of the five vascular beds examined, atherosclerosis was present in one to two beds in 34 (25%) mummies, three to four beds in 11 (8%), and in all five vascular beds in two (1%). Age at time of death was positively correlated with atherosclerosis (mean age at death was 43 [SD 10] years for mummies with atherosclerosis vs 32 [15] years for those without; p=0.0001) and with the number of arterial beds involved (mean age was 32 [SD 15] years for mummies with no atherosclerosis, 42 [10] years for those with atherosclerosis in one or two beds, and 44 [8] years for those with atherosclerosis in three to five beds; p<0.0001).
METHODS

We compared the radiographic imaging of tumors with the assay of circulating tumor DNA, CA 15-3, and circulating tumor cells in 30 women with metastatic breast cancer who were receiving systemic therapy. We used targeted or whole-genome sequencing to identify somatic genomic alterations and designed personalized assays to quantify circulating tumor DNA in serially collected plasma specimens. CA 15-3 levels and numbers of circulating tumor cells were measured at identical time points.

RESULTS

Circulating tumor DNA was successfully detected in 29 of the 30 women (97%) in whom somatic genomic alterations were identified; CA 15-3 and circulating tumor cells were detected in 21 of 27 women (78%) and 26 of 30 women (87%), respectively. Circulating tumor DNA levels showed a greater dynamic range, and greater correlation with changes in tumor burden, than did CA 15-3 or circulating tumor cells. Among the measures tested, circulating tumor DNA provided the earliest measure of treatment response in 10 of 19 women (53%).

CONCLUSIONS

This proof-of-concept analysis showed that circulating tumor DNA is an informative, inherently specific, and highly sensitive biomarker of metastatic breast cancer. (Funded by Cancer Research UK and others.)

Analysis of Circulating Tumor DNA to Monitor Metastatic Breast Cancer


BACKGROUND

The management of metastatic breast cancer requires monitoring of the tumor burden to determine the response to treatment, and improved biomarkers are needed. Biomarkers such as cancer antigen 15-3 (CA 15-3) and circulating tumor cells have been widely studied. However, circulating cell-free DNA carrying tumor-specific alterations (circulating tumor DNA) has not been extensively investigated or compared with other circulating biomarkers in breast cancer.

METHODS

We compared the radiographic imaging of tumors with the assay of circulating tumor DNA, CA 15-3, and circulating tumor cells in 30 women with metastatic breast cancer who were receiving systemic therapy. We used targeted or whole-genome sequencing to identify somatic genomic alterations and designed personalized assays to quantify circulating tumor DNA in serially collected plasma specimens. CA 15-3 levels and numbers of circulating tumor cells were measured at identical time points.

Focal segmental glomerulosclerosis (FSGS) is induced by microRNA-193a and its downregulation of WT1


ABSTRACT

Focal segmental glomerulosclerosis (FSGS) is a frequent and severe glomerular disease characterized by destabilization of podocyte foot processes. We report that transgenic expression of the microRNA miR-193a in mice rapidly induces FSGS with extensive podocyte foot process effacement. Mechanistically, miR-193a inhibits the expression of the Wilms’ tumor protein (WT1), a transcription factor and master regulator of podocyte differentiation and homeostasis.
Decreased expression levels of WT1 lead to downregulation of its target genes PODXL (podocalyxin) and NPHS1 (nephrin), as well as several other genes crucial for the architecture of podocytes, initiating a catastrophic collapse of the entire podocyte-stabilizing system. We found upregulation of miR-193a in isolated glomeruli from individuals with FSGS compared to normal kidneys or individuals with other glomerular diseases. Thus, upregulation of miR-193a provides a new pathogenic mechanism for FSGS and is a potential therapeutic target.

6)

Characterisation of retinoblastomas without RB1 mutations: genomic, gene expression, and clinical studies


SUMMARY

BACKGROUND
Retinoblastoma is the childhood retinal cancer that defined tumour-suppressor genes. Previous work shows that mutation of both alleles of the RB1 retinoblastoma suppressor gene initiates disease. We aimed to characterise non-familial retinoblastoma tumours with no detectable RB1 mutations.

METHODS
Of 1068 unilateral non-familial retinoblastoma tumours, we compared those with no evidence of RB1 mutations (RB1+/+) with tumours carrying a mutation in both alleles (RB1−/−). We analysed genomic copy number, RB1 gene expression and protein function, retinal gene expression, histological features, and

FINDINGS
No RB1 mutations (RB1+/+) were reported in 29 (2.7%) of 1068 unilateral retinoblastoma tumours. 15 of the 29 RB1+/+ tumours had high-level MYCN oncogene amplification (28—121 copies; RB1+/+MYCNA), whereas none of 93 RB1−/− primary tumours tested showed MYCN amplification (p<0.0001). RB1+/+MYCNA tumours expressed functional RB1 protein, had fewer overall genomic copy-number changes in genes characteristic of retinoblastoma than did RB1−/− tumours, and showed distinct aggressive histological features. MYCN amplification was the sole copy-number change in one RB1+/+MYCNA retinoblastoma. One additional MYCN tumour was discovered after the initial frequencies were determined, and this is included in further analyses. Median age at diagnosis of the 17 children with RB1+/+MYCNA tumours was 4.5 months (IQR 3.5—10), compared with 24 months (15—37) for 79 children with non-familial unilateral RB1−/− retinoblastoma.

INTERPRETATION
Amplification of the MYCN oncogene might initiate retinoblastoma in the presence of non-mutated RB1 genes. These unilateral RB1+/+MYCNA retinoblastomas are characterised by distinct histological features, only a few of the genomic copy-number changes that are characteristic of retinoblastoma, and very early age of diagnosis.

7)

Early detection of cancer in the general population: a blinded case–control study of p53 autoantibodies in colorectal cancer


Abstract

BACKGROUND
Recent reports from cancer screening trials in high-risk populations suggest that autoantibodies can be detected before clinical diagnosis. However, there is minimal data on the role of autoantibody signatures in cancer screening in the general population.

METHODS

Continues from p.11
Informative p53 peptides were identified in sera from patients with colorectal cancer using an autoantibody microarray with 15-mer overlapping peptides covering the complete p53 sequence. The selected peptides were evaluated in a blinded case-control study using stored serum from the multimodal arm of the United Kingdom Collaborative Trial of Ovarian Cancer Screening where women gave annual blood samples. Cases were postmenopausal women who developed colorectal cancer following recruitment, with 2 or more serum samples preceding diagnosis. Controls were age-matched women with no history of cancer.

RESULTS
The 50640 women randomised to the multimodal group were followed up for a median of 6.8 (inter-quartile range 5.9–8.4) years. Colorectal cancer notification was received in 101 women with serial samples of whom 97 (297 samples) had given consent for secondary studies. They were matched 1:1 with 97 controls (296 serial samples). The four most informative peptides identified 25.8% of colorectal cancer patients with a specificity of 95%. The median lead time was 1.4 (range 0.12–3.8) years before clinical diagnosis.

CONCLUSION
Our findings suggest that in the general population, autoantibody signatures are detectable during preclinical disease and may be of value in cancer screening. In colorectal cancer screening in particular, where the current need is to improve compliance, it suggests that p53 autoantibodies may contribute towards risk stratification.

Dr. Loukas Kaklamanis
A chemical found in red meat can encourage the growth of fatty deposits (grey) on the walls of arteries (orange). A PASIEKA/SCIENCE PHOTO LIBRARY

Photo published by Nature/News by C.Woolston, 7th April 2013

L-carnitine, normally found in red meat, increases the serum levels of trimethylamine-N-oxide (TMAO) which alters the metabolism of cholesterol resulting in increased atherosclerosis. Vegans and vegetarians even when they take L-carnitine, they produce less TMAO than meat eaters. Their faecal studies showed very different types of bacteria in their intestines.

In their animal studies, mice fed with L-carnitine doubled the risk of arterial plaque formation. When the mice were also fed with intestinal-cleaning antibiotics, L-carnitine did not increase the risk of atherosclerosis.

These fascinating results, provided that could be validated in larger perspective studies, might have a major impact in changing human approach to diet.

Dr. Loukas Kaklamanis
MORE QUESTIONS?
Please contact the organizers:
Heinrich.Popper@meduni-graz.at; Phone (0660) 316 380 44036
edith.kaiserferchner@meduni-graz.at; Phone 0043 (0) 316 382 4427

GETTING TO GRAZ BY PLANE
For scheduled flights to Graz see http://www.fluguhren-graz.at

MORE INFORMATION ABOUT GRAZ
http://www.graaztourismus.at

The course is approved by ESCOP
the European School of Pathology
European Society of Pathology

Zelis Austria will provide the
microscopes for the course

ZELIS

ESCOP
European School of Pathology

Adult Cardiovascular Pathology

Thursday 16 – Friday 17 May 2013
NIHU Education Centre
National Heart and Lung Institute
Imperial College London, Dovehouse Street, London SW3 6LY

Course Organiser: Dr Mary Sheppard
www.imperial.ac.uk/medicine/people/mary/sheppard/ 

This course approaches the practical problems that face the diagnostic pathologist when dealing with cardiovascular pathology, which is the most common cause of death in the western world today. The approach to a cardiac autopsy, cardiac anatomy and cardiac dissection will be emphasised. Topics covered include: sudden cardiac death, vascular and heart disease, cardiomyopathies, inherited cardiac diseases, myocarditis, and post-operative death. A large collection of cardiac specimens and a cardiac pathology museum are also included for study during the two-day course.

Course fees: £505 Full Rate / £375 Daily Rate
£225 Special Rate for SPIRS / £125 Special Daily Rate for SPIRS

CPO Credits Sought

Course Programme, Faculty List, and Online Registration at www.imperial.ac.uk/mbi/ocsp/ 

Pathology and underlying genetics of inheritable human cancer and developmental defects

25 and 26 April 2013
Leiden

www.boerhaavenscholing.nl
IOANNINA UNIVERSITY COURSES IN PATHOLOGY (IUCP)

BREAST PATHOLOGY - ONCOLOGY

Director: Emeritus Prof. Niki J. Agnantis

28 - 31 May 2013
HOTEL PALLADION, IOANNINA, GREECE

Scientific Information: http://www.iucp.gr

Secretariat Information: Conferre Ltd, Ioannina, Greece
Tel: (+30) 2651068540, Fax: (+30) 2651068611
Email: info@conferre.gr

Fee, venue and registration

Course fee
Course fee (including course book, course materials, lunches, drinks and closing dinner): € 450. Reduced fee for students with a letter of verification from supervisor: € 350.

Venue
Leeuwen University Medical Center
Building 3, Lecture room J and computer room 21-402

Registration
Registration and payment through our website: www.boerhaavescm.org. The deadline for registration is 15 October 2013. There is a limited number of places available (max. 25). Participants will be registered on a first come first served basis.

Written confirmation of participation will be sent upon receipt of the registration form and payment.

Boerhaave CME

The Leiden University Medical Center (LUMC) is a modern knowledge centre.
The medical staff members of the LUMC are passionate about improving patient care through scientific research.
The Boerhaave CME offers more than 200 continuing medical education (CME) courses to train doctors for this purpose. We are the largest post-graduate education institute in the field of medicine in The Netherlands.

Boerhaave CME
P.O. Box 9600, Postbus 9600, 2300 RC Leiden

Further Information

Boerhaave CME
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Website: www.boerhaavescm.org

Practical, clinical, radiological and pathological diagnosis of skeletal tumours

25, 26 and 27 November 2013
Leiden

www.boerhaavescm.org
Kidney and Urinary Tract - Postgraduate Course

One and a half day course with lectures and interactive sessions for surgical pathologists. Up-to-date information on neoplastic and non-neoplastic diseases of the kidney and the urinary tract.

When:
Starts: Friday, June 7, 2013, 8:00 h.
Ends: Saturday, June 8, 2013, 14:00 h.

Where:
Pathology, University Hospital Basel, Schönbeinstrasse 40, CH-4031 Basel, Switzerland

Course costs and registration:
CHF 100.- (including seminars, workshops, lunch, buffet, and refreshments). Please see our website: http://pathologie.unispital-basel.ch "Aktuelles/Basel Seminars in Pathology"

Organization:
Lukas Huberndorf, Basel, Switzerland
Helmut Hopfer, Basel, Switzerland

Speakers:
Ian S. Roberts, Oxford, United Kingdom
Holger Moch, Zürich, Switzerland
Mahul B. Amin, Los Angeles, U.S.A.
Peter A. Humphrey, St. Louis, U.S.A.
Thomas Gasser, Basel/Liestal, Switzerland

For additional information contact Helmut Hopfer (Helmut.Hopfer@usz.ch) or see our website (http://pathologie.unispital-basel.ch/"Aktuelles"