

**GUIDE BOOK 2013**



# **8<sup>TH</sup> YES MEETING**

**EIGHTH YOUNG EUROPEAN SCIENTIST MEETING**

**19-22 SEPTEMBER 2013**

**FACULTY OF MEDICINE OF PORTO – PORTUGAL**

INFO ONLINE @  
**WWW.YESMEETING.ORG**



# YES GUIDE 2013

8th YES - Young European Scientist Meeting, 2013

In this guide you can find all the useful information about 8th YES - Young European Scientist Meeting, 2013. Check the details for the Committees, Scientific and Social programmes, related information and so on.

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### FORMER PRESIDENTS' MESSAGE - THE YES EXPERIENCE

Starting YES from scratch...

While a medical student and after presenting a poster in a conference in Berlin, the thought of starting a Meeting in Porto to gather students and biomedical sciences came to my mind. At that time, I felt that there was an unmet need to bring together undergraduates involved in research projects and renowned scientists, in an informed atmosphere and with the goal of encouraging students to pursue a scientific career. Some of my good friends from medical school got very excited with the idea and started to contact different companies and people to make the first YES happen. I believe that for all of us who started the YES from scratch, it's been very rewarding to see how the meeting evolved through the years, growing in the number of participants, always with brilliant speakers and building partnerships with student associations across the world. My wish is to keep following the success of YES Meeting and later become part of YES again... possibly as a speaker! Have fun and enjoy!

Filipe Carvalho Founder and 1st YES Meeting President

When I was first invited to be a member of the I YES Meeting Committee, I could not imagine the fast growth this Project actually had. At the beginning, we had a little cell as an icon which immediately turned into a target, where each one had his own goal. Ours was calling all young scientists across Europe to join us in our city.

The I YES Meeting was a giant surprise, having a Nobel Prize and almost 300 attendants! Not bad for a project discussed in the faculty corridors by a group of students, guided by another student.

And suddenly, for the II YES Meeting, I've seen myself as the only available person, once everyone from the first team was graduating, not being able to maintain an active participation as an organizer. The main committee was totally reformed, and I had the honor of being the President, a responsibility I held for two years.

I won't describe each YES edition, since every fact can be found in documents or websites. Instead, I want to share how YES changed my perspective of life ways, people relationships, work methods and Science fields. It was a really rewarding experience I will never forget and here I truly want to thankful to all the team that worked with me.

I'm so glad our "little baby" is now a strong, happy and vigorous 7 years old child! I believe this will be one more unforgivable edition. I hope you take home a little bit of this international working spirit.

João Maciel - 2nd and 3rd YES Meeting President

YES Meeting, the Young European Scientist Meeting is a renowned international conference, bringing each year top specialists in medical research fields, promoting at the same time new investigation from students all over the world. In each meeting hundreds of students have the chance to share knowledge and experience, both in science as well as in the plurality of many different cultures. It all started with the idea of a group of students and it grew each year, involving interested and enthusiastic people who dedicate their time to a cause without any interest besides the development of education, research and new advances in medical areas.

My history in the YES Meeting started in its very first edition, as a presenting student, also in my first year in medical school. I remember the anxiety, all the other students from

such different backgrounds, the amazing social programme and all the great experiences. Next year I was a part of the organizing committee, and saw the idea from a whole new perspective. Two years passed and in the IV edition I was honored to be the YES Meeting President. We were an entire new team, having to plan everything in a very different context than before. After all the meetings, discussions, problems and achievements in the end we were a perfect team, each own contributing with their specific abilities and savoir-faire. The actual days of the IV YES meeting arrived, after many unslept nights and hard work... as usual it was a great success. Ending my "career" as an active part of this initiative, I have plenty of unforgettable experiences. Besides this, it is indeed a dream of many that came true and kept on succeeding, which makes me feel very proud to have had the chance to be a part of it.

I wish all the best for the seventh edition of this unique event, and hope that it continues through endless times, maintaining all its values and motivations.

Cristina Duque 4th YES Meeting President

To me the YES Meeting was one of the most exciting experiences in my life, both from the organization perspective and the presenting point of view. It was a very enriching activity, that promotes scientific knowledge sharing, but also the creation of new relationships with colleagues from around the world, promoting synergies between students, faculty and medical schools around the world. In my view it represents an important opportunity for many young medical students to start their contact with the academic and scientific world and from there on develop their interest in science and research. The continuous growth of the YES Meeting since the very first edition make me proud and honored of having been a part of such a remarkable legacy, still with so much more potential, that yearly is able to benefit students from all around the world, with an unforgettable scientific experience.

Tiago Taveira - 5th YES Meeting President

The YES Meeting has been and is, for many years now, an established meeting point for students with a very special scientific curiosity from all over the world. As part of the organization, I have seen an increasing number of participants coming to Porto to join their fellows, to present their research and to attend jaw-dropping lectures. Some of



these talks were delivered by great scientists, physicians and even Nobel Prize winners, namely Rolf Zinkernagel and Aaron Ciechanover. We learnt more about breathtaking topics, such as cellular tensegrity, facial transplant and even how to grow a mouse from a fibroblast. There was also time to discuss global health issues like the environmental changes, and we started interesting debates in “mornings with scientists”. But there was also time for “hands on” workshops and for social activities from Serralves Museum to Ribeira. In the end, we all left YES with the desire of coming next year. And here I am, coming in 2012 as a participant, very proud of what we have done in the past, and very grateful to the current OC, that has done a terrific job in providing us an outstanding scientific experience.

Delfim Duarte - 6th YES Meeting President

### MESSAGE FROM THE YES COMMITTEE

Dear YES participants,

It is with great joy that we address to you in this 8th edition of the YES Meeting.

This year, for the first time there will be a Pre-Course! A series of workshops with the objective of making the participants as much comfortable as possible with tasks such as doing bibliographical research, giving speeches and oral presentations, writing scientific articles and so on...

As always, it has been a challenge and a pleasure to organize such an interesting meeting and you can now have a glimpse at this year's programme.

In the lectures panel we will have Ada Yonath, Nobel Prize in Chemistry 2009.

On the other hand, we will receive Tal Golesworthy who gave several lectures at the well known TED Talks and will tell us all about "Vascular Repair", also David Tannahill who recently published a paper about his discoveries on the DNA structure and will lecture us about the "DNA, not just a double helix"

For the first time, there will be a very special and very dear symposium entitled "+Humans" which will focus on the personal approach a health care professional should be proficient on...hear about how a medical student started a movement to make professionals aware of how they should behave when dealing with patients...

This is just a glimpse since many more speakers and themes will be discussed throughout the 3 days of the meeting

In this 3-day scientifically challenging meeting, you will have the chance to participate in 2 workshops and an unique social program was also specially designed for those who want to know more about Porto and want to develop a global network with fellow colleagues and make new friends over a beer.

Remember, we need you to make this an unforgettable scientific experience!

Our best regards,

8th YES Meeting Organizing Committee

## THE TRUTH ABOUT THE YES MEETING 2013

YES Meeting was born in 2006, when a student from the Faculty of Medicine, University of Porto, had the idea of joining together students' presentations with professional researchers' lectures.

The aim of this project was to make students feel they have real value in Science and, in some cases, help them decide for a future carrier in research.

The 8th YES Meeting scientific programme includes:

1. Symposiums and round tables on major themes of biomedical interest: Neurosciences, + Humans, Internal Medicine, Cardiothoracic Surgery and Nobel Prize Session.
2. Students' presentations on themes: Neuroscience; Immunology & Physiology, Internal Medicine, Oncology & Molecular Biology and Surgery.
3. Workshops on Curious Cases in Hematology, Developong the Chest Radiography, Is Doctor House a Surgeon?, Time Management, U, the ICU Team, What are you Afraid of?, Small Surgery, Laparoscopy, Invasive Hemodynamic Evaluation, Relaxation Techniques, Treatment of Toxicologic Emergencies, All Different All Equal, Training Basic Skills in a Delivery Simulator and Eye Surgery where students can learn and interact.

Besides this, our social programme includes day and night events such as visits to historic places of interest, a walk downtown to sight-see the main touristic attractions, typical Portuguese meals and an introduction to Porto's famous nightlife.

We couldn't leave you without saying goodbye, so we planned a semi-formal Farewell Dinner where the awards will be announced.

If you are here presenting your work, we wish you the best luck. If not, we truly hope that you'll enjoy this year's YES Meeting



# IFMSA PARTNERSHIP

Dear YES participants,

This year YES Meeting will proudly be once more, IFMSA's official scientific meeting.

The International Federation of Medical Students' Associations (IFMSA) is one of the largest international student forums, bringing together more than 1.2 million medical students representing 96 countries from all 4 corners of the globe. The IFMSA believes and works towards creating culturally sensitive medical students who are able to appreciate health problems throughout the world, work relentlessly to alleviate the burdens of those problems and join forces with relevant partners to create healthier communities, and thus a healthier world. Our official recognition by the UN as the voice of International medical students, and official relationships with major UN agencies like WHO, UNESCO, UNICEF, UNFPA and others ensure that IFMSA is considered a major partner when it comes to issues relating to global health.



# IFMSA

International Federation of  
Medical Students' Associations



## COMMITTEES

### YES MEETING 2013 STAFF COMMITTEE

**Tiago Magalhães**

YES President

**Fábio Carneiro**

YES Vice-President & Scientific Programme

**Ana Cunha**

Workshops

**Ana Lúcia Rouxinol**

Fundraising

**Bárbara Alves**

Public Relations

**Diogo Leal**

Workshops

**Gabriela Gonçalves**

Social Programme

**Inês Gonçalves**

Social Programme

**Joana Brandão**

Scientific Programme

**Joana Rei**

Scientific Programme

**Liliana Teixeira**

Public Relations

**Manuel Silva**

Design & Informatics

**Marisa Martins**

Scientific Programme

**Sérgio Costa**

Treasurer

## **COMMITTEES**

### **YES MEETING 2013 SCIENTIFIC COMMITTEE**

**Adelino Leite Moreira**

Faculty of Medicine, University of Porto, PT

**André Moreira**

Faculty of Medicine, University of Porto, PT

**António Taveira-Gomes**

Faculty of Medicine, University of Porto, PT

**Davide Carvalho**

Faculty of Medicine, University of Porto, PT

**Daniel Moura**

Faculty of Medicine, University of Porto, PT

**Deolinda Lima**

Faculty of Medicine, University of Porto, PT

**Francisco Rocha Gonçalves**

Faculty of Medicine, University of Porto, PT

**Isaura Tavares**

Faculty of Medicine, University of Porto, PT

**José Manuel Romão**

Hospital Geral de Santo António, Porto, PT

**Luís Delgado**

Faculty of Medicine, University of Porto, PT

**Manuel Sobrinho Simões**

Institute of Molecular Pathology and  
Immunology of the University of Porto, PT

**Paulo Bettencourt**

Faculty of Medicine, University of Porto, PT

**Raquel Soares**

Faculty of Medicine, University of Porto

## COMMITTEES

### YES MEETING 2013 HONOUR COMMITTEE

**Aníbal Cavaco Silva**

President of the Portuguese Republic

**Paulo Macedo**

Ministry of Health

**Agostinho Marques**

Dean of the Faculty of Medicine, University of Porto

**Miguel Seabra**

Science and Technology Foundation

**Leonor Parreira**

Science, Technology and Higher Education

**José Marques dos Santos**

Rector of the University of Porto

**Jorge Gonçalves**

Vice-Rector of the University of Porto

**Miguel Guimarães**

Medical Association - North Section President

**Maria Amélia Ferreira**

Medical Education Office, Faculty of Medicine,  
University of Porto



## ADA YONATH

Sunday 22nd - 13h15

### THE FRUITS OF CURIOSITY

Yonath, who is the world pioneer of ribosome crystallography, has spent most of her scientific career working to unravel the structure of the ribosome, a universal cellular complex of numerous components that functions as the cell's "factory" that translated the genetic instructions into the cell's workers, the proteins. She initiated these studies in 1980, long before most others thought it is feasible and consequently she introduced advance techniques, all of which are because routine and are now in broad use. In 2000 Yonath's two decades' long research effort culminated in solving the spatial structure of two of the ribosome's subunits and entered the list compiled by editors of the prestigious Science magazine as one of the ten most important scientific developments of that year. In 2001, she showed how several clinically relevant antibiotics bind to bacterial ribosomes and paralyze them. She also revealed the mechanisms used by disease-causing bacteria to acquiring antibiotics resistance, thus paving the way improving existing therapies and for structure based drug design.

Yonath was born to a poor family in Jerusalem, Israel, Ada Yonath lost her father, who was trained as a rabbi, by the age of 11. Nevertheless, she completed her high school education, and earned B.Sc & M.Sc degrees at the Hebrew University in Jerusalem and a Ph.D. degree at the Weizmann Institute of Science (WIS). After a short postdoctoral period at Carnegie Mellon and MIT in USA, in the seventies she established the first laboratory for protein crystallography in Israel, which was the only laboratory of this kind in the entire country for almost a decade. Currently Prof. Yonath is the WIS Kimmel Professor of structural biology and the Director of the Kimmelman Center for Biomolecular Structure and Assembly. In parallel, during 1986-2004 she headed the Max-Planck-Research-Unit in Hamburg, Germany.

She is a member of the US National Academy of Sciences; the American Academy of Arts and Sciences; the Israel Academy of Sciences and Humanities; the European Academy of



Sciences and Art; the Korean Academy for Science and Technology; the European Molecular Biology Organization; the Microbiology Academy and the International Academy of Astronautics. She holds honorary doctorates from Hebrew, Tel-Aviv, Ben-Gurion, Open and Bar-Ilan universities in Israel; KEK Institute, Japan; Oslo University, Norway; Fujian U, China; NYU, NY; Mount Sinai U, NY; Toulouse U., France and Oxford U, UK.

Her awards include the 1st European Crystallography Prize; the Israel Prize; the Paul Karrer Gold Medal; the Israel PM EMET award; the Rothschild Prize; the Louisa Gross Horwitz Prize of Columbia University, NY; the Paul Ehrlich-Ludwig Medal; the Linus Pauling Gold Medal; the Anfinson Prize; the Wolf Prize; the Massry Award; the UNESCO Award for Women in Science; the Albert Einstein World Award for Excellence; the Erice Peace Prize; the DESY pin; Exner medal; the Nobel Prize for Chemistry; the Indian PM Gold medal; the Panama Government Medal; the Cite of Florence Prize.



## ANDREA BANFI

Saturday 21st - 09h00

### **CELL AND GENE THERAPY FOR CONTROLLED ANGIOGENESIS IN REGENERATIVE MEDICINE**

Andrea Banfi directs the Cell and Gene Therapy group at Basel University Hospital, in the Departments of Biomedicine and of Surgery.

His research focus is the understanding of the basic principles governing the growth of blood vessels and translating this knowledge into the development of novel therapies for: 1) ischemic diseases, such as myocardial infarction and peripheral ischemia; and 2) controlled vascularization in tissue engineering and regenerative medicine applications. The goal is to restore the blood supply in ischemic tissue, or to ensure the induction of a functional vascular network in tissue engineered constructs, by the delivery of growth factors that control the formation of new blood vessels. This is achieved by genetically engineering suitable progenitors to express controlled levels and combinations of angiogenic factors. This approach has the potential to provide both angiogenic stimulation and tissue regeneration, combining the specific advantages of cell therapy and gene therapy.

Vascular endothelial growth factor (VEGF) is the master regulator of vascular growth. However, uncontrolled expression leads to vascular tumors (angiomas). It has been previously found that the transition between normal and aberrant angiogenesis depends on the VEGF amount in the microenvironment around each producing cell rather than on the total dose, since VEGF remains tightly localized in tissue. The group is therefore developing novel methods to deliver the Vascular Endothelial Growth Factor gene alone or in combination with maturation factors, in order to increase its safety and efficacy *in vivo*, through the use of transduced progenitors, gene therapy vectors and controlled release of recombinant proteins by smart biomaterials. They are further applying these methods to mesenchymal progenitors to achieve bone and cardiac regeneration.

Furthermore, taking advantage of a highly controlled cell-based gene delivery platform

developed, the group is pursuing a systematic investigation of the mechanisms that regulate the vascular switch between normal and aberrant angiogenesis in vivo, in order to identify novel and more specific molecular targets for therapeutic angiogenesis approaches. Research is funded by Swiss agencies (SNF and Swiss Heart Foundation), the European Union 7th Framework Program (FP7) and industrial funds.

The Cell and Gene Therapy group has several collaborations in Basel, as well as nationally and internationally, such as at EPFL in Lausanne, and at Columbia University in New York. It is also part of 3 European Consortia working on the control of angiogenesis in regenerative medicine: ANGIOSCAFF ([www.angioscaff.eu](http://www.angioscaff.eu)), Disc Regeneration ([www.disc-regeneration.eu](http://www.disc-regeneration.eu)) and MAGISTER ([www.magister-project.eu](http://www.magister-project.eu)).





## GREGORY PASTORES

Sunday 22nd - 12h30

Gregory M. Pastores MD was born in New York and is an Associate Professor of Neurology and Pediatrics at the NYU School of Medicine in New York, and Director of the Neurogenetics Laboratory for the Department of Neurology at NYU. He graduated from the University of Sto. Tomas in Manila (1983) and received his training in Pediatrics and Genetics at the Mount Sinai Medical Center in New York and at the Mayo Clinic in Minnesota. He is Board Certified in Pediatrics, Clinical Genetics and Clinical Molecular Genetics. He is also the founding member of European Taskforce on Brain and Neurodegenerative Lysosomal Storage Diseases and of the Spanish Foundation for the Study and Treatment of Gaucher disease (FEETEG). He has published over 100 original reports in renowned scientific magazines and is the author and co-author of two books: "Neurology of Hereditary Metabolic Diseases in Children" and "Lysosomal storage disorders: Principles and Practice", besides having written over 10 book chapters.

Dr. Pastores has extensive clinical and research experience in the diagnosis and treatment of patients with the lysosomal storage disorders and with inherited diseases that primarily afflict individuals of Ashkenazi Jewish ancestry. He has also been engaged in the development and testing of treatment for Gaucher disease, MPS I and VI, Pompe disease and a late (adult)-onset form of Tay-Sachs disease (GM2-gangliosidosis).

His current interest lies in the molecular genetics of inherited diseases that involve the nervous system: focusing on ascertaining factors that modify phenotype in patients with Gaucher disease (GBA deficiency), given the observed imperfect concordance between genotype and clinical manifestations, he has discovered an association between GBA mutations and Parkinson disease, which has opened an avenue for investigations, therefore using Gaucher disease as a rare disease model of a common disease (Parkinson disease).





## PROGRAMME OUTLINE

### THURSDAY, 19TH SEPTEMBER - PRE-COURSE

09h00 Check-in. Until 18pm

"Make my article publishable"

"Bibliographic Research: an overall Thrust"

### FRIDAY, 20TH SEPTEMBER

08h00 Check-in. During the morning

09h00 Opening session with Keynote Speaker

David Tannahill, DNA, not just a double helix

Helder Maiato, Ensuring mitotic fidelity (what can go wrong)

11h00 Internal Medicine + Physiology & Immunology Posters

Coffee-Break

12h00 Neurosciences symposium

13h30 Lunch

15h00 Guided Visit through Porto + Guided Visit to Serralves Museum of Contemporary Art + Guided Visit to the National Museum Soares dos Reis

19h00 + Humans symposium

20h00 Dinner

### SATURDAY, 21ST SEPTEMBER

09h00 Internal Medicine symposium

09h45 Oncology & Molecular Biology + Surgery Posters

Coffee-Break

10h45 Cardiothoracic Surgery symposium

12h45 Lunch

14h30 Parallel Oral Sessions (Faculty of Medicine)

## PROGRAMME OUTLINE

15h45 Workshops 1st round (Faculty of Medicine)

17h00 Coffee-Break

17h15 Workshops 2nd round (Faculty of Medicine)

19h00 Plenary session (Faculty of Medicine)

20h30 Social Dinner

### **SUNDAY, 22ND SEPTEMBER**

09h30 Speed Meeting

11h00 Posters Presentation + Coffee-Break  
Neurosciences

12h00 Internal Medicine symposium

Prof. Maria Mota, Malaria Research Group, IMM

Prof. Gregory Pastores, NYU Neurogenetics Lab

13h15 Nobel Prize Session

Prof. Ada Yonath

14h00 Lunch

16h00 Social Programme

21h00 Farewell dinner (Taylor's Port Wine Cellars)

Due to the complexity of the Hospital layout, we divided it in different containment areas in order to make it easier for you to get to the proper Session/Workshop. The different areas are divided in various colors. Please check in the back of your badge where your Session/Workshop will take place. There will be coloured maps and arrows in the Hospital to help you.

## EXTENDED PROGRAMME

### THURSDAY, 19TH SEPTEMBER

09h00 **CHECK-IN**

### FRIDAY, 20TH SEPTEMBER

08h00 **CHECK-IN**

09h00 **OPENING SESSION**

09h00 Tiago Magalhães YES Meeting President

09h05 Agostinho Marques. Dean of The Faculty of Medicine, University of Porto

09h10 J. Marques dos Santos. Rector of the University of Porto

09h15 F. Rocha Gonçalves. Faculty of Medicine, University of Porto

09h20 Paulo Macedo Minister of Health

09h30 "DNA, not just a double helix"

David Tanahill

Wellcome Trust Sanger Institute, Cambridge

10h15 "Ensuring mitotic fidelity (what can go wrong)"

Hélder Maiato

IBMC

11h00 **COFFEE BREAK - INTERNAL MEDICINE AND PHYSIOLOGY & IMMUNOLOGY POSTER PRESENTATIONS**

12h00 **"OXYGEN CHALLENGE IMAGING IN ACUTE ISCHAEMIC STROKE"**

KRISHNA DANI

University of Glasgow

13h00 **LUNCH**

15h00 **SOCIAL PROGRAM - GUIDED VISIT THROUGH PORTO + GUIDED VISIT TO SERRALVES MUSEUM OF CONTEMPORARY ART + GUIDED VISIT SOARES DOS REIS MUSEUM**



## EXTENDED PROGRAMME

19h00 **" + HUMANS "**

**"COM-PASSION FOR CARE"**

Salmaan Sana  
COM-passion for Care

**"PALIATIVE CARE"**

Isabel Galriça Neto  
Unidade de Cuidados Paliativos, Hospital da Luz, Lisboa

20h30 **DINNER**

## SATURDAY, 21ST SEPTEMBER

09h00 **CELL AND GENE THERAPY FOR CONTROLLED ANGIOGENESIS IN REGENERATIVE MEDICINE**

Andrea Banfi  
Laboratory of Cell & Gene Therapy, Basel University Hospital

09h45 **COFFEE BREAK - SURGERY AND ONCOLOGY & MOLECULAR BIOLOGY POSTER PRESENTATIONS**

10h45 **"MINIMAL INVASIVE NEONATAL SURGERY"**

Jorge Correia Pinto  
Escola de Ciências da Saúde, Universidade do Minho

11h30 **"VALVULAR REPAIRS"**

Tal Golesworthy  
Energy Institute

12h15 **LUNCH**

14h30 **PARALLEL ORAL SESSIONS** - Faculty of Medicine

(Check where the sessions will take place and the corresponding color on the back of your badge)

## EXTENDED PROGRAMME

### **ONCOLOGY & MOLECULAR BIOLOGY** - White Section; Norte Amphitheater – 1st flr

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**PS 73 - The relationship between factor v leiden and prothrombin g20210a mutations and the first major thrombotic episode in polycythemia vera and essential thrombocythemia**

Roxana Costache

**PS 116 - Selected gene expression signature and methylation profile in prostate cancer cell lines**

Katarzyna Grębicka

**PS 184 - The role of Vismodegib in Hematological Neoplasias Treatment**

Cátia Domingues

**PS 46 - Breast Cancer pathway: ARE DOCTORS AWARE?**

Filipe Machado

**PS 117 - Relevance of imprinted genes in human fetal growth**

Amílcar Cordeiro

### **PHYSIOLOGY & IMMUNOLOGY** - Pink Section; Poente Amphitheater – 3rd flr

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**PS 148 - Antibacterial effects of raspberry concentrate in in vitro conditions**

Aleksandar Bokan

**PS 96 - TNF gene polymorphism rs1800629 in Serbian kidney transplant patients**

Jovana Milic

**PS 38 - Analysis of stress responses to labor and public performance through changes in salivary cortisol concentrations**

Aleksandra Vejnovic

**PS 141 - Interleukin 10 single nucleotide polymorphisms rs1800896 and rs1800871 in Serbian kidney transplant patients**

Milica Djoric

**PS 142 - Kinetics of inflammatory markers in acute ischemic stroke and their relevance in stroke-induced immunosuppression**

Anna Bajnok

## EXTENDED PROGRAMME

### NEUROSCIENCES - Green Section; Student's Lounge – 01 flr

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**PS 127 - Sexual and sphincter dysfunction in patients with multiple sclerosis.**

Djordje Mijailovic

**PS 167 - EGCG prevented the diabetes-induced hyperactivity of spinal nociceptive neurons: a possible involvement in opioidergic spinal system**

Diogo Raposo

**PS 104 - Total number of ER $\alpha$ -immunoreactive neurons of the principal division of the bed nucleus of the stria terminalis in female rat brain during the estrous cycle**

Claudia Leite

**PS 164 - Expression changes in GABAAR receptor subunits in a model of epileptiform activity in organotypic hippocampal slice cultures (OHSC)**

Inês Fernandes

**PS 105 - Effect of the natural compound Resveratrol in osteoarthritic pain: a behavioural experimental study**

Tiago Aguiar

### INTERNAL MEDICINE - Red Section; Nascente Amphitheater – 3rd flr

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**PS 75 - non-susceptibility of coagulase-negative staphylococci isolated from blood cultures - do we have a problem?**

Katarina Katic

**PS 175 - How to achieve quality in medical education? Inter-rater agreement about item-writing flaws in multiple-choice questions: the case of clinical anatomy**

Bruno Guimarães

**PS 111 - Results of mesenchymal stem cell (MSC) treatment of Crohn's disease in Russia**

Yulia Orlova

**PS 182 - The role of IgA-antiendomysial antibody in the diagnosis of Celiac Disease in a pediatric sample**

Paulo Guedes

### **PS 188 - Myocardial infarction as a complication during hospitalisation due to ischemic stroke**

Magdalena Danuta

**SURGERY** - Green Section; Novo A Amphitheater – 2nd flr

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### **PS 140 - comparative evaluation of zinc oxide eugenol versus gelatin sponge soaked in plasma rich in growth factor in the treatment of dry socket**

Dejan Stekic

### **PS 124 - Predicting cardiotoxicity: finding echocardiographic prognostic markers in a breast cancer patient population**

Mariana Saraiva

### **PS 128 - Postoperative stroke is less frequent after off-pump CABG compared to on-pump surgery**

Sabina Licholai

### **PS 168 - comparison of changes in lipid profile after roux-en-y gastric bypass and laparoscopic sleeve gastrectomy**

Janik Piotr

### **PS 47 - Metabolic Changes after Simultaneous Pancreas- Kidney Transplantation**

Aron Ghimessy

### **15h45 WORKSHOPS 1ST TURN**

(Check on the workshops section where your workshop will take place)

### **17h00 COFFEE-BREAK**

### **17h15 WORKSHOPS 2ND TURN**

(Check on the workshops section where your workshop will take place)

### **19h00 PLENARY PRESENTATIONS** Brown Section; Aula Magna – 3rd flr

## **ONCOLOGY & MOLECULAR BIOLOGY**

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### **PS 78 - Evaluation of the MicroRNA Biogenesis Machinery in Chick Embryo Development**

Carlos Serra



## **PHYSIOLOGY & IMMUNOLOGY**

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**PS 103 - Cellular electrophysiological and antiarrhythmic efficacy of new sodium/calcium exchanger inhibitors in the canine heart.**

András Horváth

## **NEUROSCIENCES**

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**PS 118 - Structural and functional implications of phosphorylation of PRRXL1 homeodomain transcription factor**

Ricardo Reis

## **INTERNAL MEDICINE**

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**PS 85 - cystic fibrosis: study of cftr gene sequence variations in the pediatric portuguese population**

Liliana Gonçalves

## **SURGERY**

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**PS 122 - Neoadjuvant Therapy and Liver Transplantation for Hilar Cholangiocarcinoma: Is Pretreatment Pathological Confirmation of Diagnosis Necessary?**

Fatih Kaya

## **20h00 DINNER WITH SOCIAL PROGRAMME**

**TRADITIONAL DINNER**

**TUNA FEMININA DE MEDICINA LIVE PERFORMANCE**

**ESKADA NIGHT CLUB**

## **SUNDAY, 22ND SEPTEMBER**

### **09h30 SPEED MEETING**

(Speed dating with the participation of YES Meeting Speakers)

### **10h30 COFFEE BREAK - NEUROSCIENCES POSTER PRESENTATIONS**

## 11h30 **INTERNAL MEDICINE**

### 12h00 **"CURRENT TRENDS IN MALARIA RESEARCH"**

Maria Mota

Malaria Research Group, IMM

### 12h30 **"LYSOSOMAL STORAGE DISORDERS: INSIGHTS INTO THE NEURODEGENERATIVE PROCESS"**

Gregory Pastores

NYU Neurogenetics Lab

### 13h00 **NOBEL PRIZE SESSION - "THE FRUITS OF CURIOSITY"**

Ada Yonath

Weizmann Institute of Science

## 14h00 **LUNCH**

### 16h00 **SOCIAL PROGRAM**

**PORT WINE TASTING AT ARAB HALL IN PALÁCIO DA BOLSA**

**VISIT TO THE PORT WINE CELLARS**

**AWARD CEREMONY**

### 21h00 **FAREWELL DINNER**

### 01h00 **RESEARCHERS' NIGHT**

## WORKSHOPS

The workshops are going to be held on Sunday 21st September at 15h45. The workshops will be held in different rooms across the Faculty of Medicine. For your convenience please refer to a member of our staff. Due to the complexity of the Hospital layout, we divided it in different containment areas in order to make it easier for you to get to the proper workshop. The different areas are divided in various colors. Please check in the back of your badge where your workshop will take place. There will be coloured maps and arrows in the Hospital to help you.

### ALL DIFFERENT, ALL EQUAL

LOCATION - Novo B Amphitheater; floor - 2nd (Green Section)

It is said we should never have preconcepts about people. Despite, human being is programmed to have some preconcepts, that, altogether with the clear discrimination seen on every single society, make us treat people, even if in a subconscious manner, different.

This workshop will explore the discrimination and provide you with some tips to deal with different people with similar eyes.

CHAIR: MARIA CUNHA

### CURIOUS CASES IN HEMATOLOGY

LOCATION - Clinicas 3 Amphitheater; floor - 2nd (Red Section)

Blood is like a cocktail of cells in perfect harmony with each other. It allows our organism to have the nutrients, oxygen and get rid of the trash with high performance and efficiency. Unfortunately, not always is the story so happy, and hemathological diseases happen. It is not easy to get the diagnosis right of this diseases, as they can mimetize so many symptoms you would relate to other conditions. Will you be able to take the challenge and learn how to be wary of them?

CHAIR: MANUEL SOBRINHO SIMÕES

### DEVELOPING THE CHEST RADIOGRAPHY

LOCATION - Radiology Department; floor - 2nd (Red Section)

This workshop intends not only to show you images of some conditions you will definitely see through your life and teach you how you can reach the diagnosis by looking to a

X-Ray or a CT scan. As we are in crisis worldwide, it is more and more a main concern of the government that we, as health professionals, spend as little as we can to get to the same results. Therefore, you should know when to ask an exam, why you are asking it, and if it will change some decision you made before. With this workshop we want our participants to be aware of the good practices they should follow in the future.

CHAIR: JOSÉ MIGUEL PEREIRA; ISABEL RAMOS

### Eye Surgery

LOCATION - Norte Amphitheater; floor - 1st (White Section)

Last year it was a success and therefore we will bring you again the live-streaming, interactive eye-surgery, where, as the name says, you can virtually be into the operation room and ask questions to the main surgeon that will be, at the same time, your workshop leader.

CHAIR: AUGUSTO MAGALHÃES

### Invasive Hemodynamic Evaluation

LOCATION - Physiology Department; floor - 4th (Orange section)

This workshop aims to explain how to perform and interpretate invasive hemodynamic techniques.

CHAIR: ADELINO LEITE-MOREIRA; MANUEL PINTO

### Is Doctor House a Surgeon?

LOCATION - Nascente Amphitheater; floor - 3rd (White Section)

You can only imagine the amount of organs stuck into our abdomen. They are disposed all together in this small area and they work perfectly... Unless one of them is injured. Join the group, discuss diagnosis and treatments of cases you could only watch in Dr. House before!

CHAIR: ANTÓNIO TAVEIRA GOMES

### Laparoscopy

LOCATION - Novo A Amphitheater; floor - 2nd (Green Section)

In this "blockbuster" workshop you will, once more, be given the opportunity to learn from an expert the basics of laparoscopic surgery. After a short introduction, you'll have the chance to try it by yourself with laparoscopic endotrainers. Curious about what your



hands are capable of?

CHAIR: ANTÓNIO TAVEIRA GOMES

## **RELAXATION TECHNIQUES**

LOCATION - Students Lounge; floor - 01 (Green Section)

Stress and all-around anxiety are an important part of our society. Learn how to cope with these situations in this workshop: relax! It's good for your health, good for your mind and good for everyone around you.

CHAIR: MARGARIDA FIGUEIREDO

## **SMALL SURGERY**

LOCATION - Poente Amphitheater; floor - 3rd (Red Section)

Small surgery workshop is back! Learn and test your skills doing some basic suture techniques.

CHAIR: PINTO SOUSA

## **TIME MANAGEMENT**

LOCATION - CIM Room 3 (Orange Section)

Time is free, but it's priceless. You can't own it, but you can use it. You can't keep it, but you can spend it. Once you've lost it you can never get it back. Harvey Mackay Time management is one of the key attributes in anyone's lives regardless of your field of work. Learn how to best deal with your time in a workshop structured to better suit the needs of Biomedical Students.

CHAIR: ISABEL LOURINHO

## **TRAINING BASIC OBSTETRIC SKILLS IN A DELIVERY SIMULATOR**

LOCATION - Biomedical Simulation Center; floor - 7th (Pink Section)

And if a pregnant woman starts delivering her baby in your bus? Do you know what to do? Maybe this workshop can give you some help! Learn and watch the experts. Some of the participants will have the opportunity to train their obstetric skills in a realistic delivery simulator.

CHAIR: DIOGO AYRES DE CAMPOS; CARLA SÁ COUTO

## **TREATMENT OF TOXICOLOGIC EMERGENCIES**

LOCATION - Pharmacology Amphitheater (Orange Section)

How to use the basic science of poisons and drugs to support medical decision to care for patients with acute intoxications. A series of clinical cases will be used to show how doctors should think and act using the knowns and the unknowns.

CHAIR: DANIEL MOURA

## **U, THE ICU TEAM**

LOCATION - Biomedical Simulation Center; floor - 7th (Pink Section)

In this workshop you will be integrated in a team trying to save a traumatized man with minutes to live if anything is done in the meanwhile. With our sophisticated software, you will be able to deal with a real-size, dynamic simulator, and save it from his inevitable death. Or won't you? Come and show us you capable to accomplish the mission!

CHAIR: JORGE TAVARES; MARCOS GOUVEIA; CARLA SÁ COUTO

## **WHAT ARE YOU AFRAID OF?**

LOCATION - Psychiatry Department (Yellow Section)

Everybody is afraid of something: a spider, the first day of school, a job interview, the first kiss... but imagine your fear was so strong you were completely dominated by it! Some phobias can be truly incapacitating and there is still some stigma around people with phobias. Learn how to deal with this patients with this amazing workshop. You will be terrified!!

CHAIR: RUI COELHO

## SOCIAL PROGRAMME

### GUIDED VISIT THROUGH PORTO

FRIDAY, 20TH SEPTEMBER, 15H00

A cultural walk around the most well known places in Porto. You will see various famous monuments and places that made the city of Porto so emblematic. We have a special treat for everyone going on the tour so don't miss this opportunity to know our city!

### GUIDED VISIT TO SERRALVES MUSEUM OF CONTEMPORARY ART

FRIDAY, 20TH SEPTEMBER, 15H00

A guided visit to the museum, as well as the possibility of a pleasant walk to the wonderful gardens around this building. The number of participants is limited.

### GUIDED VISIT TO NATIONAL MUSEUM SOARES DOS REIS

FRIDAY, 20TH SEPTEMBER, 15H00

A guided visit to the many collections of the museum, since Ceramics Sculpture, Engraving, Jewellery, Furniture, Gold and Silverware, Painting, Textiles, Glassware and other featured artists.

The Museu Nacional Soares dos Reis occupies the Carrancas Palace, a building from the end of 18th century that in the meantime has suffered several adaptations to its new function.

### DINNER - TUNA FEMININA DE MEDICINA - LIVE PERFORMANCE

SATURDAY, 21ST SEPTEMBER, 20H30

Enjoy a wonderful dinner in the Medical Faculty of Porto, with the live music act by the Tuna Feminina de Medicina do Porto. This traditional musical group from our college are sure to impress and amuse you throughout the dinner.

### ESKADA NIGHT CLUB

SATURDAY, 21ST SEPTEMBER, 00H00

After the dinner and the traditional portuguese culture exhibition, it's time for taking the party into a whole different level. Enjoy one of the most glamorous and popular night clubs in Oporto, the Eskada porto Night Club!

## YES GUIDE BOOK

### PORT WINE TASTING, PORT WINNE CELLARS AND AWARD CEREMONY

SUNDAY, 22ND TH SEPTEMBER, 16H00

A long lasting landmark of our city is, unquestionably the Port Wine. On Sunday afternoon you will have the opportunity to visit one of the most beautiful Halls that can be found in Oporto, the Salão Árabe (Arab Hall) inside Palácio da Bolsa, while you experience the typical Port Wine. You will also visit the Port Wine Cellars which provides you an unforgettable experience about the port wine, its history and tradition.

The Award ceremony will be held after the dinner.

### FAREWELL DINNER PARTY AND AWARD SESSION CEREMONY

SUNDAY, 22TH SEPTEMBER, 21H00 (TAYLOR'S PORT WINE CELLARS)

Say goodbye to another fantastic YES Meeting and prepare to come next Year with a whooping semi formal dinner party.



## ABOUT PORTO...

### MUSEUMS

#### **CASA-MUSEU GUERRA JUNQUEIRO**

The museum housed in a lovely 18<sup>th</sup> century building displays the private collection of Portuguese writer Guerra Junqueiro.

Rua D. Hugo, 32

#### **CASA-MUSEU MARTA ORTIGÃO SAMPAIO**

This museum contains the collections of Marta Ortigão, which were donated to the City of Porto. The main attractions are the paintings and jewellery collections. The jewellery consists of 18<sup>th</sup> to 20<sup>th</sup> century pieces. The paintings include the works of Silva Porto, Marques de Oliveira, Sousa Pinto, Artur Loureiro, Aurélia de Sousa, and Sofia de Sousa.

Rua Nossa Sr.<sup>a</sup> de Fátima, 291

#### **MUSEU DE ARTE CONTEMPORÂNEA DE SERRALVES**

A visit to the Museum of Modern Art, on the western edge of the city. It is best to left it out of a first day exploration of Porto. The museum is on the grounds of the impressive Casa de Serralves, situated in a large park, and puts on temporary exhibitions from different arts.

Rua de Serralves, 977

#### **MUSEU DO CARRO ELÉCTRICO**

The Electric Tramcar Museum explores the history of Tramcars. The first tramcars in Porto were the horse-pulled "American Cars" which came into operation in the early 1870s. The museum's collection includes this and other types of tramcars covering over 100 years of the city's history.

Alameda Basílio Teles, 51

### **MUSEU MILITAR DO PORTO**

The Military Museum, which began in 1920 with an exhibition on the Liberal Revolution of 1820, today houses a collection of light weapons, equipment, uniforms and heavy artillery from the 16<sup>th</sup> to 20<sup>th</sup> centuries. Of particular interest is the collection of miniature soldiers which portrays the history of warfare.

Rua do Heroísmo, 329

### **MUSEU NACIONAL DE SOARES DOS REIS**

The Museu Nacional Soares dos Reis, former Museu Portuense and first art museum in Portugal, was born in 1833, when D. Pedro IV of Portugal decided to establish in Porto a Museu de Pinturas e Estampas (Paintings and Prints Museum). The aim of the foundation of this Museum was the preservation of the artistic heritage that came mainly from extinct convents, and the simultaneous promotion of its use for cultural and pedagogical purposes. The Museum was settled in 1940 in Palácio dos Carrancas, currently considered a public interest property, and it was built in the late 18<sup>th</sup> century, by a wealthy family of Porto.

Rua D. Manuel II

### **MUSEU ROMÂNTICO**

Hidden away to the west of the Jardim do Palácio de Cristal is the Romantic Museum, fully furnished as a Portuguese house of the 19<sup>th</sup> century. The room in which King Charles Albert of Sardinia (b. 1798) died in 1849 is also on view.

Rua Entrequintas, 220

### **MUSEU DO VINHO DO PORTO**

Located in an 18<sup>th</sup> century warehouse where the wines of Companhia Geral da Agricultura das Vinhas do Alto Douro were once stored. This museum is a centre with relevant information regarding Port wine, motivating visitors to discover the city's commercial history.

Rua de Monchique, 45

## SIGHTS

### Foz do Douro

About 5km/3mi downstream from Porto, on a road which runs immediately above the steep bank of the Douro, with fine views back over the city, lies São João da Foz (or Foz do Douro), a suburb of Porto, and a very popular bathing resort, beautifully situated at the mouth (foz, from Latin fauces) of the Douro. The Douro Litoral beach is fringed by palms, and from the breakwater with the harbour light there is an impressive view of the coast and the mouth of the river, commanded by the Castle (Castelo da Foz) (1570). Further northwest, on the road to Matosinhos, is the 17<sup>th</sup> century Castelo do Queijo, built to protect the coast against pirates from North Africa.

### Casa da Música

Although the brash modernity of the House of Music concert hall first seems outlandish or even bizarre, particularly in a city that dates to pre-Roman times and cherishes its century-old monuments, one realizes that this hall could only have been built in a country such as Portugal, which takes the results of architectural competitions seriously. Anywhere else, it would have been watered down, or abandoned.

Avenida da Boavista

### Estação de S. Bento

Built on the site of an ancient convent, it was completed in 1916. Now, only regional trains pass through here. Inside, the immense panels of tiles created by Jorge Colaço, reproducing historical scenes, add a rare artistic beauty to the station.

Praça Almeida Garrett

### Igreja do Carmo

Situated close to the Clergymen Tower and Church (Igreja e Torre dos Clérigos), the Igreja do Carmo is a remarkable construction, presenting an amazing panel of tiles on an exterior wall with scenes describing the foundation of the Carmelite Order.

Praça Gomes Teixeira

### **IGREJA DE SÃO FRANCISCO**

On the Porto waterfront stands the church of St. Frances, dating from 1383. Though not quite imposing from the outside, it has a lavishly Baroque decorated interior created in the 17<sup>th</sup> and 18<sup>th</sup> centuries. Pillars and columns within the vault are festooned with gold-gilded cherubs and flower garlands, entwined animals and fruit cornucopia. This stunning view is set off by wide Gothic arches made of marble, which soar into the roof.

Rua do Infante D. Henrique

### **IGREJA AND TORRE DOS CLÉRIGOS**

A monument of the Baroque style, built between 1754 and 1763 by the Italian architect Nicolau Nasoni, Torre dos Clérigos became the emblem of Porto. From the top of the Tower, six floors and 76 metres high, after climbing an endless spiral staircase with 225 stairs, the visitor enjoys dazzling views over the city, the river Douro and its estuary.

Rua S. Filipe de Nery

### **JARDIM DO PALÁCIO DE CRISTAL**

A little way southwest of the Soares dos Reis Museum is the flower filled Jardim do Palácio de Cristal, the setting for the Pavilhão Rosa Mota, the sports arena, with seating for 10,000 spectators and also a venue for concerts, exhibitions, etc., which in 1952 replaced the former "Crystal Palace". From the south side of the park, where a chapel commemorating King Charles Albert of Sardinia was built in 1851, there is a superb view over the city, the river and the sea.

Rua Manuel II

### **SÉ CATEDRAL**

Built in the 12<sup>th</sup> century, in the Roman style, it was later modified for several times and the original architecture was altered. Inside, it is worth admiring the paintings by Nicolau Nasoni, the silver altarpiece of the Holy Sacrament, João Gordo ("Fat John") Chapel and the cloister. At the southern tower, there are still two standard measures engraved in the stone, the last vestiges of the Medieval fair which took place in the large Cathedral's grounds.

Terreiro da Sé



## **PONTE D. Luís I**

In accordance with the Law of 11/02/1879, the government opened a competition for the construction of a metal bridge over the Douro River, to replace the previous suspended bridge. The winning proposal was the project of engineer Teófilo Seyrig, from the Belgian company Societé de Willebroeck. Teófilo Seyrig had already been the author of the plan and head of the team in the project of Ponte D. Maria Pia (D.Maria Pia Bridge) as Eiffel's associate. This time he was the sole responsible for this work of the new and grand Ponte D. Luís I (D. Luís I Bridge). The construction works began in 1881 and the inauguration occurred on 31<sup>st</sup> October 1886). The arch comprises 172m of cord and is 44.6m tall.

## **RIBEIRA**

The genuine city is visible at the quarter of ribeira ("River-bank"), right by the river. Narrow and winding streets, dark arcades, typical houses with colourful façades set in a place which preserves the charm of sites marked by history, full of contrasts and curious characteristics. At night, the Ribeira acquires liveliness and animation, being one of the most sought spaces due to the numerous pleasant restaurants, esplanades and nightclubs.

## **CAIS DE GAIA**

On the other side of the river lies Cais de Gaia, a recently remodelled area that hovers the Douro and gazes at the beautiful city of Porto. There you can find many of the most popular restaurants, bars and clubs of the city. By the night fall, Cais de Gaia becomes superb, not only because of its' vivid nightlife, but also for the charming view over the blinking "light-filled" Ribeira. For more information on how to get to Cais de Gaia from the YES Meeting Hotel, please check the "Local Map" section

## Food

### FRANCESINHA

A Francesinha (literal translation: Little French Girl) is a Portuguese meal from Porto, made with wet-cured ham, fresh sausage, steak or roast meat and covered with a large quantity of cheese. The sandwich is toasted and served in a shallow bowl, smothered with a thick, very spicy beer and tomato-based sauce. There are a lot of variations to Francesinha, some with champignon and cream, prawns, pork, chicken, tuna or even with vegetables only (although some don't recognize it as real Francesinhas).

### TRIPAS À MODA DO PORTO

When native son Henrique the Navigator geared up to conquer Ceuta in the early 15<sup>th</sup> century, Porto's residents slaughtered their cattle, gave the meat to Prince Henrique's fleet, and kept only the entrails. This dramatic generosity came in the wake of the Plague, when food supplies were crucial. The dish Tripas à Moda do Porto commemorates their culinary sacrifice; to this day, the people of Porto are known as Tripeiros (tripe-eaters).

## WHERE TO EAT

### ABADIA

Enjoy panoramic view and traditional Portuguese cuisine. Specialities are codfish and Tripas à Moda do Porto.

Rua do Ateneu Comercial do Porto, 22-24

### CAFÉ MAJESTIC

Those seeking refreshment should visit the Café Majestic. This Art Nouveau style establishment has a unique atmosphere and stays open until 2AM.

Rua de Santa Catarina, 112

### CAPA NEGRA

Great Portuguese cuisine. Specialities include Francesinha and crepes with ice-cream.

Rua do Campo Alegre, 191

### REGALEIRA

This is one of the best places to eat fantastic seafood.

Rua do Bonjardim, 87

### O ESCONDIDINHO

Decorated according to old houses from the Northern part of Portugal, this restaurant tries to combine the traditional food with gourmet. It has been visited by many figures of Portugal, such as Francisco Sa Carneiro and Mario Soares.

Rua de Passos Manuel 144 4000-382

### D. TONHO

Type of food – Francesinha.

Cais Ribeira 13 Porto, 4050-509

### RESTAURANTE FILHA DA MAE PRETA

Cais Ribeira 40, 4050-510

### SHIS

This restaurant is not cheap, but it delights every single taste bud of your mouth. Situated just next to the beach, it never disappoints people you are fan of gourmet food.

## YES GUIDE BOOK

Praia Do Ourigo, 4150-000

### **PIZARIA AL FORNO**

If you are more into Italian style, this is the place for you.

Rua do Adro da Foz 4, 4150h

### **BARS & CLUBS** (NOT INCLUDING THE MANY YOU CAN FIND AT RIBEIRA OR CAIS DE GAIA)

#### **ARMAZÉNS DO CHÁ**

Located downtown, in a building of the XIX century that used to be a coffee producing factory, Armazém do Chá is one of the very prestigious bars in Porto. With 3 floors, Armazém do Chá has many areas such as living room with pleasant sofas, cafeteria, wine bar, dance room, stage for live concerts and a gallery zone to expositions.

Rua Jose Falcão, 180, 4050-315

#### **BREYNER 85**

Rua do Breiner, 85 4050-126

#### **CAFÉ ANCORA DE OURO, AKA “O PIOLHO”**

You can't go to Porto and miss this café. With its 100 years of history, this café received in the past many congregations of students who fought against Portuguese ditacture and it still nowadays being the most popular place among university students of Porto.

Praça de Parada Leitão 43-57, 4050-456

#### **CAFÉ GALERIAS DE PARIS**

This café is placed downtown in one of the most popular streets of Porto s night. Being very close to Piolho, people usually stop here to listen to live music, eat their delicious chocolate cake or drink beer. The decoration is very peculiar, with a retro style that characterizes bars among Porto.

Rua Galeria de Paris – Clérigos

#### **CASA AGRICOLA**

Casa Agricola remains one of the last testimonies of ancient, rural Porto. A merchant from St. Domingo's Street, Antonio d'Almeida Saraiva built it, in the XVIII th century. Similarly to other wealthy people, he preferred to live in the suburbs, rather than the already noisy city. Today the house and its chapel is what have left from the Quinta de Nossa Senhora



do Bom Sucesso (literally our lady of good success). It is said that this huge farm - one of the most important of it's time - spread from the present Campo Alegre st. and reached the Agramonte graveyard, which was visited by countless pilgrims looking for the success of the saint. In this house the future is built on history.

Rua do Bom Sucesso 241, 4150

### **CASA DO LIVRO**

A bar downtown that was in times the very known bookshop Casa do Livro (Book s House). Now rebuilt, this place inherited the name and the books that still spread for the several rooms of the bar. Nonetheless, where in the past there were only books, now are also served cocktails, given live concerts, plays or performances. Here, the taste for the detail is notorious: with antique chairs with green and golden velvet, a piano in the center of one of the rooms, the huge bookshelves and the Venus of Boticelli taking care of the place.

Rua Galeria de Paris 85 4050-284

### **CONTAGIARTE**

A place where you can connect with different sounds and cultures. On Fridays you can listen to retro music. Saturday night is the Latin night, with Cuban and Brazilian music.

Rua Alvares Cabral, 372 4050-040

### **LAIS DE GUIA**

A beach bar in Matosinhos, very famous for it's Caipirinha.

Av. Norton de Matos, Praia Moderna 4450-208 Matosinhos

### **MAUS HÁBITOS**

A beach bar in Matosinhos, very famous for it's Caipirinha.

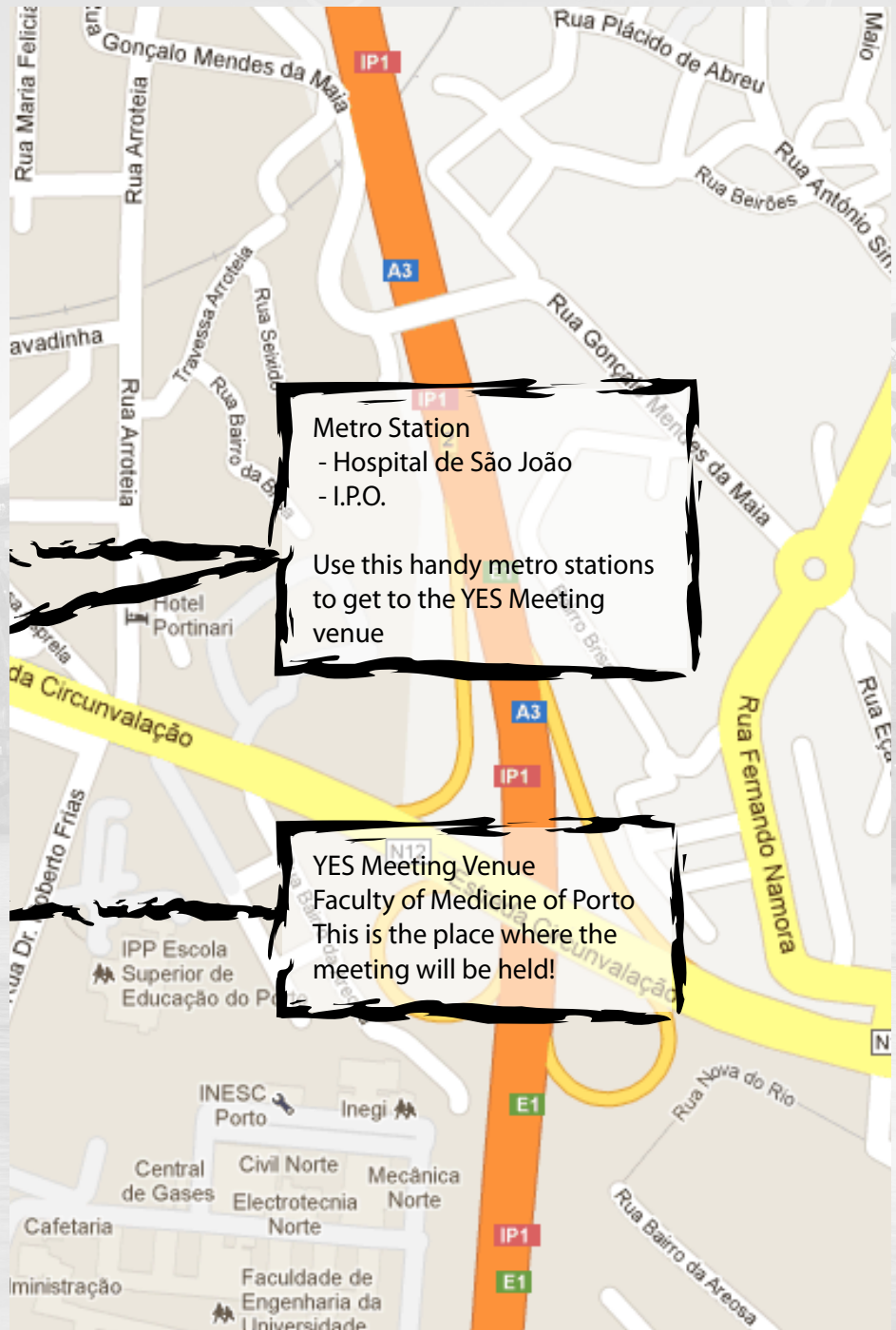
Rua Passos Manuel 178, 4º 4000-382

### **TWINS**

If you like bars more urban and cosmopolitans, you cannot miss the new Twins Bar that opened downtown.

Rua Candido dos Reis n.12 4050-151





## USEFUL INFORMATION

### ADMISSION

Participants are requested to wear their YES Badges at all times during the congress. Admission to the meeting rooms, social program events, lunches and coffee-breaks is limited to those wearing YES Badges.

### INFORMATION BOARD

An information board is located near the Information Desk. All news and changes not available at this YES Meeting Guide can be found there.

### WORKSHOPS

Application for workshops was previously done online.

### YES MEETING STAFF

You can identify YES Committee members and YES Assistance Staff members by their coloured identification cards and blue shirt. May you have any question or problem, please feel free to contact us any time.

### INSURANCE

Congress organizers cannot accept any liability for personal injuries or for loss of or damage to property belongings to congress participants, either during or as a result of the YES Meeting. Participants shall make their own arrangements for health and travel insurance.

### INTERNET ACCESS / WIRELESS LAN

Free internet stations are available in the YES Meeting exhibition area.

### LANGUAGE

The official language of the event is English. No simultaneous interpretation facilities are provided during the conference.

### MOBILE PHONES

Mobile phones must always be switched off inside lecture halls.

### SMOKING POLICY

Smoking in the Meeting area will not be allowed.



**COFFEE-BREAKS AND LUNCHES**

From September 16th to the 18th, coffee-breaks and lunch will be served free of charge to participants wearing YES Badges.

**CURRENCY AND SALES TAX**

The Portuguese currency is Euro (€). Major credit cards are accepted virtually everywhere. ATM cards with the "Maestro"-sign are accepted at all ATM machines (Multibanco - MB) for cash withdrawal as well as payment cards at many shops. Sales tax is normally included in quoted prices.

**ELECTRICITY**

220 volts AC, 50Hz. Round two-pin European plugs are universally used in Portugal.

**FIRST AID**

Please contact a staff member or the Reception desk.

**PHOTOGRAPHY, FILMING AND AUDIO RECORDING**

Unless previous permission has been granted by the speakers or poster presenters, photography, video and audio recording is strictly prohibited during the scientific sessions.

**PERSONAL PROPERTY**

Please take good care of your personal belongings. Neither the Faculty of Medicine nor the YES Staff will be held responsible for any loss or damage to your personal property.

**LOST AND FOUND**

If you loose anything, please ask the Information Desk about it. May you find anything in the YES Meeting premises, please deliver it at the Information Desk.

## USEFUL CONTACTS

### YES MEETING HEADQUARTERS

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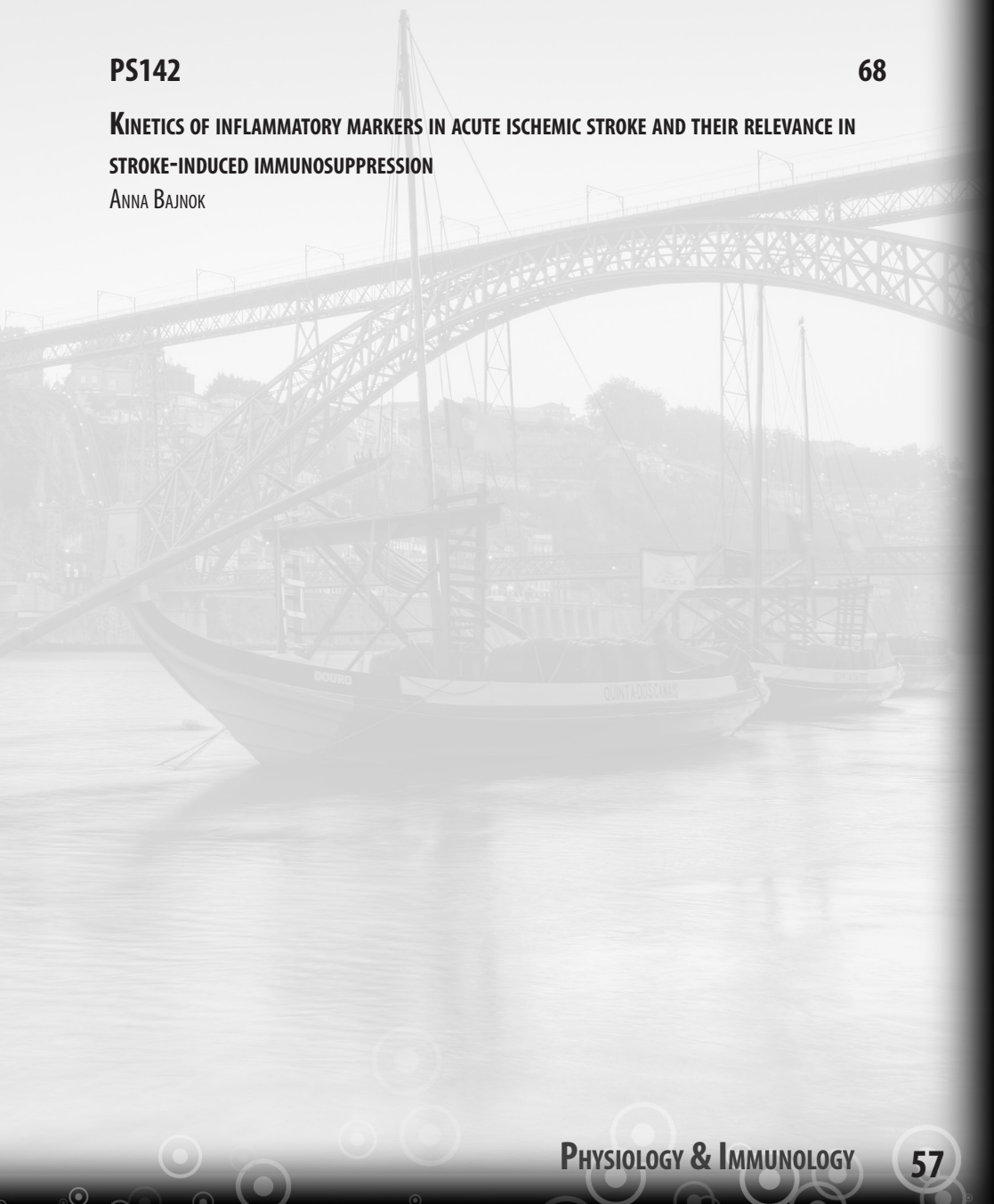
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### **ANALYSIS OF STRESS RESPONSES TO LABOR AND PUBLIC PERFORMANCE THROUGH CHANGES IN SALIVARY CORTISOL CONCENTRATIONS**

ALEKSANDRA VEJNOVIC (1), Doc. DR. NIKOLA CURIC (2)

1- FACULTY OF MEDICINE, UNIVERSITY OF NOVI SAD, 2- DEPARTMENT OF PATHOPHYSIOLOGY, FACULTY OF MEDICINE, UNIVERSITY OF NOVI SAD

#### **AIM**

Analysis and comparison of intensity and dynamics of salivary cortisol concentration changes as indicator of stress response to labor and public performance.

#### **INTRODUCTION**

Stress response is complex reaction of the organism to the threat of homeostasis disruption. There are numerous physical and psychosocial factors that can activate this reaction. Hypothalamic-pituitary-adrenal axis and cortisol have important role in stress response. Measurement of cortisol concentration provides the assessment of intensity and adequacy of stress response. Salivary cortisol measurement method has many advantages.

#### **METHODS**

Two groups were included in this study (10 women in labor and 12 musicians). All participants underwent psychophysical stress, labor and public performance, respectively. From each participant five saliva samples were collected using Salivette, at different times in relation to stressful event. Salivary concentrations were determined by electrohemiluminescent method. Obtained values were statistically analyzed utilizing Student's  $t$ -test and correlation between parameters.

#### **RESULTS**

Salivary cortisol levels in all samples were significantly higher in group of women in labor than in group of musicians ( $p < 0,05$ ). In both groups, the highest cortisol level was recorded one hour after stressful event (131,92 nmol/l- women in labor, 30,28 nmol/l- musicians). Increase in cortisol level in women in labor was bigger, on average 8,51 times, whereas in musicians 4,38 times. Significant correlation was found between areas under cortisol concentration curve in period during stressful event and in period after it, in group of musicians. However, such a correlation was not found in group of women in labor.

#### **CONCLUSION**

Stress response patterns of two groups are very similar in period during stressful event, while there is difference in stress response in period after stress due to influence of other factors.

**PS148****ANTIBACTERIAL EFFECTS OF RASPBERRY CONCENTRATE IN IN VITRO CONDITIONS**

ALEKSANDAR BOKAN (1), VERA GUSMAN (1,2)

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AIM

Determination of potential antibacterial effects of red raspberry fruit (*Rubus idaeus* L.).

**INTRODUCTION**

A contemporary antibacterial therapy significantly reduces the period of acute infectious diseases and prevents the development of various complications associated with ethiological agents of these diseases. However, there is a rise in the occurrence of microbial strains resistant to a wide range of antimicrobial agents. The task of the pharmaceutical industry is to provide adequate antimicrobials which provide positive effects even on the latest genetically modified microbial pathogens. As a source of many solutions, nature offers different plants whose effects have not yet been tested and still have not been given the importance as potential anti-inflammatory, anticarcinogenic or antibacterial agents.

**METHODS**

Antibacterial effect of the concentrate of red raspberry fruit, obtained in sterile conditions through a modified disk diffusion method, was later studied in order to determine its antibacterial effects. The following standard ATCC bacterial strains have been used: *Staphylococcus aureus* ATCC 25923, *Enterococcus faecalis* ATCC 29212, *Bacillus cereus* ATCC 11778, *Listeria monocytogenes* ATCC 19111, *Escherichia coli* ATCC 25922, *Salmonella Typhimurium* ATCC 14028, *Klebsiella pneumoniae* ATCC 700603, *Cronobacter muytjensii* ATCC 51329 and *Pseudomonas aeruginosa* ATCC 27853.

**RESULTS**

Red raspberry concentrate displayed an antibacterial effect on the following bacterial species: *Staphylococcus aureus* > *Listeria monocytogenes* > *Bacillus cereus* > *Enterococcus faecalis* > *Escherichia coli* > *Cronobacter muytjensii* > *Pseudomonas aeruginosa* > *Salmonella Typhimurium*. *Klebsiella pneumoniae* was the only species which was unaffected by the growth-inhibitory effect of the raspberry concentrate.

**CONCLUSION**

The red raspberry fruit or any of its processed form is an affordable and easily accessible nutrient that can be used in pharmaceutical, chemical and food industries as a new antibacterial agent with broad-spectrum effects.

## PS103

**CELLULAR ELECTROPHYSIOLOGICAL AND ANTIARRHYTHMIC EFFICACY OF NEW SODIUM/CALCIUM EXCHANGER INHIBITORS IN THE CANINE HEART.**

ANDRÁS HORVÁTH(2), ZSÓFIA KOHAJDA(1), CLAUDIA CORICI(2), NORBERT NAGY(1), KÁROLY ACSAI(1), PÉTER BILICZKI(2), JOUKO LEVIJOKI(3), PIERO POLLESELLO(3), TUULA KOSKELAINEN(3), LEENA OTSOMAA(3), ANDRÁS TÓTH(2), JULIUS GY. PAPP(1,2), ANDRÁS VARRÓ(1,2), LÁSZLÓ VIRÁG(1,2), NORBERT JOST(1,2)

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**AIM**

The aim of the study was to investigate the selectivity of the ORM-10103 and ORM-1096 compounds in canine heart muscle preparations. We tested the compounds on different repolarizing potassium currents such as the transient outward, inward rectifier, the slow and fast components of the delayed rectifier potassium current and on the L-type calcium current. We also tested the effects of the ORM-10103 on experimentally induced early (EAD) and delayed (DAD) after depolarizations.

**INTRODUCTION**

The sodium/calcium exchanger (NCX) is considered to be a major regulator maintaining the  $\text{Ca}^{2+}$  homeostasis in the myocardium. Since the extrusion of one  $\text{Ca}^{2+}$  is coupled with the entry of 3  $\text{Na}^{+}$  into the cell, the forward mode of the NCX is accompanied by a net inward current; when the intracellular  $\text{Ca}^{2+}$  level is elevated, this can cause substantial depolarization, leading to EAD and DAD, which are generally thought to play important roles in arrhythmogenesis. It may be speculated, therefore, that specific blockers of NCX are potentially antiarrhythmic in dysrhythmias related to a  $\text{Ca}^{2+}$  overload. This hypothesis has not been tested directly so far, since the available NCX inhibitors (KB-R7943 and SEA-0400) also decreased the L-type  $\text{Ca}^{2+}$  current ( $\text{I}_{\text{CaL}}$ ) which in turn is known to decrease the intracellular  $\text{Ca}^{2+}$  load, thereby indirectly changing the magnitude of NCX.

**METHODS**

Transmembrane ion current measurements were performed by using the whole cell configuration of the patch clamp technique in canine single left ventricular myocytes, and action potentials were recorded from canine and guinea-pig papillary muscles and Purkinje fibres using the conventional microelectrode technique.

**RESULTS**

ORM-10103 and ORM-10962 significantly reduced both the inward and outward NCX currents with estimated  $\text{EC}_{50}$  values of 780 nM vs. 51 nM and 960 nM vs. 67 nM, respectively. ORM-10103 (10  $\mu\text{M}$ ) and ORM-10962 (1  $\mu\text{M}$ ) did not significantly decrease the amplitude of  $\text{I}_{\text{Ca}}$  in canine ventricular myocytes. ORM-10103 (10  $\mu\text{M}$ ) did not affect the amplitude and the maximum rate of depolarization ( $V_{\text{max}}$ ) of the slow response



action potentials recorded from guinea-pig papillary muscles, which also suggested the lack of its effect on the L-type  $\text{Ca}^{2+}$  current. ORM-10962, even at a high concentration ( $1\text{ }\mu\text{M}$ ), did not influence  $\text{IK}_1$ ,  $\text{I}_{\text{to}}$ ,  $\text{IKr}$  and  $\text{IKs}$  currents. The same applies to ORM-10103 ( $3\text{ }\mu\text{M}$ ) except that it slightly decreased the  $\text{IKr}$  tail current. The amplitudes of pharmacologically induced early and delayed afterdepolarizations were significantly decreased by ORM-10103 ( $3$  and  $10\text{ }\mu\text{M}$ ) in a concentration-dependent manner.

## CONCLUSION

The present study provides evidences for the strong NCX-inhibitory activity of ORM-10103 and ORM-10962. ORM-10962 is more potent and selective for NCX than ORM-10103. It is concluded that specific inhibition of the NCX current can abolish triggered arrhythmias and may result in a powerful antiarrhythmic electrophysiological effects.

## PS141

### **INTERLEUKIN 10 SINGLE NUCLEOTIDE POLYMORPHISMS RS1800896 AND RS1800871 IN SERBIAN KIDNEY TRANSPLANT PATIENTS**

MILICA DJORIC (1), VERA PRAVICA (2), EMINA SAVIC (2), JOVANA MILIC (1)

1 – SCHOOL OF MEDICINE, UNIVERSITY OF BELGRADE; 2 – INSTITUTE OF MICROBIOLOGY AND IMMUNOLOGY, SCHOOL OF MEDICINE, UNIVERSITY OF BELGRADE

#### **AIM**

Our aim was to investigate if interleukin (IL)-10 single nucleotide polymorphisms (SNP) -1082 G/A (rs1800896) and -819 C/T (rs1800871) correlate with acute graft rejection and delayed graft function in kidney transplant patients.

#### **INTRODUCTION**

Kidney transplantation is the treatment of choice in chronic renal failure. Immune response is the main problem in this type of treatment. It has been suggested that gene polymorphisms for cytokines (tumor necrosis factor (TNF), interferon gamma (IFN- $\gamma$ ), IL-10, etc.) could affect early immune response to graft tissue. IL-10 is an anti-inflammatory cytokine that induces downregulation of MHC class II molecules and costimulatory molecules on antigen presenting cells while inhibiting TH1 cytokines production. It is mostly secreted by regulatory T-cells.

#### **METHODS**

The study included 91 kidney transplant recipients that had undergone kidney transplantation at least 1 year prior to the commencement of the study. During the first 12 months after transplantation frequency of acute rejection and delayed graft function were recorded. Serum creatinine concentration and creatinine clearance were also measured. Genomic DNA was isolated from peripheral blood, sampled with EDTA, using the GeneJET whole blood genomic DNA purification mini kit (Fermentas Thermo Fisher Scientific Inc, Germany). The purity of DNA was determined by measuring absorbance at 260 and 280 nm, respectively. SNPs were detected using real-time PCR based detection method with commercial TaqMan probes (Applied Biosystems Inc, USA). Statistical test used in this study was Fisher exact probability test.

#### **RESULTS**

Our results didn't show the correlation of IL-10 polymorphisms -1082 G/A (rs1800896) and -819 C/T (rs1800871) with acute rejection and delayed graft function. However, both were in correlation with early acute rejection (less than 10 days). Patients who had allele A of -1082 G/A (rs1800896) polymorphism or allele T of -819 C/T (rs1800871) were less likely to suffer from acute rejection in the first 10 days post transplantation.

#### **CONCLUSION**

It has been indicated that alleles G in SNP rs1800896 and C in rs1800871 are associated with high production of IL-10 in vivo. Our study implies that high producers of IL-10 could be more likely to suffer early acute

rejection. We can speculate that high production of IL-10 may be in the response to high pro-inflammatory activity immediately after transplantation.



## PS96

### **TNF GENE POLYMORPHISM rs1800629 IN SERBIAN KIDNEY TRANSPLANT PATIENTS**

JOVANA MILIOÖ (1), VERA PRAVICA (2), EMINA SAVIOÖ (2), MILICA DJORIOÖ (1)

(1) SCHOOL OF MEDICINE, UNIVERSITY OF BELGRADE

(2) INSTITUTE OF MICROBIOLOGY AND IMMUNOLOGY, SCHOOL OF MEDICINE, UNIVERSITY OF BELGRADE

#### AIM

The aim of this study was to examine whether -308 G/A (rs1800629) TNF polymorphism correlate with acute graft rejection (AR), delayed graft function (DGF) and biochemical parameters of kidney function such as serum levels of creatinine and creatinine clearance in kidney transplant patients.

#### INTRODUCTION

The main indication for kidney transplantation is chronic renal failure. This treatment is commonly accompanied by immune response which can cause severe damage to patients, so immunosuppressive therapy is used in order to prevent graft rejection. Importance of gene polymorphisms for cytokines such as tumor necrosis factor (TNF) in immune response to graft tissue is widely examined. TNF is pro-inflammatory cytokine which is mostly produced by mononuclear phagocytes, but it can also be produced by activated T-lymphocytes and NK cells. Better definition on extent of TNF involvement of individual TNF genetics in allogenic immune response could provide rationale for more adequate immunosuppressive protocols.

#### METHODS

The study included 91 kidney transplant recipients that had undergone kidney transplantation. During the first 12 months after transplantation frequency of AR and DGF graft function were recorded. Serum creatinine concentration and creatinine clearance were also measured. Genomic DNA was isolated from peripheral blood, using the GeneJET whole blood genomic DNA purification mini kit (Fermentas Thermo Fisher Scientific Inc, Germany). The purity of DNA was determined by measuring absorbance at 260 and 280 nm, respectively. SNP was detected using real-time PCR based detection method with commercial TaqMan probes (Applied Biosystems Inc, USA). Non-parametric statistical tests were used in this study.

#### RESULTS

Study results did not show the correlation of -308 G/A (rs1800629) TNF gene polymorphism with AR and DGF. However, statistically significant difference has been shown between mean values of creatinine clearance and TNF gene polymorphism genotypes. Patients with GG genotype had higher creatinine clearance 3, 6 and 12 months after transplantation than the patients with AG or AA genotype (57.35 ml/min Vs. 46.81 ml/min after 3 months,  $p<0.01$ ; 62.74 ml/min Vs. 51.51 ml/min after 6 months,  $p<0.05$ ; 61.64 ml/min Vs. 51.25 ml/min after 12 months,  $p<0.05$ ).

#### CONCLUSION

Preliminary results of this study did not show that TNF gene polymorphism has influence on AR and DGF, despite of fact that previous investigations in this area show important role of TNF in these immune processes. This finding can be explained by small number of patients that were commenced to the study, so further



analysis is required. AA homozygotes of functional TNF polymorphism at the position -308 (rs1800629) are characterized as genetically high TNF producers, while presence of G allele can suppress activity of T cell line promoter. This is in agreement with our results indicating that patients with GG genotype demonstrate higher values of clearance creatinine due to lesser inflammation after transplantation.



## PS196

### THE EFFECT OF DIABETES IN THE DISTRIBUTION OF ADENOSINE RECEPTORS IN THE KIDNEY OF HYPERTENSIVE RATS

CARLA CARVALHO (1), CARLA ABREU (1), DANIELA PATINHA (2), JOANA AFONSO (2), CARMEN DINIZ (1), MANUELA MORATO (1,2), ANTÓNIO ALBINO-TEIXEIRA (2)

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AIM

This work aimed at studying the distribution of adenosine A1 and A2B receptors in the kidney of spontaneously hypertensive rats (SHR) with and without streptozotocin (STZ)-induced diabetes.

#### INTRODUCTION

Diabetes damages the kidney, being diabetic nephropathy a prime cause of end-stage renal disease[1]. Adenosine regulates several renal physiological functions[2]. Most diabetic patients also have hypertension, aggravating the prognosis[3].

#### METHODS

On day 0, male SHR rats (12 weeks) were i.p. injected with STZ (65 mg/kg-1; diabetic group) or vehicle (control group). On day 21, animals were anesthetized with pentobarbital sodium (50 mg/kg-1; i.p.) and the left kidney was removed, fixed in formalin and included in paraffin. Tissue sections (4 µm) were incubated with primary antibodies against adenosine receptors (anti-A1 and anti-A2B), the resulting immuno-complexes detected with a biotinylated secondary antibody and the chromogenic reaction enhanced with ABC using DAB as substrate. DAB-immunostained sections were imaged using bright field optics on a microscope and acquired using a CDD camera connected to a computer. Statistical analysis was performed by Mann-Whitney test and Dunn's post hoc test, using GraphPad software.

#### RESULTS

In both groups, the adenosine A1 receptor immunoreactivity was located in mesangial cells while that for the adenosine A2B receptor was mainly observed in podocytes, but also in mesangial cells. Both immunoreactivities were more marked in superficial than in deep glomeruli. In all glomeruli, the immunoreactivity for the adenosine A1 receptor was lower in the STZ group while that for the adenosine A2B receptor was higher in the STZ group, when compared to the control group. Immunoreactivity for both receptors was also observed in the distal convoluted tubule, and in the loop of Henle for adenosine A1 receptors. No immunoreactivity was observed in the proximal convoluted tubule. In these renal structures, the immunoreactivity was similar between experimental groups. The collecting duct also presented

immunoreactivity for both receptors. However, for the adenosine A1 receptor it was lower in the STZ group, whilst for the A2B receptor, it was higher in the STZ group, when compared to the control group.

## CONCLUSION

The results of the present study, although only semi-quantitative for now, suggest that in SHR animals, STZ-induced diabetes alters the renal expression of adenosine receptors which might be triggered by the diabetes-induced higher concentration of endogenous adenosine described in the literature.

Aknowledgements: Abbot Diabetes Care and FEDER/QREN/COMPETE and Strategic Programs (FCT project grants: PTDC/SAU-FCF/67764/2006; PEst-C/SAU/LA0002/2011; PEst-C/EQB/LA0006/2011]. Patinha D. grant: QREN/POPH (FCT-SFRH/BD/43187/2008).

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## PS142

### **KINETICS OF INFLAMMATORY MARKERS IN ACUTE ISCHEMIC STROKE AND THEIR RELEVANCE IN STROKE-INDUCED IMMUNOSUPPRESSION**

ANNA BAJNOK

FACULTY OF MEDICINE, SEMMELWEIS UNIVERSITY

AIM

In this study, we aimed to describe the kinetics of selected clinical inflammatory markers (CRP, WBC, neutrophil count, suPAR, CD64 neutrophil and monocyte antigen) in order to identify an inflammatory marker that best represents this biphasic immunological response after AIS. We also aimed to describe the prevalence of immunosuppressive CD4+ CD25high Treg cells, activated (CD11b+) monocytes, as well as the prevalence of CD177+ neutrophils and monocytes.

#### INTRODUCTION

The clinical relevance of the bidirectional relation between the central nervous system (CNS) and the immune system has gained increasing attention in acute ischemic stroke (AIS) over the recent years. While acute stroke patients may survive the initial CNS insult, subsequent complications might develop over time, of which infection is the most common and thus the chief cause of morbidity and mortality in stroke survivors. Animal data clearly support a biphasic effect of stroke on the immune system. The initial phase is characterized by a local and then a generalized inflammatory response, which is followed by systemic immunosuppression, referred to as stroke-induced immunosuppression (SIIS). Therefore, from a clinical point of view, it is of great importance to distinct the inflammatory response induced by CNS damage and that later caused by evolving infection, however markers of infection currently used in clinical practice are unreliable in this regard.

#### METHODS

Peripheral blood samples were taken from 12 AIS patients free of infection within 6 hours and one week after the insult and 14 age-matched individuals with negative neurological history as control. Plasma suPAR and CRP concentrations were measured. WBC and neutrophil count values were determined using a Beckman Coulter analyzer. The prevalence of CD4+ CD25high Tregs, CD64+ and CD177+ neutrophils and monocytes were assessed using flow cytometry.

#### RESULTS

We found elevated suPAR levels 6 hours after the insult compared to controls, and this elevation was still present 1 week later. The level of CRP and WBC and neutrophil counts were not elevated in the 6 hour group, but showed elevation 1 week after the insult. The prevalence of CD177+ neutrophils and monocytes was higher in both stroke groups compared to controls. The prevalence of immunosuppressive Treg cells showed a decrease 6 hours after the insult but showed an increasing tendency 1 week later. The number of CD64+ neutrophils was highly elevated in the 6 hour group compared to controls, and decreased below the baseline in the 1 week group (5.95 [5.41-8.75] % vs. 32.38 [9.21-43.93] % vs. 4.06 [1.73-6.77] %,  $p < 0.05$ ).



## CONCLUSION

Based on our results we can state, that of selected clinical inflammatory markers the prevalence on CD64+ neutrophils sensitively follows the biphasic kinetics of the immunological response following AIS, therefore it is a suitable candidate for the indication of the developing inflammatory response due to infection, since its levels are expected to rise again in this condition.

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VAKALIOSZ ATHÉNA (1), KOCIS-BOGÁR KRISZTINA (2), DR. PERCEL FORINTOS DÓRA (3)

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ALEXANDER A. POTAPOV 1, SERGEY A. GORYAYNOV 1, ANTON G. GAVRILOV 1, VLADIMIR A. OKHLOPKOV 1, LYUDMILA V. SHISHKINA 1, VSEVOLOD A. SHURKHAY 1, PETR V. ZELEKOV 1, VIKTOR B. LOSCHENOV 2, TATYANA A. SAVELEVA 2, PAVEL V. GRACHEV 2, MARIA N. HOLODTSOVA 2, SERGEY G. KUZMIN 3, DENIS A. GOLBIN 1, ANASTASIA P. CHUMAKOVA 4

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### EVALUATION OF THE MTHFR A1298C VARIANT IN LEUKOARAIOSIS

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#### AIM

The aim of the present study was to examine whether the MTHFR A1298C genetic variant, which is also believed to be unfavorable, is associated with the presence of leukoaraiosis (LA) and whether there is an unfavorable synergistic effect between the unfavorable MTHFR C677T allele and the MTHFR A1298C variants as regards the frequency of LA.

#### INTRODUCTION

Vascular demyelination of the white matter of the brain is referred to as leukoaraiosis (LA). This very frequent entity is associated with a cognitive decline, thereby resulting in a deteriorating quality of life. Besides poorly controlled hypertension and aging, its development is reported to be associated with an elevated serum homocysteine level. Although the methylenetetrahydrofolate reductase (MTHFR) C677T genetic variant is associated with an elevated serum homocysteine level, it has not been proved to be an independent risk factor for LA.

#### METHODS

The clinical and genetic data on 198 LA patients and 235 neuroimaging alteration-free controls were analyzed.

Genomic DNA was extracted from 200  $\mu$ l of peripheral blood anticoagulated with EDTA by the desalting method (Miller et al. 1988.).

The genetic variants of MTHFR C677T and A1298C were identified by LightCycler probe system (Szolnoki et al. 2006.).

Statistics. We used Chi-squared test.

#### RESULTS

The presence of the A1298C or the 1298CC variant was calculated to be a risk factor for LA, as compared with the absence of both of them. The clustering of the heterozygous A1298C and C677T variants was proved to involve the risk of LA.

#### CONCLUSION



Our results suggest that the MTHFR A1298C variant confers an independent genetic risk of LA, and this pathological role may be amplified by the MTHFR C677T variant.



## PS53

### CHILDHOOD TRAUMATIC EVENTS IN THE BACKGROUND OF PSYCHOTIC SYMPTOMS

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#### AIM

Our hypothesis was that in the history of psychotic patients with more positive than negative symptoms, childhood traumatic events are more common. Dissociation and PTSD as possible mediating factors were also examined.

#### INTRODUCTION

It is widely accepted that childhood physical or sexual abuse is a risk factor for psychotic symptoms later in life. Several data suggest that childhood traumas can cause both biochemical and structural anomalies in the brain which may have an effect on the exacerbation of psychotic symptoms.

The connection between traumatic events and psychosis is supported not only by neurobiological processes but similarities between psychosis and posttraumatic stress disorder (PTSD) symptoms described by several studies. According to Ehlers and Clark's cognitive model, traumatic experiences are processed in a data-driven fashion, and this leads to fragmented memories of the traumatic events which can return involuntarily in the form of flashback memories in PTSD. This fragmentation of memories and the self can be observed in schizophrenia spectrum disorders too, and the role of hippocampus in the integrity of memories and the self must be mentioned. There are also results which demonstrate that PTSD and dissociation may be possible mediators between life events and the clinical manifestation of schizophrenia spectrum disorders.

#### METHODS

Patients with schizophrenia or schizoaffective disorder answered our questionnaires (N=50):

SCID I(First, Spritzer, Gibbon, Williams, 2000)

SAPS (Andreasen, 1984)

SANS (Andreasen, 1983)

Life Events Questionnaire, shortened (Paykel, 1991)

DES (Carlson, Putnam, 1986)

Impact of Events Scale (Horowitz, 1979)

For the statistical analysis we used SPSS 20.

#### RESULTS

Childhood physical abuse committed by the parents had a significant positive correlation with positive symptoms ( $r=0,356$ ;  $p=0,016$ ;  $n=45$ ), especially with hallucinations ( $r=0,317$ ;  $p=0,30$ ;  $n=47$ ) and a

significant negative correlation with the negative symptom emotional withdrawal ( $r=-0,307$ ;  $p=0,048$ ;  $n=42$ ). The presence of dissociation was positively associated with childhood physical abuse ( $r=0,401$ ;  $p=0,014$ ;  $n=38$ ) and with positive psychotic symptoms ( $r=0,417$ ;  $p=0,10$ ;  $n=38$ ) as well. With PTSD no significant correlations were found.

## CONCLUSION

As a result, we can say that childhood traumas are more common in the history of psychotic patients with more positive symptoms. Furthermore, we can assume dissociation to be a mediating factor between childhood traumas and psychosis. However, the mediating role of PTSD has not been proved. In order to gain further statistical support, a wider sample and regression analyses are necessary.

## PS84

### **QUANTITATIVE BIOSPECTROSCOPY AND FLUORESCENCE DIAGNOSTICS WITH 5-ALA IN SURGERY OF INTRACRANIAL MENINGIOMAS**

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#### **AIM**

To expand the application of fluorescence diagnostics and biospectroscopy with 5-ALA and to assess the role of these methods in meningioma surgery.

#### **INTRODUCTION**

Fluorescence diagnostics and laser spectroscopy with 5-ALA was shown to be effective in surgery of malignant gliomas. However, only few authors report fluorescence- or spectroscopy-guided meningioma resections.

#### **METHODS**

The study included 12 patients (three male and six female patients, median age was 61 years) with intracranial meningiomas. All patients were operated with the aid of 5-ALA-induced fluorescence navigation in Burdenko Neurosurgery Institute in 2011-2012. In all cases laser biospectroscopy was performed. We compared fluorescence spectra from tumorous tissues with those of the intact brain.

#### **RESULTS**

Tumor fluorescence was observed in all cases. Generally meningiomas demonstrated intensive, bright fluorescence. The maximal peaks in the fluorescence spectra ranged from 9.39 to 121.93 (median – 32.64) and the mean values of spectra ranged from 5.44 to 59.35 (median – 24.31). We also investigated fluorescence spectra of the intact brain tissues in all cases, the values ranged from 0.32 to 5.98 (median – 1.9).

Radical resection (Simpson I-II) was achieved in 10 cases. In all resections, however, visual evaluation of fluorescence helped to achieve a more careful dissection of small tumor fragments, especially those that infiltrate the bone flap, the arachnoid, the pia and the dura mater. In two cases of meningiomas with abundant blood supply fluorescence intensity decreased during the course of the resection. In this case biospectroscopy helped to distinguish between tumorous and intact tissues.

We observed 10 patients after discharge. Relapse occurred in the only one case where a subtotal resection of



multiple atypical convexital and basal meningiomas was achieved at the surgery.

## CONCLUSION

Our data indicate that qualitative and quantitative assessment of 5-ALA-induced fluorescence enables additional and more precise visualization of meningiomas during their resection. Fluorescence navigation affects surgical strategy and enables quick differentiation between normal and pathological tissues within the operative wound. We consider this method to be particularly useful for operating on the sites of tumor invasion into the adjacent tissues. Further investigation is needed to assess how the method affects relapse-free survival and postoperative treatment strategy.

## PS105

### **EFFECT OF THE NATURAL COMPOUND RESVERATROL IN OSTEOARTHRITIC PAIN: A BEHAVIOURAL EXPERIMENTAL STUDY**

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#### **AIM**

The aim of our study was to evaluate the potential beneficial effects of resveratrol in the nociceptive-related behaviour of rats with OA induced by a sodium monoiodoacetate (MIA) knee injection.

#### **INTRODUCTION**

Osteoarthritis (OA) is a joint related inflammatory disease and is a major clinical problem characterized by biomechanical impairment and also by incapacitating chronic pain, persistent at rest and exacerbated by movement, therefore representing a huge obstacle on patients' quality of life. OA-associated pain is currently treated with drugs with numerous side effects and not completely effective. Resveratrol is a polyphenol receiving considerable attention as a promising natural compound to be used as either a potential therapy or as a preventive agent for numerous diseases due to its anti-oxidant, anti-aging, anti-carcinogenic and anti-inflammatory properties. Despite resveratrol anti-inflammatory therapeutic application has been evaluated mainly in the gastrointestinal tract, its beneficial effect may extend to other sites and pathologies, including arthritis.

#### **METHODS**

All procedures were performed according to the ethical guidelines for the study of experimental pain in conscious animals. OA was induced by injection of 2mg of mono-iodoacetate (in 25  $\mu$ L saline) in the left knee joint of adult rats. Starting at 14 days of OA, one group of rats received twice a day, during 2 weeks, an intraperitoneal injection of resveratrol in dimethylsulphoxide (DMSO) (10 mg/Kg of a 5 mg/mL resveratrol solution in 10% DMSO) (RESV+DMSO Group). During the same period, another group of rats received a similar injection of 10% DMSO (DMSO Group). At days 0 (before MIA injection), 7, 14 (before DMSO/RESV+DMSO injection), 21, 28 (during DMSO/RESV+DMSO treatment) and 35 (before sacrifice), the movement-induced nociceptive response was evaluated using the Knee-bend test. Both groups were sacrificed by perfusion at day 35 of OA.

#### **RESULTS**

In the first 14 days after OA induction, the Knee-Bend scores were identical for both groups, indicating an increasing nociceptive sensitivity to induced movements of the knee. After day 14, with the administration of RESV+DMSO or DMSO, remarkable differences between both groups were noticed. While in the DMSO group the knee bend scores remained high throughout the 2 weeks of injection, in the OA rats treated with resveratrol a progressive reduction of the nociceptive response to the knee bend test was detected, more

obvious after 2 weeks of treatment (at day 28). After this time point and until day 35, the DMSO Group of rats manifested a subtle increase in the Knee-Bend scores, while the RESV+DMSO Group showed a stabilization of the nociceptive response.

## CONCLUSION

The attenuation of the nociceptive behavioural response in rats treated with Resveratrol during the 2 week period suggests that this natural compound can play an important role in ameliorating arthritis-related nociception and therefore be used in the future as an alternative therapy to the currently used drugs.

## PS138

### **THE REACTION OF SOMATOSENSORY CORTEX NEURONS TO POSTERIOR THALAMIC NUCLEUS STIMULATION IN WAG/Rij RATS, GENETICALLY PREDISPOSED TO ABSENCE EPILEPSY.**

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#### **AIM**

The aim of this research is to detect the role of sensory systems in development of absence epilepsy.

#### **INTRODUCTION**

The prominent EEG hallmarks of absence epilepsy are spontaneous spike-wave discharges.

It was found, that in WAG/Rij rats, which genetically predisposed to absence epilepsy, the spike-wave discharges occurs in the somatosensory cortex, whiskers associated area.

Whiskers associated area in the somatosensory cortex is the largest projection area of the rat — Es cerebral cortex and occupies about 30% of the total area of the neocortex. There is an interaction of afferent flow coming through the lemniskus and paralemniskus ways.

#### **METHODS**

Experiments were performed on WAG/Rij rats, as a genetic model of absence epilepsy. As a control group Wistar rats, not suffering from absence epilepsy, were used.

In acute experiments under urethane narcosis, the reactions of the single somatosensory cortex neurons to stimulation of the posterior thalamic nucleus (Po) — paralemniskus input to the cortex - were studied.

#### **RESULTS**

We found that in rats of the Wistar group, the reaction of cortical neurons to single electrical PO stimulation has three types of responses:

short-latency (12 ms), short duration discharge; long- latency (32-40 ms) long- duration (90 ms) discharge, and a reaction including of short- latency and long- latency reactions (complex reaction). Also, there is predominance of short-latency responses. WAG/Rij rats have no complex reaction and predominance of the long-latency responses.

#### **CONCLUSION**

These data indicates the violation of the paralemniskus cortex entry functioning in predisposed to absence epilepsy rats. Becomes obvious type of this violation. It may shed light on the fundamental processes underlying the disease.



**PS118****STRUCTURAL AND FUNCTIONAL IMPLICATIONS OF PHOSPHORYLATION OF PRRXL1****HOMEODOMAIN TRANSCRIPTION FACTOR**

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1 - THESE AUTHORS MADE AN EQUAL CONTRIBUTION TO THIS WORK, 2 - DEPARTMENT OF EXPERIMENTAL BIOLOGY, FACULTY OF MEDICINE & IBMC - INSTITUTE FOR MOLECULAR AND CELL BIOLOGY, UNIVERSITY OF PORTO, PORTUGAL, 3 - CENTER FOR NEUROSCIENCE AND CELL BIOLOGY, UNIVERSITY OF COIMBRA, PORTUGAL, 4 - QOPNA, MASS SPECTROMETRY CENTRE, DEPARTMENT OF CHEMISTRY, UNIVERSITY OF AVEIRO, PORTUGAL  
AIM

Identification of PRRXL1 phosphorylation sites and their implication in PRRXL1 conformation-dependent activity.

**INTRODUCTION**

PRRXL1 is a paired-like homeodomain transcription factor with a recognized role in the connectivity and survival of 1st and 2nd order nociceptive neurons at both the spinal cord (SC) and the brainstem. The dorsal horn of knockout mice SC shows loss of laminae I-III neurons, and the mice present reduced sensitivity to noxious stimuli. Immunoblot analysis of PRRXL1 reveals a multiple band pattern which is eliminated by phosphatase treatment, suggesting that PRRXL1 is phosphorylated.

**METHODS**

PRRXL1-HA fusion protein was immunoprecipitated from transfected ND7/23 cells and analysed by Mass Spectrometry. PRRXL1 phospho-site mutants were generated by site-directed mutagenesis. PIN1 binding was assayed through GST-pulldown and co-immunoprecipitation. The transcriptional and DNA-binding activities of PRRXL1 mutants were determined by luciferase-reporter and DNA pull-down assays. Phospho-PRRXL1 (S119) antibody was generated by rabbit immunization and sequential affinity purification from rabbit sera. Structural data was inferred from limited trypsin proteolysis and Ferguson Plot analysis.

**RESULTS**

Mass spectrometry analysis revealed six unique phospho-sites: T110, S119, S231, S233, S238 and S251. Four of these phospho-sites precede a highly conserved proline residue. This constitutes the binding site for the phospho-specific prolyl-isomerase PIN1, here shown to interact with PRRXL1 and whose knockdown diminished PRRXL1 transcriptional activity. PRRXL1 band pattern analysis through tryptic proteolysis and Ferguson Plot demonstrated that the upper bands display different structural properties. These bands are recognized by the pS119 specific antibody. Although phospho-site mutation did not impair PRRXL1 dimerization, DNA-binding or nuclear trafficking, the mutants displayed phospho-site specific modulation of PRRXL1 transcriptional activity.

## CONCLUSION

This work shows that phosphorylation is a major modulator of PRRXL1 transcriptional activity. PRRXL1 activity modulation occurs through variations in its conformation, which are mediated by changes in intra and intermolecular interactions and by proline isomerization. Of the identified phosphorylated residues, S119 seems to be the strongest determinant of PRRXL1 conformation.

**PS127****SEXUAL AND SPHINCTER DYSFUNCTION IN PATIENTS WITH MULTIPLE SCLEROSIS.**

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FACULTY OF MEDICAL SCIENCES, UNIVERSITY OF KRAGUJEVAC

**AIM**

The aim of our study is to determinate existence of sexual dysfunction, disorders of bladder and bowel control in patients with multiple sclerosis and to determinate their correlation with anxiety and depression in these patients.

**INTRODUCTION**

Sexual dysfunction, disorders of bladder and bowel control are very common symptoms in patients with multiple sclerosis. These problems are disturbing to patients and often correlated with anxiety and depression.

**METHODS**

In our study, we used Multiple Sclerosis Quality of Life-54 questionnaire which is translated and adapted for patients in Serbia, Hamilton Rating Scale for Depression and Hamilton Anxiety Rating Scale.

Statistical data processing, we used the Pearson correlation test and Student's t test.

**RESULTS**

In this study we enrolled 120 patients with multiple sclerosis, 68

females and 52 males. The average age of respondents was 47.36 years, and

average duration of illness 17 years. Bladder disturbances were presented in 88 patients (73.3%). Most frequent urinary symptoms were: urgency of micturition (91%), frequency of micturition (81%), hesitancy (81%) and urge incontinence (77.2%) of all patients with bladder dysfunction. Fecal incontinence occurred in 36 (30%) and constipation in 64 (53.3%) of patients. Sexual dysfunction was observed in 82.35% of female patients and 55.17% of male patients. Most frequent symptoms of sexual dysfunction in female patients were trouble achieving orgasm and loss of libido and in male patients difficulty achieving or maintaining an erection and difficulty achieving orgasm and/or ejaculation. The average values of Multiple Sclerosis Quality of Life-54 questionnaire domains Sexual function is 48.60 and Satisfaction with sexual function 51.66. We found positive correlation between the bladder dysfunction and values of Hamilton anxiety rating scale ( $r=0.223, p=0.12$ ) and Hamilton rating scale for depression ( $r=0.29, p=0.15$ ), but they were not statistically significant. We found statistically significant positive correlation between the bladder dysfunction and duration of disease ( $r=0.360, p=0.025$ ). Statistically significant negative correlation was between domain of the Sexual Dysfunction and Anxiety ( $r=-0.418, p=0.022$ ), and negative, statistically significant correlation between depression and Sexual dysfunction ( $r=-0.354, p=0.027$ ). Also we found statistically significant negative correlation between the domain of Satisfaction with sexual function and Anxiety ( $r=-0.417, p=0.011$ ) and Depression ( $r=-0.464, p=0.005$ ).

**CONCLUSION**

Our results suggest that there is a huge incidence of bladder and bowel control disorder and sexual dysfunction in patients with multiple sclerosis. Also, there was a significant correlation between these disorders with anxiety and depression in these patients.



## PS167

**EGCG PREVENTED THE DIABETES-INDUCED HYPERACTIVITY OF SPINAL NOCICEPTIVE NEURONS: A POSSIBLE INVOLVEMENT IN OPIOIDERGIC SPINAL SYSTEM**

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AIM

In the present study we aimed to evaluate the effects of treating streptozotocin (STZ)-diabetic rats with Epigallocatechin Gallate (EGCG), a potent antioxidant present in green tea, in pain behavioral responses, in oxidative stress damage and neuronal activation at the spinal cord. Moreover, the involvement of oxidative stress damage on spinal mu-opioid-receptor (MOR)-neurons was studied.

**INTRODUCTION**

Diabetic neuropathy is frequently associated with neuropathic pain, which is due to hyperactivity of the nociceptive spinal cord neurons. Although the mechanisms underlying this hyperactivation remain unclear, recent data showed that it was reversed by antioxidant treatment with alpha-lipoic acid, which also ameliorated pain behavioral responses.

**METHODS**

Diabetes was induced by an intraperitoneal injection of STZ in male Wistar rats. Control animals (CTR) received vehicle solution. Three days post-injection, one set of STZ-diabetic rats started EGCG treatment (2g/L in the drinking water - STZ+EGCG), while CTR and STZ-diabetic (STZ+H<sub>2</sub>O) animal maintained normal water consumption. Mechanical hyperalgesia and tactile allodynia were behaviorally evaluated by Randall-Sellito and dynamic plantar aesthesiometer before, at 4 weeks and at the end of treatment. Animals were sacrificed 10 weeks post-injection. The spinal cord was removed and sections were immunoreacted against 8-hydroxy-2'-deoxyguanosine (8-OHdG), a marker of DNA/RNA damage. The spinal expression of 8-OH-dG was quantified by densitometry at L4-L5 spinal segments. Double immunofluorescence reactions against Fos (marker of neuronal activation) or MOR and 8-OHdG were performed to evaluate the role of oxidative stress on spinal nociceptive processing.

**RESULTS**

The STZ-diabetic rats developed hyperglycemia, which was maintained until the end of the experiments and was not affected by the treatment with EGCG. Despite the maintenance of hyperglycemia after EGCG treatment, the STZ-diabetic rats showed attenuation of mechanical hyperalgesia and a total reversal of tactile allodynia. This improvement of behavioral signs of diabetic neuropathy was associated with a significant reduction of 8-OHdG expression and with a significant decrease in the number Fos-immunoreactive neurons. Moreover, there was also a decrease in the number of neurons co-expressing Fos and 8-OHdG. Spinal MOR expression was unaltered by diabetes, but 8-OHdG was shown to be expressed by MOR-immunoreactive neurons in the STZ-diabetic rats.

## CONCLUSION

The treatment with EGCG prevented the diabetes-induced hyperactivity of spinal nociceptive neurons, probably by diminishing the oxidative stress damage at the spinal dorsal horn. This is likely to contribute to the anti-hyperalgesic and anti-allodynic effects elicited by EGCG treatment.

By showing that spinal MOR neurons express 8-OHdG, this study points for a role of oxidative stress in the loss of opioid-induced analgesia observed in diabetic neuropathic pain.

**PS104****TOTAL NUMBER OF ER $\alpha$ -IMMUNOREACTIVE NEURONS OF THE PRINCIPAL DIVISION OF THE BED NUCLEUS OF THE STRIA TERMINALIS IN FEMALE RAT BRAIN DURING THE ESTROUS CYCLE**

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**AIM**

To evaluate the total number of ER $\alpha$ -ir neurons in the BNSTpr of three-month-old female Wistar rats during the estrous cycle.

**INTRODUCTION**

The BNST is a relay nucleus of the rostral forebrain closely related to the amygdala. It is extensively connected to some preoptic and hypothalamic nuclei involved in the neuroendocrine regulation of the reproductive behavior [1]. The effects of estrogens on the BNSTpr are essential for its role in the regulation of sexual and defensive behaviors. The BNST is known to express abundantly both types of nuclear estrogen receptors (ER) and their expression is modulated by hormone levels [2,3]. Estrogen receptor content significantly changes over the estrous cycle, with brain levels being highest during metestrus, attenuated on diestrus, and lowest during proestrus and estrus [4].

**METHODS**

The estrous cycle of 3-mo-old rats was monitored daily by vaginal smear cytology. Prior to perfusion, blood samples were taken directly from the heart and estradiol and progesterone serum levels were assayed. The animals were perfused, the brains were sectioned and the uteri were surgically isolated and weighed. The BNST-containing sections were processed for immunohistochemistry using an anti-rabbit ER $\alpha$  antibody. The estimates of the total number of neurons were obtained by using stereological methods. The results were statistically analyzed using a one-way ANOVA.

**RESULTS**

The total number of ER $\alpha$ -ir neurons in the BNSTpr significantly altered over the estrous cycle, being about 35% lower during proestrus and estrus when compared with metestrus and diestrus.

**CONCLUSION**

These results suggest that gradual combinations of ovarian hormone levels have the ability to modulate the expression of ER $\alpha$  in the neurons of the BNSTpr. On the one hand, the prominent surge in progesterone levels which is observed in proestrus is correlated with a decrease in ER $\alpha$  expression. On the other hand, slight estradiol levels which are observed in metestrus and diestrus are correlated with an increase in ER $\alpha$  expression. This may be a way to the hormone control of the relay mechanism of the BNSTpr for the olfactory information to the hypothalamic nuclei involved in the control of sexual behavior.

This work was supported by National Funds through FCT.

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## PS164

# EXPRESSION CHANGES IN GABAAR RECEPTOR SUBUNITS IN A MODEL OF EPILEPTIFORM ACTIVITY IN ORGANOTYPIC HIPPOCAMPAL SLICE CULTURES (OHSC)

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AIM

To determine, by quantitative PCR, the changes occurring in the expression of ionotropic GABAAR receptor subunits, in a model of epileptiform activity established in OHSC.

## INTRODUCTION

The glycinergic and the GABAergic transmissions play an inhibitory role in the control of neuronal excitability and information processing, as well as in neuronal plasticity and synchronization of the central nervous system. Gamma-aminobutyric acid (GABA) is the main inhibitory neurotransmitter in the brain. It is formed from glutamate in the GABAergic terminals and released into the synaptic cleft, activating three main types of receptors: GABAA, GABAB and GABAC receptors. The ionotropic receptors, GABAAR and GABACR, have different subunits. The numerous GABAA receptor subunits ( $\alpha 1$ – $\alpha 6$ ,  $\beta 1$ – $\beta 3$ ,  $\gamma 1$ – $\gamma 3$ ,  $\delta$ ,  $\epsilon$ ,  $\theta$ ,  $\mu$ ,  $\nu$ , and  $\zeta$ ) typically form heteropentameric receptors that differ in their function, pharmacology and cellular localization. Several studies performed both in humans with epilepsy, as well as in epilepsy animal models, demonstrated the occurrence of abnormalities in GABA-mediated synaptic transmission. Alterations in GABAAR subunit expression have been reported in adult animals beginning immediately after prolonged seizures and continuing as animals become chronically epileptic. In this work we have used an in vitro model of epileptiform activity in OHSC, to further understand these changes.

## METHODS

This project aims to determine the expression changes in the subunits of ionotropic GABAA receptor in a model of epileptiform activity in OHSC. It requires several steps: 1. Organotypic hippocampal culture preparation from 6 day old rats (P6). 2. Induction of epileptiform activity by incubation in a low magnesium solution, for 7 hours, after 14 days of culture. CTL OHSC will be kept in the same medium, but with added magnesium. 3. RNA extraction from OHSC CTL and insulted OHSC. 4. cDNA synthesis by in vitro transcription from RNA. 5. Evaluation, by qPCR, of changes in the expression of GABAA receptor subunits ( $\alpha 1$ – $\alpha 5$ ,  $\beta 1$ – $\beta 3$ , and  $\gamma 2$ ).

## RESULTS

Quantitative PCR with specific primers for GABAAR subunits, namely  $\alpha 1$ – $\alpha 5$ ,  $\beta 1$ – $\beta 3$ , and  $\gamma 2$ , has shown that the expression of GABAAR  $\beta 2$  and  $\beta 4$  transcripts is increased in slices which undergo the low magnesium protocol. GABAAR  $\beta 5$  transcript expression depicts a tendency for decrease. The expression of the other GABAAR subunits, namely  $\alpha 1$ ,  $\alpha 3$ ,  $\alpha 1$ ,  $\beta 2$ ,  $\beta 3$  and  $\gamma 2$ , show no significant changes.

## CONCLUSION

The results indicate that the expression of some GABAAR subunits are altered in the in vitro model of epileptiform activity established in organotypic slice cultures. The obtained alterations, in particular the increase in GABAAR  $\bar{I}_{\pm 2}$  and  $\bar{I}_{\pm 4}$  transcripts, are among the most prominent changes described in human temporal lobe epilepsy and related animal models of acquired epilepsy. Therefore, these findings support the use of the established model as a routine procedure to further study this pathology. However, the number of experiments must be increased in order to have more valuable data.

**PS198****CHRONIC FOOD RESTRICTION INCREASES THE NUMBER OF NEUROPEPTIDE Y-CONTAINING NEURONS AND THE DENSITY OF CHOLINERGIC VARICOSITIES IN THE HIPPOCAMPAL DENTATE****GYRUS OF AGED RATS**

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AIM

The major goal of this study was to analyze if food restriction on aged animals could prevent aging-associated changes of the total number of neurons, the number of neuropeptide Y (NPY)-containing neurons and the density of cholinergic varicosities on the hippocampal dentate hilus.

**INTRODUCTION**

Growing evidence shows that prolonged dietary caloric restriction in rodents have several beneficial effects, including increasing of the mean and maximum lifespan, retarding age-associated decrease of the metabolic, structural, and physiological functions and maintenance of cognition. Most of the caloric restriction studies are performed in young animals and the information of the effects of the food restriction in old animals is very scarce. Therefore, we have analyzed the effects of food restriction on the total number of neurons in the hippocampal dentate hilus and on the number of hilar NPY neurons, due to their important roles in the regulation of feeding behavior, emotion and memory. Furthermore, we have also analyzed the hilar density of cholinergic varicosities, since acetylcholine is thought to be involved in the neurotrophic support of NPY neurons.

**METHODS**

Young control rats (2-month old) were fed for 6 months ad libitum with standard rodent laboratory chow. Aged rats (18-month old) were randomly assigned to an aged control group and to an aged food-restricted group. Aged control rats were fed for 6 months ad libitum with standard rodent laboratory chow and food-restricted rats were fed 60% of the calories consumed by controls for 6 months. After treatments the animals were perfused and processed for glycolmethacrylate embedding and immunocytochemistry. The density of cholinergic varicosities (VAcT) and the number of neurons and the number of NPY-containing neurons were estimated in the dentate gyrus hilus. The handling and care of the animals followed the Principles of Laboratory Animal Care (NIH Publication No. 86-23, revised 1985) and the European Communities Council Guidelines in Animal Research (86/609/UE). All efforts were made to minimize the number of animals used and their suffering.

**RESULTS**

It was found that the total number of neurons, the total number of NPY-IR neurons and the density of VAcT varicosities in the hilus were decreased in old rats when compared to the young controls. Although there were no differences in total number of hilar neurons between aged food-restricted rats and control old rats, food restriction increased the total number of NPY-IR neurons and the VAcT varicosities density compared

to the control age-matched group.

## CONCLUSION

Our results corroborate previous works demonstrating that aging induces reduction of the total number of hilar neurons, NPY-IR neurons and VACHT varicosities density. Furthermore, the present results also show that food restriction appears to have an important role in the prevention of aging-related reduction of NPY-IR neurons and cholinergic varicosities density.



## PS563

**CHRONIC ETHANOL TREATMENT AND WITHDRAWAL DO NOT AFFECT THE TOTAL NUMBER OF CHOLINERGIC NEURONS OF THE PEDUNCULOPONTINE TEGMENTAL NUCLEUS OF THE RAT: AN UNBIASED STEREOLOGICAL STUDY**

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AIM

There is not much literature about the effects of chronic ethanol treatment (CET), withdrawal and nerve growth factor (NGF) on the cholinergic cell counts in the mesopontine tegmentum. Thus, the present study was designed to investigate whether there exist CET and withdrawal-related changes in the total number of choline acetyltransferase-immunoreactive (ChAT-ir) neurons in the pedunculopontine tegmental nucleus (PPTg) of male Wistar rats and to examine the role played by exogenous NGF in the phenotype of these neurons.

**INTRODUCTION**

The mammalian brain cholinergic system plays part in several functions such as locomotion, sleep, memory, attention and emotion. This system comprises two major anatomically distinct parts: the cholinergic nuclei of the basal forebrain and the cholinergic nuclei of the brainstem. In the case of the brainstem, acetylcholine is expressed by neurons of the PPTg and laterodorsal tegmental nuclei in the mesopontine tegmentum. The PPTg is a morphologically and neurochemically heterogeneous nucleus that has been typically associated with the ascending reticular activating system (ARAS) due to its projections. However, despite the substantial information regarding the basal forebrain nuclei, the pontomesencephalic ones have been barely studied. Indeed, there is considerable evidence showing that the basal forebrain cholinergic neurons undergo atrophic or degenerative changes after CET and withdrawal but it is not well established whether brainstem cholinergic neurons are vulnerable or impervious to these treatments.

**METHODS**

Twenty Wistar male rats were assigned to control, ethanol-treated, withdrawn and NGF-treated withdrawn groups. At the end of the experiments, rats were perfused and brainstems sections were processed for ChAT immunostaining and for Nissl staining. The total number of ChAT-ir neurons was estimated on blind-coded slides by using the optical fractionator.

**RESULTS**

The PPTg of adult male rats contains a mean of 2353 ChAT-ir neurons. Statistical analysis revealed no CET, Withdrawal and NGF-related changes in the total number of PPTg cholinergic neurons.

**CONCLUSION**

On the contrary to what has been observed by other authors in the basal forebrain cholinergic nuclei, we found no significant differences in the total number of ChAT-ir neurons in the PPTg of chronic ethanol treated,

withdrawn and NGF-treated rats. Therefore, the brainstem neurons seem to be more resistant to ethanol and withdrawal-associated degenerative changes than their BF counterparts. This lower vulnerability may be partially explained by the higher expression of protective mechanisms against ethanol induced oxidative stress, as stated in the literature. Despite considerable research conducted over several decades, greater anatomical and neurochemical knowledge of the brainstem cholinergic nuclei is needed in order to better understand their still cryptical functional roles.



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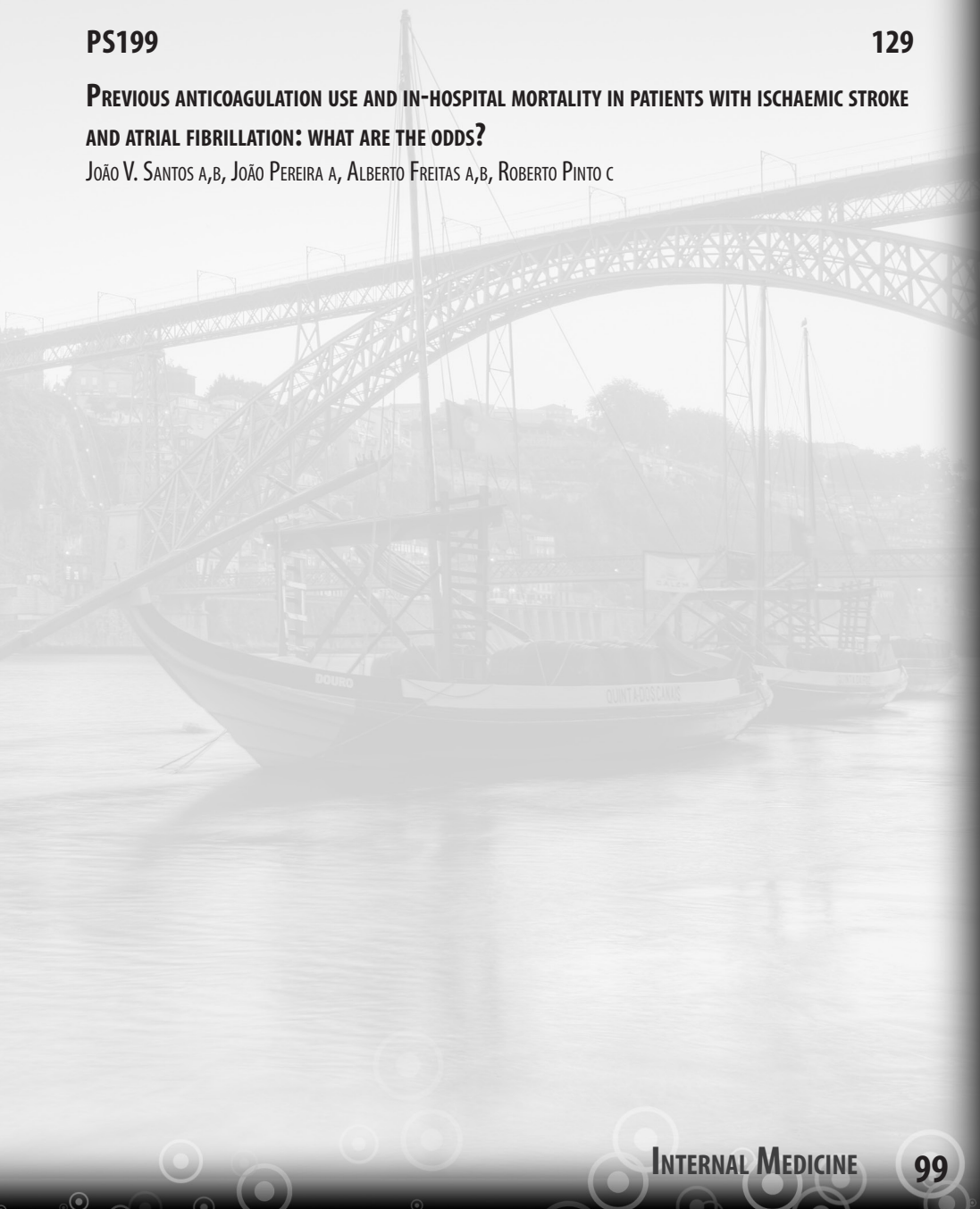
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## PS6

### RISK FACTORS AND PREVENTION OF FALLS IN THE FRAIL ELDERLY

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AIM

The goal of this present paper refers to the fall risk assessment and prevention of future falls in the elderly.

#### INTRODUCTION

The fall is defined as any event characterized by the drop or descend under the force of gravity, as to a lower place, through loss or lack of support. Each year, one in every three adults aged > 65 falls. The contributing factors for falls are multiple, as a result of the interaction between the individual intrinsic factors related to age and/or pathology and the extrinsic environmental factors.

#### METHODS

We analysed 81 frail elderly patients, aged between 75-85 years old, 39 males and 42 females, from the "Sevamed Medical Clinic", between 2011-2012, with polypathology, which experienced at least one fall before admission. The patients were interviewed about their medical history and they were submitted to conventional drug therapy, monitored by general practitioner; at the same time they underwent rehabilitation therapy, especially exercises, tailored to the needs of older adults, prescribed and monitored by a rehabilitation therapist.

#### RESULTS

We demonstrated that exercise can improve functional status and therefore can reduce the risk for falls. Our program for fall prevention includes a very close interdisciplinary collaboration between the general practitioner and the rehabilitation providers. We noticed an increase in muscle strength, with improving of functional status after medical treatment and exercise program, very well coordinated, with the exercises being adapted to the patients' needs.

#### CONCLUSION

The falls are a very frequent incident in the frail elderly patients, which are caused by a close interaction between the patient's pathology and medication. The multidisciplinary approach of the patients who experienced a fall is necessary and can reduce the risk for future falls through exercise, in a carefully adapted rehabilitation program.



## PS58

**CHRONIC EROSIVE AND ULCERATIVE DISEASES IN CHILDREN: CHARACTERISTICS FEATURES OF THESE PATHOLOGY IN PRESENT DAYS.**

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**AIM**

The aim of the study was to investigate the characteristics of chronic erosive-ulcer diseases in children with likely changes, given endoscopic picture, age and sex of the child, as well as duration of the illness.

**INTRODUCTION**

Despite all the advances in pediatrics gastroenterology in recent times, every year in Ukraine there are records of more than 50,000 children with chronic gastroduodenitis and more than 1,000 children with peptic ulcer disease. There remains a large number of patients with prolonged, recurrent, complicated course, indicating lack of adequate knowledge of all aspects of the disease and requires further study of the problem.

**METHODS**

We analyzed the case histories of 32 children with uncomplicated peptic ulcer and duodenal ulcer in stage I (exacerbation), and 47 patients with chronic erosive gastroduodenitis (EGD) in the acute stage, were treated in the department of gastroenterology in 2nd hospital of children, Simferopol Ukraine from the period of 2010-2012 years. Verification of the diagnosis was based on complaints, anamnesis vitae and morbi, clinical examination, as well as additional methods of examination esophagogastroduodenoscopy (EFGDS), bacterioscopic and breathing techniques (Helik test) to detect *Helicobacter pylori* (HP) and intragastric pH-metry.

**RESULTS**

Analysis of the data were as follows; Ulcer: girls 7 - 10 years in 9.4% of cases, between 11- 17 years old 37.5%, boys: 7-10 years in 12.5% of cases, from 11-17 years in 40.6%. EGD: Girls 7 - 10 years in 8.5% of cases, 11 - 17 years in 46.8%, boys from 7 - 10 years in 12.8% of cases, between 11 - 17 years - 31.9%. Results shows that in most cases "fresh" ulcerative defect was of average size (0.3-0.5 cm) and was often localized: on the frontal bulbs of duodenum in 40.6% of cases, on the back - in 34.4%, on the side - in 15.6%. Children with EGD dominated blemishes from 0.1 - 0.3 cm in front of the bulbs duodenum in 25.5% of cases, the greater curvature of the stomach - in 19%, in the antrum in 14.8% of cases. Duration of duodenal ulcer in children were in most cases up to 1 year from the initial presentation of the disease in children with gastroduodenitis - 1 to 3 years.

In 68.3% of children with ulcerative-erosive changes of gastroduodenal mucosa by HP infection presented II degree, at 16.5% - III degree, at 15.2% - I degree.

**CONCLUSION**

Given the findings of our study, we arrived at the following conclusions:

1. Duodenal ulcer was common in boys of high school ages, and gastroduodenitis - girls of the same age.
2. "Fresh" ulcerative defects were more of average sizes ranging from (0.3-0.5 cm) and located on the front of the duodenal bulb.
3. Erosion in the majority of cases occurred in the greater curvature of the gastric mucosa with size between 0.1-0.3 cm
4. Contamination of gastroduodenal mucosa by HP in most cases is of II degree.

PS74

## METHODS AND DYNAMICS OF MORBIDITY AND FEATURES OF ACUTE RESPIRATORY DISEASES AND OBSTRUCTIVE BRONCHITIS IN CHILDREN IN RECENT YEARS.

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AIM

The purpose is to study the dynamics of acute respiratory disease and obstructive bronchitis in children, and features of their clinical course.

### INTRODUCTION

Every year the world has a sick rate of over 500 million people. According to statistics, every person in a year on an average of 2 times is usually ill with acute respiratory disease, and in children, it averages on 6-8 times a year. In 60% of cases, acute respiratory infections occur with complications, such as acute bronchitis, pneumonia, etc. In recent years among children of all age groups, frequent manifestations of bronchial obstruction, develops in 45% of cases of ARD.

### METHODS

These statistics shows the medical records of children who were treated at the Central Regional Clinical Hospital (CRCH) in the years 2005, 2011 and 2012.

### RESULTS

In 2005: acute respiratory infections - 429 cases, acute bronchitis – 76, pneumonia – 34, obstructive bronchitis – 27. In 2011: acute respiratory infections – 786, acute bronchitis – 178, pneumonia – 59, obstructive bronchitis – 129. In 2012: acute respiratory infection - 815, acute bronchitis – 158, pneumonia – 73, obstructive bronchitis – 104.

The years 2005 and 2011 had the highest rate of obstructive bronchitis according to studies. In respect to children's age, obstructive bronchitis had the following incidence rate: children from one to three years of age were 32.9% in 2005: in 2011-25.7%. Those between 3 to 7 years in 2005 were 11.8%, and in 2011 – 14.2%. School-age children had sick-rate as follows; in 2005 – 19.74%, and in 2011 – 23.8%. In addition, obstructive bronchitis in 2005 occurred in 63.2% of boys and 36.8% of girls; 2011 occurred in the rate of 64.7% in boys, and 35.6% in girls. It was noted also, that 6.5% of children aged 1-5 years, who were being treated for obstructive bronchitis in 2005, were hospitalized with a diagnosis of asthma exacerbation in 2011.

### CONCLUSION

1) The incidence of acute respiratory infections in recent years has increased, compared to 2005, by more than 1, 5 times; consequently, the incidence of obstructive bronchitis in children has increased on an average

of 38.2%.

- 2) It has been observed that the incidence of obstructive bronchitis in boys is 2 times higher than in girls.
- 3) The rate of pneumonia increased in children before 1 year of age, on 2 times between 2005 and 2012.
- 4) The peak incidence of bronchial obstruction is observed in children within their first three years of life. Up to 7% of cases of obstructive bronchitis have been noted to transforming into asthma.
- 5) Since there is a high tendency for acute respiratory infections and complications such as obstructive bronchitis to change into bronchial asthma, it then shows that specific prevention to avoiding such effect remains important.
- 6) The increase in the incidence pneumonia in children, calls for an increase in the necessity of intensifying the vaccination of children against pneumococci of different groups.



PS75

## NON-SUSCEPTIBILITY OF COAGULASE-NEGATIVE STAPHYLOCOCCI ISOLATED FROM BLOOD CULTURES - DO WE HAVE A PROBLEM?

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AIM

The aim of this study was to determine the presence of the most common coagulase-negative staphylococci isolated from blood cultures and to determine susceptibility pattern of the methicillin-resistant isolates.

### INTRODUCTION

Coagulase-negative staphylococci represent a major cause of bacteremia in patients with medical implants and in immunocompromised patients, although considered to be contaminants through the years. Their importance as potential agents of hospital-acquired infections has been enlightened in recent years. The number of methicillin-resistant isolates is increasing with growing resistance to other antibiotics. Multiresistant strains may colonize the hospital environment and thus become the source of antimicrobial resistance.

### METHODS

The study was performed at the Centre for Microbiology, Immunology and Virology of the Institute for Pulmonary Diseases in Sremska Kamenica (Serbia) in 3-year period. The study included 136 blood cultures with coagulase-negative staphylococci. Identification was performed by using the BBL Crystal Identification Systems Gram-positive ID kit. For each strain antimicrobial susceptibility was determined by the disk diffusion method.

### RESULTS

Among 136 coagulase-negative staphylococci the most prevalent was *Staphylococcus haemolyticus* 56 (41.2%), followed by *Staphylococcus epidermidis* 54 (39.7%), *Staphylococcus hominis* 12 (8.82%) and *Staphylococcus capitis* 5 (3.68%). Methicillin-resistant were 82 (60.3%) isolates. Multiple resistance was observed in 70 (83.4%) methicillin-resistant isolates. The resistance rates of methicillin-resistant strains were for gentamicin 91.5%, for erythromycin 89%, for ciprofloxacin 85.4% and for clindamycin 70.7%. All strains were sensitive to vancomycin and linezolid. There were no smooth resistance trends for any of the examined antibiotics although some evidence for year-to-year fluctuation have been detected.

### CONCLUSION

The most common isolates are *Staphylococcus haemolyticus* and *Staphylococcus epidermidis*. A significant number of strains were methicillin-resistant with multiple resistance. The treatment of infections induced by these strains may become a great challenge, as therapeutic capacities of the existing antibiotics have been rapidly exhausted. It is therefore crucial to take the preventive measures including a rational use of antibiotics and prevention of multiresistant coagulase-negative staphylococci spread.



## PS61

**IMPORTANCE OF RISK FACTORS FOR OSTEOPOROSIS AND BONE MINERAL DENSITY IN AORTIC VALVE STENOSIS**

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**AIM**

The aim of this study was to evaluate the relationship between risk factors for osteoporosis and bone density and the severity of aortic valve stenosis.

**INTRODUCTION**

Aortic valve stenosis and osteoporosis are prevalent conditions in the elderly. The progression of aortic valve stenosis and the phosphorus-calcium metabolism seem to be associated. Recently, it has been proposed that mechanisms related to inflammation might determine the association between aortic valve stenosis and phosphorus-calcium metabolism deregulation, causing demineralization in the bone and valvular and arterial calcification.

**METHODS**

We included 52 patients non-consecutive, aged between 65 and 85 years, hospitalized with aortic valve stenosis and/or significant coronary disease with surgical criteria from September 2012 to February 2013. Aortic valve stenosis was evaluated according to the mean valvular gradient:  $\leq 20$  mmHg (or sclerosis)

(n=17), between 20 and 40 mmHg (n=13) or  $\geq 40$  mmHg (n=22). Coronary disease was defined as absence of significant stenosis (n=14), significant coronary disease of a major epicardial vessel (n=6) and multi-vessel disease (n=32). Patients were divided in four groups according to the grade of aortic valve stenosis (Groups A - mean valvular gradient  $\leq 20$  mmHg - and B - mean valvular gradient  $> 20$  mmHg) and the extension of coronary disease (Groups C - none or one major epicardial vessel disease - and D - multi-vessel disease). All patients answered to a questionnaire about the risk factors for osteoporosis, atherosclerosis and medication. The majority (n=44) was submitted to an osteodensitometry to evaluate the bone density in the femur and in the lumbar spine.

### RESULTS

Apart from age, 35 patients (67%) had at least one risk factor for osteoporosis. In those whose bone density was measured, 26% had osteopenia and 22% had osteoporosis. Only three were treated with biphosphonates at the time of hospitalization. The frequency of risk factors for osteoporosis and the values of bone density/T-Score were not significantly different between the groups studied.

### CONCLUSION

Although risk factors for osteoporosis and reduced bone density are frequent in patients older than 65 years and with aortic valve stenosis and/or coronary disease with surgical criteria, it was not possible to evaluate their correlation with the severity of heart disease, namely with the grade of aortic valve stenosis. We concluded that the progression of aortic valve stenosis lesions and bone demineralization seem to be independent mechanisms.



## PS85

# **CYSTIC FIBROSIS: STUDY OF CFTR GENE SEQUENCE VARIATIONS IN THE PEDIATRIC PORTUGUESE POPULATION**

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## **AIM**

In Portugal, the prevalence of Cystic Fibrosis (CF) is still unknown. So, the aim of this work is to investigate the type and frequency of sequence variations in the CFTR (Cystic Fibrosis Transmembrane conductance Regulator) gene, by screening a random and representative sample of the pediatric Portuguese population.

## **INTRODUCTION**

Cystic Fibrosis (CF) is the most common autosomal recessive genetic disease in the Caucasian population, affecting approximately 1 in every 2500 births, with significant variations according to ethnic group and geographical location. CF is caused by mutations in the CFTR gene that result in loss or reduction in ion transport mediated by the CFTR channel across the apical membrane of epithelial cells.

After the CFTR gene identification in 1989, it was expected that only a limited number of mutations could cause CF, however, almost 2000 different sequence variants have already been reported in the CFTR gene. Nonetheless, the molecular and functional consequences of many of these sequence variations are still unknown. In fact, less than 10 mutations occur with a frequency greater than 1%, being the most common mutation, F508del, responsible for approximately 66% of patients with CF.

## **METHODS**

This study was performed in DNA samples, extracted from buccal mucosa cells of 197 children representative of the Portuguese population, followed by PCR amplification and direct sequencing of 27 exons and flanking intronic regions of the CFTR gene.

## **RESULTS**

Screening of CFTR gene in 197 samples allowed the identification of 17 different sequence variations. Two sequence variations were detected in only one sample (IVS8T5(TG)12/L967S) whereas single sequence variations were identified in 46 samples. No sequence variation was detected in the remaining 150 samples. The most frequent sequence variation was IVS8T5, with an allelic frequency of 3%, followed by the G576A-R668C complex allele with an allelic frequency of 1.8% and V754 and L997F with an allelic frequency of 1.3%. The F508del CF mutation was found in two samples, with an allelic frequency of 0.5%. The 17 different sequence variations detected, when detected in homozygosity or compound heterozygosity may be associated with a CF or CFTR-related phenotype. Apart from these sequence variations different already known polymorphisms were also detected in 193 samples analyzed.

## **CONCLUSION**

In this preliminary study, 17 different sequence variations were detected in the 47 of the 197 samples analyzed, corresponding to a 24% of sequence variations carrier's frequency. This frequency is similar to that reported in other countries (25-30%). Two mutations were identified in a girl, IVS8T5(TG)12/L967S, which may be associated with a phenotype of the CFTR-related disorders. With the present results we expect to determine the CF prevalence, as well as to contribute for a better knowledge of the CFTR gene sequence variations spectrum in Portuguese population, which will improve the CF diagnosis in these patients.

**PS111****RESULTS OF MESENCHYMAL STEM CELL (MSC) TREATMENT OF CROHN'S DISEASE IN RUSSIA**

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AIM

to figure out the results of stem cell treatment of Crohn's disease and evaluate the effectiveness and advantages of this method

**INTRODUCTION**

Recently the number of Crohn's disease cases has increased in Europe. In the European part of Russia, the prevalence is 3.7 per 100,000 people. Unique to the disease in our country is a three times greater prevalence of the severe forms of Crohn's disease, which have a high mortality rate. Even when the doctor uses the best possible form of therapy, remission is achieved in only 50% of the cases. So the transplantation of mesenchymal stem cells becomes a treatment option, as it is effective in restoring the intestinal wall and creates minimal interference for the patient.

**METHODS**

Two groups of patients were involved: Gr1 (n=30) received traditional therapy (control group) and Gr2 (n=30) received traditional therapy plus MSC treatment (the primary group). To determine the effectiveness of the treatment several tests were made: estimating TNF-alfa, INF-g and IL-4 using mucosal biopsies of the colon membrane, TNF-alfa, INF-g, IL-1beta and IL-4 in the serum before and after treatment. Before and after the transplantation of allogenic mesenchymal stem cells in serum humoral the immune status of IgM, IgG and IgA was estimated using the test kits "Protein circuit".

**RESULTS**

All patients after MSC transplantation had a decline in clinical inflammatory activity ranging from 8.2 to 1.2 points. The endoscopic activity index after transplantation decreased from 6.2 to 2.0 points. There was also mentioned the multidirectional regulating effect of MSCs: stimulating the functional activity of the depressed immune system, reducing the autoimmune reactions intensity, the immunopathological processes activity in the colon lining.

**CONCLUSION**

New approaches to the treatment of Crohn's disease showed significant results. Our results of therapy of Crohn's disease using mesenchymal stem cells are unique, cases described before show MSC treatment of single patients. We believe that the advantages of the standard cell-based therapies can be explained as system and local anti-inflammatory effect of stromal cells.

## PS119

### THE FREQUENCY OF COLONIZATION OF PERIRECTAL REGION WITH EXTENDED-SPECTRUM BETA-LACTAMASE-PRODUCING ENTEROBACTERIACEAE

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AIM

The aim of this study was to determine the most common extended-spectrum beta-lactamase-producing Enterobacteriaceae in perirectal region and the frequency of infections caused by phenotypically identical strains.

#### INTRODUCTION

Perirectal region is normally colonized by many bacteria, among which are Enterobacteriaceae. However, in this region, recently was noticed the presence of resistant strains of Enterobacteriaceae. Since their resistance to antibiotics is based on production of beta-lactamase, the enzymes which provide them protection from many groups of antibiotics, they are called extended-spectrum beta-lactamase-producing Enterobacteriaceae. Moreover, there was assumption that resistant bacterial strains from perirectal region could be spread through organism and cause infections of other parts of the body. Because of resistance to many antibiotics used empirically, infections caused by resistant strains became an emerging problem.

#### METHODS

Retrospective study included perirectal swab samples obtained from 242 patients in intensive care unit in Institute for Pulmonary Diseases of Vojvodina in 18-months period in 2011-12. Bacterial identification and extended-spectrum beta-lactamase production testing were performed in Center for Microbiology, Immunology and Virology. Biochemical tests and commercial system for identification Gram-negative bacteria (BBL Crystal Identification Systems Enteric/Nonfermenter ID kit, Beckton Dickinson, USA) were used for bacterial strains identification. Beta-lactamase production was tested using double-disk synergy test. The presence of phenotypically same bacteria in urine, blood and sputum samples was controlled in order to determine the occurrence of infections by bacteria which have been initially localized only in perirectal region.

#### RESULTS

Of the 242 samples on admission, in 19 (7.8%) extended-spectrum beta-lactamase-producing Enterobacteriaceae were identified. Among 58 patients with 2 samples, 31 (53%) had negative sample on admission and positive control sample. The most common isolate was *Klebsiella pneumoniae* in 21 samples. Then, *E. coli* in 6 samples and *P. mirabilis* and *E. cloacae* in 2 samples each. Among 50 patients with positive sample, infection of urinary, respiratory tract or blood was detected in 22 (44%) patients. Infection of urinary tract was the most common. In the most number of cases, *Klebsiella pneumoniae* caused the infection.

#### CONCLUSION



High percentage of colonization with extended-spectrum beta-lactamase-producing Enterobacteriaceae was detected. Isolated strains were associated with the occurrence of urinary, respiratory tract and blood infections.



## PS123

### **GLUTATHIONE S-TRANSFERASE M1 AND T1 POLYMORPHISM IN RELATION TO MARKERS OF LIPID AND PROTEIN OXIDATIVE DAMAGE IN HAEMODIALYSIS PATIENTS**

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#### AIM

To determine whether the deletion polymorphisms of genes coding for antioxidant enzymes glutathione S-transferase (GST) M1 and T1 modulate the degree of oxidative damage in end stage renal disease (ESRD) patients.

#### INTRODUCTION

Increased oxidative stress is a hallmark of ESRD. GSTs are involved in detoxification of xenobiotics and protection of important biomacromolecules from oxidative damage. Genetic polymorphism is found in several genes coding for GSTs, the most significant of which clinically are deletion polymorphisms of GSTM1 and GSTT1 gene.

#### METHODS

GSTM1 and GSTT1 genotypes were determined in 100 ESRD patients by multiplex PCR (polymerase chain reaction). Markers of oxidative damage, malondialdehyde (MDA) adducts, were measured by ELISA (enzyme linked immunosorbent assay). Total oxidative status (TOS) and advanced oxidative protein products (AOPP) were determined by spectrophotometry.

#### RESULTS

The presence of GSTM1 null or GSTT1 null genotypes influence the degree of lipid peroxidation, resulting in significant increase of plasma MDA adducts level in those carrying these genotypes ( $p < 0.01$ ). A strong combined effect of the deletion of both genes in terms of susceptibility towards the oxidative damage was found in ESRD patients. Namely, when patients were stratified according to GSTM1 and GSTT1 genotype, the highest level of plasma MDA adducts was noted in those with GSTM1 null/GSTT1 null genotype. Protein oxidative damage was significantly higher in patients carrying GSTM1 null genotype ( $p < 0.05$ ). When GSTM1 and GSTT1 genotypes were combined, the highest level of AOPP was observed in patients carrying both GSTM1 and GSTT1 null genotypes. When TOS was measured, no difference was noticed in patients carrying either of GSTM1 or GSTT1 variants.

#### CONCLUSION

GSTM1 null and GSTT1 null genotypes are, independently or in combination with one another, associated with enhanced susceptibility to oxidative lipid and protein damage in haemodialysis patients. Our results suggest a possibility for GST genotype based stratification of ESRD patients which could improve the attempts towards individualization of antioxidant treatment.

## PS125

**GLUTATHIONE S-TRANSFERASE A1 AND P1 POLYMORPHISMS AFFECT PROTEIN OXIDATIVE DAMAGE IN END STAGE RENAL DISEASE**

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AIM

We hypothesized that the polymorphisms in antioxidant enzymes GSTA1 and GSTP1 modulate the degree of oxidative protein damage in ESRD patients.

**INTRODUCTION**

Kidney tissue has high metabolic activity and oxygen demand- characteristics that increase the potential for endogenous formation of reactive reactants.

Glutathione S-transferases A1 (GSTA1) and P1 (GSTP1) are members of GST family of proteins, which are involved in the detoxification of xenobiotics and protection of oxidative damage. Since the oxidative damage is thought to have a role in end stage renal disease (ESRD) development, it seems reasonable to assume that GSTA1- or GSTP1-low-activity genotypes might also influence the level of oxidative stress in these patients and thus contribute to endogenous predisposition to oxidative damage in the setting of disrupted redox balance.

**METHODS**

GSTA1 and GSTP1 genotypes were determined in 100 ESRD patients by polymerase chain reaction–restriction fragment length polymorphism (PCR–RFLP). Thiol groups concentration was measured spectrophotometrically and nitrotyrosine were measured by enzyme immunoassay.

**RESULTS**

Individual GSTA1 low-activity and GSTP1 low-activity polymorphisms influenced the vulnerability to protein oxidation, resulting in the decrease of the thiol groups ( $p=0.098$  and  $p=0.075$  respectively) and increase of nitrotyrosine levels ( $p=0.768$  and  $p=0.001$  respectively) in carriers of these genotypes. A strong combined effect of the polymorphism of GSTA1 and GSTP1 genotypes in terms of susceptibility towards the oxidative damage of proteins was found in ESRD patients. Namely, when patients were stratified according to GSTA1 and GSTP1 genotype, the lowest concentration of plasma thiol groups was noted in those with GSTA1 low-activity/GSTP1 low-activity genotype ( $p=0.002$ ). Additionally, combined GSTA1 and GSTP1 low-active genotypes were associated with higher nitrotyrosine levels ( $p=0.122$ ).

**CONCLUSION**

Individual GSTA1 low-activity and GSTP1 low-activity genotypes are associated with enhanced susceptibility to protein oxidative damage in ESRD patients. Since susceptibility to oxidative damage differs with respect to the GST genotype, it seems reasonable to assume that individuals' GST 'genetic profile', in addition to plausible oxidative stress biomarkers, should be also considered in the optimization of antioxidant treatment.





## PS132

**EFFECT OF BMI AND PHYSICAL ACTIVITY ON LUNG FUNCTION OF CHILDREN**

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**AIM**

The purpose of this study is to evaluate the impact of body mass index (BMI) on lung function of children and verify the influence of physical activity in pulmonary function at this age group.

**INTRODUCTION**

The proportions of childhood obesity are alarming, mainly in Europe, where being overweight is the most common disorder among children. Obese people have a greater risk of respiratory symptoms as breathless, mostly during exercise, even without any respiratory pathology. Physical activity is one of the modalities of treatment and control of obesity, but adhesion are low because patients feel respiratory discomfort or dyspnea. So it is important to understand the influence of childhood obesity and the role of the physical activity in lung function values.

**METHODS**

Forty-five children were evaluated by a questionnaire, anthropometric measures and respiratory function tests, in order to measure forced expiratory volume in 1 second, forced vital capacity and Tiffeneau index. All parents signed the consent form approved by Ethics Committee of Fernando Pessoa University, Porto, Portugal. Inclusion criteria were: age between 7-11 years old and correct fulfilling of the questionnaire. Children who had cardiopulmonary pathology, allergic disease or could not perform the spirometry test were excluded. Data were analyzed using IBM SPSS Statistics 21. ANOVA or Kruskal-Wallis test were used to compare lung function between three groups of children, according to BMI: normal weight, overweight and obese. Student's *t* or Mann-Whitney tests were used to compare lung function between children that perform or do not perform physical activity.

**RESULTS**

Our data indicate that BMI is related with lung function variables like forced expiratory volume in 1 second. However, according to our results, lung function does not seem to be affected by physical activity.

**CONCLUSION**

This study suggests that increase of the BMI causes an increase of the values of lung function in children, until BMI is excessive to the age and leads to a decrease of pulmonary function values.

At this age group, obesity can have a negative effect on lung function when BMI is equal or superior to 30 kg/m<sup>2</sup>. Our results also suggest that low-to-moderate physical activity is not enough to cause some improvements on lung function variables at school-aged children.

## PS175

### **HOW TO ACHIEVE QUALITY IN MEDICAL EDUCATION? INTER-RATER AGREEMENT ABOUT ITEM-WRITING FLAWS IN MULTIPLE-CHOICE QUESTIONS: THE CASE OF CLINICAL ANATOMY**

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AIM

The purpose of this study was to estimate the inter-rater agreement about item classification as either standard or flawed using clinical anatomy as the focus of this study.

#### INTRODUCTION

Quality in medical education is the foundation for sound program development and for definition of standards in the outcomes of the medical courses. Assessing students with reliable and valid methods by ensuring the quality of these examinations has to be a concern of Higher Education Institutions responsible for producing physicians.

The multiple-choice question (MCQ) examination type is recurrently used to assess students in health science disciplines. Despite this fact, MCQ item have often item-writing flaws or violations to MCQ item-writing guidelines, and few educators have formal instruction in writing MCQs.

#### METHODS

Four judges (2 teacher/2 students), blinded to all item performance data, independently classified each one of 920 MCQ questions from 10 examinations (last 5 academic years) as either standard or flawed. If flawed the exact type of item flaw or flaws contained within the question (including options) was recorded.

A standard item was operationally defined for this study as any item that did not violate one or more of the 31 principles noted in a review article which summarized current educational measurement recommendations concerning item writing. The Fleiss' Kappa was used to evaluate the inter-rater agreement between 4 judges previous the consensus process.

#### RESULTS

The agreement about item classification as either standard or flawed was fair ( $\kappa=0.3$ ). The agreement was moderate/substantial for the following principles: "use positive, no negatives" ( $\kappa=0.7$ ), "use carefully none of the above" ( $\kappa=0.8$ ), "avoid all of the above" ( $\kappa=0.7$ ) and "Choice length equal" ( $\kappa=0.5$ ). All other principles showed poor or slight agreement.

#### CONCLUSION

The results showed many disagreements among judges about item classification, previous the consensus process; however, for the more prevalent principles the agreement was substantial.

In the future, it is important to measure the impact that this flaws have on the quality indicators (difficulty indices and discrimination indices) of the examinations.

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## PS179

### **PERSONALITY, ANXIETY, DEPRESSION AND ATOPIC DERMATITIS SEVERITY: A CROSS SECTIONAL STUDY**

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#### **AIM**

Evaluate the association between anxiety, depression levels, personality traits and disease severity in adult patients with Atopic Dermatitis (AD).

#### **INTRODUCTION**

AD is a multifactorial, chronic and relapsing skin disease characterized by intense pruritus, and eczematous lesions that contribute to significant emotional distress, sleep disturbance and impact on the Quality life (QoL) of patients and their families . AD patients have higher levels of anxiety and depression, of agreeableness, harm avoidance and difficulty in dealing with anger and hostility. Lower prevalence of reward dependence, self-directedness and cooperativeness, is higher than in controls. Psychological stress deregulates central and peripheral Hypothalamic-pituitary-adrenal axis increasing skin pruritus. There are few studies addressing the association of these psychological parameters with disease severity.

#### **METHODS**

Adult patients with medical diagnosis of AD recruited from the community and allergy and dermatology outpatient settings were included. Patients with Psoriasis and other immune mediated skin diseases were excluded. Anxiety and depression levels were evaluated through the Hospital Anxiety and Depression Scale (HADS) and personality traits through the NEO Five-Factor-Inventory.

Severity of AD was measured with SCORAD and QoL through DLQI (Dermatology life questionnaire).

#### **RESULTS**

From the 69 patients invited to participate in the study, 30 patients were included: 33% male, mean age (SD) 31 (10). SCORAD mean (SD) was 48 (29) – 25% mild, 39% moderate and 36% severe. Depression level was associated with a higher score of SCORAD and a lower score in DLQI ( $p < 0.05$ ), anxiety level presented no significant association.

Personality traits were significantly associated with disease severity; agreeableness had the strongest association.

#### **CONCLUSION**

In our sample, depression level and the type of personality trait namely agreeableness were associated with increased disease severity. Further studies with more patients are needed to explore this relation. The utility of psychological interventions in this subset of patients should be addressed in future studies.





## PS181

### MORTALITY TRENDS IN PORTUGAL FROM 2000 TO 2010

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AIM

The aim of this nationwide cross-sectional retrospective survey is to analyse the reality concerning the deaths occurring in Portuguese public hospitals, between 2000 and 2010.

#### INTRODUCTION

The need of ensuring the fundamental rights at the end of life and the increasing global aging justifies the definition, by the World Health Organization, of terminal care as a public health priority [1]. Place of death is an indicator of end-of-life care, reflecting the local in which patients were receiving care at the end of their lives and is influenced by individual, health and environmental factors [2]. However, this demographic indicator, specially the percentage of people who die inside and outside the hospital, is largely unreported[3]. Based on the results of the present study, it can be achieved a best allocation of the end-of-life care settings, with strong social and economic impacts.

#### METHODS

Data concerning deaths at Portuguese public hospitals was obtained through a national database of hospital admissions. Data regarding general population was obtained from the National Institute of Statistics. Statistical analysis was performed using SPSS 21.0.

#### RESULTS

A total of 1.155.151 people died in Portugal between 2000 and 2010, 41% of whom at a Public Hospital. The percentage of man who died at hospital was higher than the percentage of women. Most of the people were between 80 and 89 years old (31.5%). 72.8% of the people who died with 15 or less years old died at hospital, whereas older people tend to die gradually more outside the hospital. The region Lisboa was the one in which more people died at hospital, followed by Norte and Centro. Cardiovascular disease was the main cause of death, accounting for 35% of the cases. Concerning hospital deaths, this disease accounted only for 13.1% of the events, having respiratory problems a higher mortality rate (26.3%).

#### CONCLUSION

According to Gomes et al.[4] 8% of Portuguese population would prefer dying at the hospital, outside a palliative care unit. However, our results demonstrate that Portuguese reality is far from meeting the population desires. Thus, a change in mentality would offer more comfortable end-of-life care services to terminal patients.

Acknowledgments: The authors wish to thank ACSS for providing access to the data.

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## PS182

### THE ROLE OF IgA-ANTIENDOMYSIAL ANTIBODY IN THE DIAGNOSIS OF CELIAC DISEASE IN A PEDIATRIC SAMPLE

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#### AIM

Study the role of IgA-antiendomysial antibody in the diagnosis of Celiac Disease (CD) in a pediatric sample

#### INTRODUCTION

Small bowel biopsies have been the gold-standard in the diagnosis of CD. In The last decade there was an increase in evidence concerning the importance of specific antibodies to the diagnosis. In the new diagnosis guidelines the small bowel biopsies can be omitted under specific clinical circumstances but it is necessary to keep a temporary analysis to validate this new recommendation.

#### METHODS

Prospective study in children (>6 months and <18 years) with a high degree of suspicion of CD due to clinical symptoms or an increase risk of CD, under a diet with gluten, and a positive test for specific antibodies IgA anti-gliadin (AGA) and/or IgA anti-transglutaminase (ATA). All the patients were submitted to a small bowel biopsy and assay of IgA anti-endomysial (EMA) by indirect immunofluorescence with patient serum and monkey's esophagus.

#### RESULTS

Since April 2012, nineteen patients were enrolled. Most of them were female (73.7%) with an average age of  $7.2 \pm 3.8$  years. The diagnosis was confirmed in 17 patients (89.5%), excluded in one patient and unclear in another with a positive clinical response after a gluten free diet. The screening for CD was done because of clinical symptoms in 62.3% (12), by the presence of risk factors (DM1, auto-immune thyroiditis and family history) in 31.6% (6) and for booth in 5.3& (1). The most frequent symptoms were abdominal pain (52.6%), weight lose >10% (31.6%), flatulence (31,6%) and anorexia (26,3%). Anti-gliadin auto- antibodies were positive (>10 U/mL) in 88.2% (15). Anti-transglutaminase auto-antibodies were positive (>10 U/mL) in 94,7% (18), and a title 10x superior to the reference value (RV) was found in 52,6% (10). EMA were positive in 89.5% (17) with a high/moderate increase of 82,4%/17,6%. Comparing the values of ATA/RF, if ATA/VR <10 (n=9) the positivity of EMA was 77.8% (moderate/high 33,3%/44,4%), but if ATA/RF  $\geq 10$  (n=10) the positivity of EMA was high in 100%. All the patients with a positive EMA test also have an histologic test (Bolbus/pars descends) compatible with celiac disease according to Marsh Classification ( $p=0,056$ ). There was no correlation between EMA titles and histological severity. One patient had a negative title of ATA but a positive EMA and a histological analysis compatible with CD. In this sample the sensibility and specificity of EMA antibodies was 94.4% and 100%, respectively.



## CONCLUSION

There was a full correlation between the histological analysis and the positivity of EMA antibodies in the confirmation and exclusion of CD. The EMA antibodies appear to be particularly useful with patients with a high level of ATA, because of the high specificity of both test. The need of individual analysis of EMA results and the high dependence of good technical conditions suggests that the execution of the test should be centralized in reference labs.

## PS187

### IS SYMMETRIC DIMETHYLARGININE (SDMA) SUITABLE MARKER OF RENAL FUNCTION IN SOLITARY FUNCTIONING KIDNEY IN CHILDREN?

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AIM

The purpose of this study was to identify whether plasma symmetric dimethylarginine (pSDMA) is an useful biomarker reflecting the level of renal injury in children with solitary functioning kidney (SFK).

#### INTRODUCTION

Solitary functioning kidney is the most common defect of the urinary tract. It could be congenital or after therapeutic unilateral nephrectomy. It is a topic of concern and debate in last years because children with SFK are at potential risk of developing hypertension, albuminuria and chronic kidney disease in later life. In clinical practice, plasma creatinine is the most commonly used marker used for estimating and monitoring GFR and controlling renal functioning. However serum creatinine concentration it's not a good parameter in mild or moderate renal functioning pathology. More sensitive markers for renal functioning pathology are needed, especially in the early stages of this disturbances.

#### METHODS

We measured circulating pSDMA in 51 patients with SFK and no other urinary defects. Patients were subdivided for two groups: primary SFK (pSFK) - unilateral renal agenesis (URA) and secondary SFK (sSFK) after unilateral nephrectomy. The control group (C) consisted of 21 healthy children, aged mean  $9.92 \pm 4.85$  yrs. Immunoenzymatic ELISA commercial kits was used to measure pSDMA concentration. Plasma SDMA (pSDMA) levels were expressed in  $\mu\text{mol/L}$ . Data analysis was performed using computer program Statistica 9.0.

#### RESULTS

The age and sex of studied children did not differ from healthy controls ( $p > 0.05$ ). Plasma SDMA levels in SFK children were higher than in healthy participants ( $p < 0.05$ ). There was no difference in pSDMA concentrations between pSFK and sSFK patients ( $p > 0.05$ ). SDMA plasma levels correlated significantly with Cr ( $r = -0.32$ ,  $p < 0.01$ ) in all participants. ROC analyses performed in order to define the diagnostic efficiency of serum creatinine and pSDMA in identifying children with  $\text{Cr} < 90\text{ml/min/1.73m}^2$  among SFK and healthy participants revealed no difference between all two AUCs ( $p > 0.05$ ).

#### CONCLUSION

In children with a solitary functioning kidney increased pSDMA levels were observed. However the low sensitivity and specificity of these marker do not confirm the superiority of SDMA over serum creatinine but pSDMA can be a good biomarker of early stages of renal injury.

**PS188****MYOCARDIAL INFARCTION AS A COMPLICATION DURING HOSPITALISATION DUE TO ISCHEMIC****STROKE**

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**AIM**

The goal of this study was to determine frequency and predictors of in-hospital MI in stroke patients.

**INTRODUCTION**

In-hospital myocardial infarction (MI) can be a serious complication increasing the risk of death after ischemic stroke. The potential predictors of MI after stroke are still poorly defined.

**METHODS**

We retrospectively analyzed prospectively collected data including 901 patients with first-ever ischemic stroke admitted to stroke unit within 48 hours after symptoms onset. Multivariate logistic regression was used to determine the potential predictors of MI.

**RESULTS**

Thirteen patients (1.44%) suffered from MI during hospitalization (median time: 12 days). Patients with MI had more severe stroke (mean Scandinavian Stroke Scale score on admission:  $12.8 \pm 10.2$  vs.  $32.3 \pm 15.9$ ;  $p < 0.01$ ), more often suffered from ischemic heart disease (92.3% vs. 56.4%;  $p < 0.01$ ) and diabetes mellitus (46.2% vs. 20.6%;  $p = 0.02$ ). These patients had higher serum fasting glucose ( $8.6 \pm 4.2$  mmol/l vs.  $6.3 \pm 2.4$  mmol/l;  $p < 0.01$ ), more often had LDL-cholesterol  $> 4.1$  mmol/l (46.2% vs. 26.4%;  $p = 0.04$ ) and white blood cell count  $> 10\,000/\text{mm}^3$  (69.2% vs. 30.4%;  $p < 0.01$ ). On multivariate logistic regression analysis Scandinavian Stroke Scale score (OR: 0.93; 95% CI: 0.89-0.98;  $p < 0.01$ ) and LDL-cholesterol  $> 4.1$  mmol/l (OR: 4.17; 95% CI: 1.19-14.7;  $p = 0.03$ ) remained independent predictors of MI in patients with acute ischemic stroke.

**CONCLUSION**

Severe stroke and elevated LDL-cholesterol are independent predictors of in-hospital MI in patients with acute ischemic stroke.

## PS145

### HEART STRUCTURAL CHANGES DETECTED BY ECHOCARDIOGRAPHY IN CARDIOEMBOLIC STROKE

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#### AIM

The aim of this study was to determine the association of left atrial echocardiographic parameters and cardioembolic stroke.

#### INTRODUCTION

Left atrium enlargement is common finding in patients with cardiovascular diseases. Increased left atrium size cause the stasis of the blood flow predisposing to procoagulable state.

#### METHODS

: We enrolled 159 patients with first ever acute ischemic stroke admitted to stroke unit within 24 hours after symptoms onset. All patients underwent head CT, neurological examination, laboratory investigations, electrocardiography and transthoracic echocardiographic study on admission. Left atrial volume was calculated using elliptic model using formula:  $\pi/6 (A1 \times A2 \times A3)$  in which A1 is left atrial antero-posterior diameter, A2- left atrial superior-inferior dimension and A3- left atrial lateral-medial dimension.

#### RESULTS

Fifty-nine patients (37.11%) suffered from cardioembolic stroke. They had significantly lower left ventricular ejection fraction ( $55.20 \pm 12.90\%$  vs.  $63.92 \pm 9.10\%$ ;  $p < 0.001$ ), larger left ventricular diameter in diastole ( $49.29 \pm 9.97\text{mm}$  vs.  $46.18 \pm 7.94\text{mm}$ ;  $p = 0.032$ ), larger left atrial antero-posterior diameter ( $46.47 \pm 5.83\text{mm}$  vs.  $42.03 \pm 5.58\text{mm}$ ;  $p < 0.001$ ) and larger left atrial volume ( $69.22 \pm 26.03\text{cm}^3$  vs.  $46.84 \pm 19.43\text{cm}^3$ ;  $p < 0.001$ ). They also had higher frequency of atrial fibrillation ( $69.49\%$  vs.  $5.00\%$ ;  $p < 0.001$ ). In multivariate logistic regression analysis left atrial volume (OR:0.97, 95%CI: 0.95-0.99;  $p = 0.04$ ), atrial fibrillation (OR: 0.03, 95%CI:0.008-0.08;  $p < 0.01$ ) and left ventricle diastolic diameter (OR:0.06, 95%CI:0.015-0.233;  $p < 0.001$ ) were independently associated with stroke of cardioembolic etiology.

#### CONCLUSION

High left atrium volume, enlarged left ventricle and atrial fibrillation are independently associated with cardioembolic stroke.



## PS199

**PREVIOUS ANTICOAGULATION USE AND IN-HOSPITAL MORTALITY IN PATIENTS WITH ISCHAEMIC STROKE AND ATRIAL FIBRILLATION: WHAT ARE THE ODDS?**

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AIM

To study previous anticoagulation therapy use and its associated factors in patients with Ischaemic Stroke (IS) and Atrial Fibrillation (AFib); To explore in-hospital mortality predictive factors of AFib patients suffering from IS.

**INTRODUCTION**

Stroke is one a leading cause of morbidity and mortality on developed countries, even though the post-IS mortality has been decreasing. Patients with AFib, the most common cardiac arrhythmia, have a 5-fold increased risk of IS, leading to a greater necessity of preventive therapy. Thus, practice guidelines recommend the use of a risk score (CHADS2 or CHA2DS2VASc2) to estimate the need to prescribe anticoagulant (Ac) or aspirin/antiplatelet therapy (Asp).

**METHODS**

Data were obtained from the National Hospitalisation Database (NHD) provided by the Health System Central Administration (ACSS), with discharge dates between 2009 and 2010 in Portuguese public hospitals. Our study population was comprised of in-patients with principal diagnosis of IS (ICD-9-CM codes 433.x1, 434.x1 or 436.xx) and a secondary diagnosis of AFib or Atrial Flutter (AFI) (427.3x). Subjects with valvular prosthesis or respective complications were excluded. Adjusted odds ratios and 95% confidence interval (CI) were calculated using logistic and multinomial logistic regression models. Data analyses were conducted using IBM SPSS Statistics 20.

**RESULTS**

Among the 39,048 IS hospitalizations (after exclusion criteria), 9060 (23.2%) had a co-morbid diagnosis of AFib or AFL. Of those, 748 (8.3%) had a reported long-term use of Ac and 372 (4.1%) of Asp. 6475 (71.5%) of the patients had CHADS2 score  $\geq 2$ , of whom 503 (8.2%) were taking Ac and 304 (4.7%) Asp.

Age  $\geq 85$  was negatively associated with previous Ac (adjusted OR 0.31; CI 0.16 to 0.58). Previous stroke/transient ischaemic attack/thromboembolism (PS/TIA/TE) and valvular heart disease (VHD) were associated with significant higher rates of Ac - adjusted OR 1.53 and 2.10, respectively. Significant higher Asp use was found with PS/TIA/TE, VHD and hypertension (HT) - 3 of the CHADS2 score criteria. Yet, diabetes mellitus (DM), also CHADS2 variable, showed a negative association, with an OR of 0.71 (CI 0.55 to 0.92).

Total in-hospital mortality rate was 17.4% (1,573 deaths). Among the group submitted to Ac, the in-hospital mortality rate was 14.8% against the 14.0% of the Asp group and the 17.8% of the non-reported therapy group. Simultaneous method revealed OR of 0.76 (CI 0.56 to 1.04)

and 0.93 (0.75 to 1.15) for AC and Asp, respectively, concerning death outcome. Using stepwise method, age significantly increased in-hospital mortality, as well as CHF (OR 1.56) and DM (OR 1.19). On the other hand, HT and VHD were considered significant protective factors to in-hospital death with an associated OR of 0.63 and 0.58, respectively.

### CONCLUSION

In our population the percentage of IS associated with AFib/AFL was similar to other reported studies. Among those who, according to CHADS2 score, had definite indication for anticoagulation, only 8.2% had reported previous Ac and 4.7% previous Asp. Positively associated predictive factors for Ac were VHD, PS/TIA/TE and increasing Charlson co morbidity index. Ac use was less likely in older patients.

Positive predictors (from CHADS2 criteria) of Ac remained good predictors for Asp, reinforced by HT. Subjects with reported Ac or Asp showed a non-significant trend to die less during stay, trend that revealed significant for HT and VHD. On the other hand, age  $\geq 75$ , DM and CHF represented independent risk factors for in-hospital death.



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# ONCOLOGY & MOLECULAR BIOLOGY



## PS46

### BREAST CANCER PATHWAY: ARE DOCTORS AWARE?

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AIM

To investigate women suspected to have breast cancer in CM clinical pathway of HSJ, determining if GPs know and follow the guidelines concerning breast pathology diagnosis and if they reroute their patients correctly according to their BI-RADS classification.

#### INTRODUCTION

In breast cancer, the fifth most important cause of death worldwide, prevention and early diagnosis play an essential role in diminishing mortality. Therefore, evaluating the patients' pathway, the general practitioners' guidelines knowledge, as well as the efficient use of classifications, e.g. Breast Imaging Report and Data System (BI-RADS), is essential to assure an effective treatment, improve health care and diminish costs.

#### METHODS

Transversal and observational study. A questionnaire was delivered to GPs to assess the quality of rerouting and the knowledge of GPs concerning the national guidelines for adequate referral of breast pathology patients. The statistics gathered from the BreastCare database were also analysed. The statistical study included frequencies and percentages, means and standard deviation, as well as binomial tests and 95% confidence intervals.

#### RESULTS

All of the GPs considered mammography as the standard test for screening and know BI-RADS classification, but only 76.5% of them know "Recomendações Nacionais para o Diagnóstico e Cancro da Mama" ( $p=0.049$ ). More than 50% (95% CI) of the GPs are familiarized with breast cancer guidelines. The study achieved a high rate (70%) of women incorrectly referred to CM and showed that 53.1% of them were referred as BI-RADS Stage 2.

#### CONCLUSION

More than half of the GPs are following the guidelines and are aware of "Recomendações Nacionais para o Tratamento e Diagnóstico de Cancro da Mama" and BI-RADS classification. However, the massive rerouting of BI-RADS Stage 2 (53.1%) to a specialized center proves that women are being inaccurately rerouted and resources are being spent inadequately. The current study allowed us to unveil gaps in the National Healthcare Service, which are accountable for psychological problems and unnecessary economic expenditures.



**PS65****SYNTHESIS OF ALKYLATED FLAVONOIDS WITH POTENTIAL ANTITUMOR ACTIVITY**

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AIM

Inspired by the potential of flavonoids as antitumor agents synthesis of alkylated analogues using a natural flavone as the starting material.

**INTRODUCTION**

In the last decades, the search for new antitumor agents has been increasing among scientific community. From these studies several hit compounds have been discovered, particularly those with flavone scaffold. In fact, there are several reports showing the potential of flavones as antitumor agents (L'pez-L'czaro, 2002; Cidade et al., 2009).

One of the main interests of CEQUIME-UP is the search of new pharmacologically active compounds from natural and synthetic origin, focusing on potential antitumor compounds. In this respect, several small-molecules have been evaluated for their activity as inhibitors of the growth of human tumor cell lines (Neves et al., 2011).

**METHODS**

The synthetic approach was based on the reaction with alkyl bromides in alkaline medium under microwave irradiation.

The structure of all synthesized compounds were established on the basis of NMR techniques (<sup>1</sup>H NMR, <sup>13</sup>C NMR, HSQC and HMBC).

**RESULTS**

The biological activity of all compounds synthesized are under evaluation.

**CONCLUSION**

In result of this work, eight alkylated compounds and three prenylated derivatives were obtained. Prenylated derivatives had been previously synthesized in CEQUIMED-UP research group but alkylated derivatives were never synthesized before. The structure characterization of the synthesized compounds was established by spectroscopic methods, such as <sup>1</sup>H and <sup>13</sup>C NMR, HSQC and HMBC.

Synthesis carried out by MAOS methodology afforded reasonable yields in shorter reaction times.

## PS73

### **THE RELATIONSHIP BETWEEN FACTOR V LEIDEN AND PROTHROMBIN G20210A MUTATIONS AND THE FIRST MAJOR THROMBOTIC EPISODE IN POLYCYTHEMIA VERA AND ESSENTIAL THROMBOCYTHEMIA**

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AIM

To demonstrate a possible contribution of the Factor V Leiden and Prothrombin G20210A mutations to the thrombotic risk in patients with polycythemia vera and essential thrombocythemia, along with other biologic features of these patients

#### INTRODUCTION

Polycythemia vera (PV) and essential thrombocythemia (ET) are the most common myeloproliferative neoplasms (MPN) negative for the BCR-ABL fusion. A very known molecular marker of these diseases, the JAK2 V617F mutation, is seen in almost all patients with PV and around 50-60% of patients with ET.

PV and ET patients, even though they have an overall good prognosis in terms of survival, they are frequently prone to thrombotic events. The pathogenesis of thrombosis in PV and ET is complex and not yet fully understood. Blood hyperviscosity is a known risk factor for thrombosis in general. JAK2 V617F mutation itself is considered a thrombotic factor for these patients. We also took into account different biologic features that may contribute to the thrombotic risk of MPN patients: male gender, higher hematocrit levels, white blood cell count and the platelet count.

Factor V Leiden and Prothrombin G20210A mutations are the most frequent causes of inherited thrombophilia in caucasians. Due to their relatively high frequency in the general population, a contribution of these mutations to the thrombotic risk of MPN patients seems an attractive hypothesis. However, few studies addressed this hypothesis, and the results were conflicting.

#### METHODS

The study included 181 consecutive patients with MPN, out of which 86(47.5%) with PV and 95(52.5%) with ET. MPN group was divided in 2 sub-groups: first sub-group consisted of patients with a major thrombosis as a first event, at the time of diagnosis, or during follow-up. The second one consisted of patients who had no thrombosis by the enrollment and during follow-up time. 34 patients (39.5%) with PV and 22 patients (23.1%) with ET had a major thrombotic event.

Factor V Leiden and Prothrombin G20210A mutations were investigated by means of molecular genetics assays

#### RESULTS

Factor V Leiden was detected in 8 (9.3%) patients with PV; all 8 patients but one had major thrombotic events (OR = 13.2; 95% CI = 1.5 — 113.1,  $p = 0.005$ ). ET patients that had a major thrombotic event also had this mutation (13.6% versus 6.8%; OR = 2.1; 95% CI = 0.5 — 9.8  $p = 0.38$ ). Prothrombin G20210A mutation was seen in 8 patients with PV, but only 3 of them had major thrombotic events (OR = 0.9; 95% CI = 0.2 — 4.1,  $p = 1$ ) while in ET disorder we found 3 positive patients with the prothrombin mutation. When joining the two groups of patients (PV and ET), the only mutation that attained statistical significance was Factor V Leiden, seen much more frequently in patients with major thrombosis than in those without thrombosis (OR = 4.3; 95% CI = 1.5 — 12.5;  $p = 0.008$ ).

## CONCLUSION

Factor V Leiden is strongly correlated to the first major thrombotic episode in MPN patients, being significant in univariate and multivariate analysis.

## PS78

### EVALUATION OF THE MICRORNA BIOGENESIS MACHINERY IN CHICK EMBRYO DEVELOPMENT

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#### AIM

Characterize the expression patterns of MicroRNA (miRNA) machinery genes in the developing chick embryo.

#### INTRODUCTION

Embryo development is a process that requires flawless temporal control in order to give rise to a completely functional organism. To accomplish this, many failsafe and regulatory mechanisms were developed. Molecular clocks, evidenced by cyclic gene expression, underlie temporal control required for embryo development. Somitogenesis is one of the processes where a Molecular clock has been evidenced. Clock genes' oscillatory expression is proposed to translate temporal information into a spatial pattern that is necessary for somite formation. Molecular clocks also play a role in other processes, namely limb formation. High degree of mRNA instability is one of the mechanisms that enable clock gene oscillations and it is thought to be due to the involvement of miRNAs.

#### METHODS

Fertilized eggs were incubated at 37,8°C in a humidified atmosphere and staged according to the Hamburger and Hamilton (HH) classification.

In situ hybridization was performed in fixed embryos and limbs as previously described by Ish-Horowicz D. (1995) using antisense digoxigenin-labeled RNA probes for genes involved in miRNA synthesis (drosha2, drosha5, exportin5, dicer, pasha), a gene regulated by miRNAs (lin-41) and the molecular clock gene hairy2.

Beads soaked in FGF2 or all-trans retinoic acid (RA) were implanted in ovo into different limb mesenchymal domains in order to evaluate their effect on the expression of hairy2, lin-41 and exportin5 (XPO5). After implantation, the eggs were sealed, reincubated and collected after 4h.

#### RESULTS

miRNA machinery genes (drosha, exportin5, dicer and pasha) are co-expressed in the same tissues as hairy2 and lin-41 in various stages of embryonic development, suggesting that miRNA action on mRNAs of molecular clock genes is a possible mechanism during embryo development. RA-bead implantation induced hairy2 expression in all the tested domains, as demonstrated by Sheeba et al (2012). Similarly, XPO5



expression was also upregulated by RA-beads while the expression of *lin-41* was not. Regarding *Hairy2* expression, FGF2 soaked beads implantation appears not to have any effect. FGF2-beads induced *hairy2* expression in all the domains except the anterior limb mesenchyme. Contrarily to what was observed with RA-beads, FGF2 upregulated *lin-41* expression and *XPO5* expression.

## CONCLUSION

This work provides novel information about the expression of miRNA machinery genes during embryo development. Despite not directly assessing the involvement of this type of small RNAs in molecular clock regulation, our work show co-localization with clock mRNA expression, further suggesting miRNA involvement in the molecular clock machinery. Moreover, we also show that in chick limb, both RA and FGF act as regulators of miRNA component gene expression.

## PS113

### ESTABLISHING A NEW GENERATION SEQUENCING METHOD FOR THE DIFFERENTIAL DIAGNOSIS OF COL IV NEPHROPATHIES

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#### AIM

Our aim was to evaluate the feasibility of new generation sequencing for the differential diagnosis of AS and TBMN. Analyse the results with prediction software, and validate the identified possible disease causing variants by Sanger sequencing.

#### INTRODUCTION

Alport sy (AS) and thin basement membrane nephropathy (TBMN) are caused by mutations in the Col4A3, Col4A4 and Col4A5 collagen type IV genes. In adults the functional protein consists of one gene product of each gene. Depending on the affected genes and number of mutations the clinical outcome could be benign TBMN or severe AS; however clinical manifestation occurs only at a later age. Thus early differential diagnosis is crucial for the treatment.

Indirect linkage analysis of Col(IV) genes is cheap, but it only works on families where the inheritance of the disease was proven. Direct sequencing of all the three genes (more than 150 exons) by conventional Sanger-sequencing method is laborious and expensive. With the advances in new generation sequencing methods the cost of sequencing became affordable, but the bioinformatic analysis led to new challenges.

#### METHODS

The DNA samples of 20 families (affected and normal family members) were available in our gene bank. For the new generation sequencing we chose one patient from each family. Sample enrichment was performed by the Ion AmpliSeq(TM) Library Kit. The samples were barcoded and sequenced on IonTorrent 316 chip. The bioinformatic analysis were performed by CLC Bio software. In the 20 patients altogether we found 292 variants. The variants resulting in amino-acid change were evaluated by disease prediction softwares (Polyphen-2, SIFT, MutationTaster).

#### RESULTS

We identified 19 possible disease causing alterations. We are in the work of validating these alterations in the affected families by Sanger sequencing.

#### CONCLUSION

Knowledge of the genetic background of Col IV nephropathy is essential to avoid the misdiagnosis of TBMN and early AS. Linkage analysis of collagen type IV nephropathy patients is a cheap convenient method for family analysis, however it is often uninformative in small families. HRM analysis and conventional

sequencing is more time consuming and costly while it identifies less mutations than new generation sequencing. The identified mutations and the use of mutation prediction tools combined with clinical data may lead to a better understanding of geno-, fenotype correlations in TBMN/AS.



## PS117

### RELEVANCE OF IMPRINTED GENES IN HUMAN FETAL GROWTH

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AIM

The aim of the present study was to evaluate the levels of four imprinted genes (IGF2, CDKN1, PHLDA2 and KCNQ1) in fetal deaths, assessing their possible relation with the fetal growth.

### INTRODUCTION

Genomic imprinting refers to a normal form of gene regulation in which one allele is repressed according to parental origin. Although imprinted genes comprise a small subset of the human genome, they have been shown to be essential to fetal, placental and behavioural development.

Fetal growth restriction (FGR) is a condition in which a fetus is unable to achieve its genetically determined potential size thereby increasing their perinatal risk of morbidity and mortality. Chromosomal abnormalities are one of the major causes of growth restriction. This phenomenon happens due to an abnormal gene expression in the tissues leading to an abnormal growth of the baby.

Imprinted genes have a very special role in the fetal growth and humans' development as they can either promote it or suppress it. This is underlined by the many imprinted genes that are expressed in placenta.

Although this subject has been the focus of much attention recently, there are still few studies clarifying the role of human imprinted genes in fetal development.

### METHODS

We performed a case control study in fetal deaths. The study group was fetus with growth restriction and the control group was fetus without restriction. RNA was extracted and cDNA synthesis was performed. Quantitative Real Time PCR using TaqMan Gene Expression Assays was done to evaluate the gene expression patterns of IGF2, CDKN1C, PHLDA2 and KCNQ1 genes in FGR fetal/placental samples (n=26) and in the group control (n=13). The housekeeping gene GAPDH was used as control. GraphPad Prism 6 software was used to perform statistical analysis.

### RESULTS

Our results indicated that levels of IGF2 were significantly lower in the FGR group than in the control group ( $p<0,0001$ ), with no significant changes in the levels of the other genes. When comparing the samples according with the gestational age statistical differences were found in the IGF2 levels in the second trimester cases ( $p<0,0001$ ) and in the third trimester cases ( $p=0,0116$ ). IGF2 levels were also downregulated in the placental samples FGR group ( $p=0,0001$ ). No statistical difference was seen between the fetal samples groups ( $p=0,1029$ ).



## CONCLUSION

Because fetal death is an important complication of pregnancy, it is very important to recognize the cause and ascertain the risk for a next pregnancy.

The genomic imprinting is a phenomenon that plays a very important role in the fetal and placental development. Several imprinting genes may regulate this process and, despite the several studies performed before, additional research is still required. This study allows us to stress the importance of IGF2 gene during the fetal development.



## PS92

### EVALUATION OF GENE EXPRESSION PATTERN OF **MAD2L2, BUB1, BUB1B E KIF2C**

#### GENES IN MISCARRIAGES CASES WITH ANEUPLOIDIES

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#### AIM

The overall aim of the present study is evaluate the gene expression pattern of genes known to be involved in cell-cycle regulation (MAD2L2, BUB1, BUB1B and KIF2C), in miscarriage products with a confirmed aneuploidy.

#### INTRODUCTION

Aneuploidy, one of the most common chromosomal abnormalities in humans, is defined as a gain or loss of one or more chromosomes. The high incidence of aneuploidies, namely trisomies, have a significant clinical impact because about one third of all miscarriages are due to trisomies and children with trisomies of the 13, 18 and 21 chromosomes have phenotypic changes of varying degree, which may include, among other malformations, mental retardation, dysmorphic features, physiological alterations and early death.

Cell-cycle tight control mechanisms, namely SAC (Spindle Assembly Checkpoint), are crucial to ensure proper chromosomal segregation and therefore avoid aneuploidy. Those processes involve a large number of genes and their proteins, in particular MAD2L2, BUB1, BUB1B and KIF2C.

#### METHODS

According with the protocol previously established between Gynecology/Obstetrics Department, S'eo Jo'eo Hospital and Genetics Department, Faculty of Medicine, miscarriages or fetal death samples were sent for routine cytogenetic analysis. After karyotype, 50 trisomic samples were selected for this study (four for chromosome 13, seven for chromosome 15, eleven for chromosome 16, ten for chromosome 18, eleven for chromosome 21 and seven for chromosome 22) as well as 30 control samples with normal karyotype. The level of expression of selected genes and housekeeping gene (GADPH) was accessed by Quantitative Real-Time PCR using TaqMani Gene Expression Assays. Data obtained were analyzed using REST 2009 (Relative Expression Software Tool).

#### RESULTS

Our results showed that both BUB1B and KIF2C were upregulated in sample group in comparison to control group, by a mean factor of 6,894 and 5,665, respectively. No significant differences were found between sample group and control group for MAD2L2 and BUB1 genes.

#### CONCLUSION

Our results suggest an association between increased expression of BUB1B and KIF2C genes and aneuploidy in miscarriages or fetal death samples. However, it is important to point out that the upregulation of BUB1B

and KIF2C can be the cause of aneuploidy or, on the other hand, can be a side effect of the aneuploidy itself. So, the etiology of this upregulation should be further investigated. Additional research will also be necessary to understand the downstream effects of upregulation of BUB1B and KIF2C, namely at protein level.



## PS120

### OPTIMIZATION OF 3C LIBRARY PREPARATION TO ANALYZE CHROMOSOME CONFORMATION

#### CAPTURE IN CANCER CELL LINES

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#### AIM

Our aim was to determine whether the regulation of RAVER2 is different in cancer vs. normal cells. To do so, we investigate the looping interaction of RAVER2 in relation to CTCF binding site near the gene. We would like to optimize 3C library preparation from cancer cell lines (PC3, PC3M, PC3M Pro, PC3M LN4, HT29, Caco2, CG, Hek 293), fibroblasts (VH10, VH25, FN-1), and Bacterial Artificial Chromosome covering entire region of RAVER2 gene – as this first and main step which allows further interaction frequency analysis for RAVER2.

#### INTRODUCTION

Chromosome conformation capture (3C) is a pioneering methodology that allows to evaluate spatial organization of chromatin in vivo. 3C technology is particularly suited to identify chromatin loops formed between promoter of the target gene and its regulatory elements localized up to several hundreds of kilobases down- and upstream. We are interested in RAVER2 gene expression regulation – as is tissue specific, different expression were observed in cancer cells and in addition Raver2 protein is localized in PNC structure.

#### METHODS

The 3C technology uses formaldehyde crosslinking to covalently link interacting chromatin segments in living cells. Crosslinked chromatin is then digested with a restriction enzyme, followed by intramolecular ligation of crosslinked fragments. The crosslinks are then removed and the DNA is purified. Final template, termed the 3C library represents set of ligation products.

#### RESULTS

In order to analyze if RAVER2 gene is organized in loop structure as putative CTCF binding sites are upstream and downstream of RAVER2, firstly, HIND III was chosen as the best restriction enzyme for RAVER2 3C analysis. Secondly we followed original 3C protocol by H. Hagege and J. Dekker, which is divided to three essential steps: formaldehyde crosslinking, followed by DNA digestion and intermolecular ligation of crosslinked fragments. As first libraries had low digestion efficiency (below 40%) we modified 3C protocol by reducing formaldehyde concentration (from 2% to 1%) during crosslinking step. Furthermore, we modified digestion step by increasing HIND III amount (from 400U to 2000U). This optimization resulted in correct digestion efficiency (above 80% for all 3C libraries) verified correct library preparation.



## CONCLUSION

Decreased formaldehyde to 1% for crosslinking and increased HindIII for DNA digestion up to 2000units, resulted in correct 3C library preparation from cancer cell line and BAC and verified correct library preparation for further interaction frequency analysis.



## PS116

### SELECTED GENE EXPRESSION SIGNATURE AND METHYLATION PROFILE IN PROSTATE CANCER CELL LINES

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#### AIM

Our aim was to determine whether expression of 22 tumor suppressor genes differ in 4 prostate cancer cell lines of varying levels of malignancy and 3 fibroblasts cell lines and compare it with methylation profile in PC3 and PC3M LN4 cell line (with low and high PNC prevalence, respectively).

#### INTRODUCTION

Gene-expression profiling has been extensively used in many cancers as potential tool for cancer prognosis and cancer classification based on molecular features. While gene expression signatures have been evaluated for diagnostic in breast, colon and lung cancers, gene expression and DNA methylation profilings in prostate cancer are still at a pre-clinical exploration stage.

#### METHODS

For gene expression total RNA was isolated from prostate cancer cell lines (PC3, PC3M, PC3MLN4 and PC3MPro4) and fibroblasts cell lines (VH10, VH25 and FN1) used as control. We performed RT-PCR and amplification with specific primers and UPL probes on a LightCycler2.0. Expression of 22 target gene was normalized to expression of the housekeeping gene PBGD. The next step was evaluation of the 22 tumor suppressor genes promoter methylations. For this purpose DNA was isolated with 2 min RNase A's incubation. Then we digested samples using 2 different endonucleases: methylation sensitive and methylation-dependent. Finally Real-Time PCR was performed using SYBR® Green qPCR Master. Data were evaluated as percentage unmethylated and percentage methylated fraction of input DNA in two prostate cancer cell lines.

#### RESULTS

We found 9 genes that had lower expression in prostate cancer cell lines compared to fibroblasts cell lines. In addition, DLC1, EGFR, MGMT and DKK3 had higher expression in PC3 cell line than other prostate cancer cell lines with higher malignant levels. Interestingly we found 3 genes: ZNF185, EDNRB and GPX3 that are highly expressed in prostate cancer cell lines in comparison to fibroblasts but promoter methylation status of those genes was above 86%. We found differences in methylation status between PC3 and PC3MLN4 cell lines which differ in PNC prevalence (low and high, respectively). The DKK3, MGMT, TNFRSF10D and RARB are 98% unmethylated in PC3 whereas in PC3MLN4 – methylated from 76% (for RARB) up to 99% in DKK3. Those methylation results correlate with gene expression in PC3 which is higher for DKK3, MGMT and RARB and lower in PC3MLN4.

## CONCLUSION

Tumor suppressor genes expression differ not only between prostate cancer cell lines and fibroblasts, but also within 4 prostate cancer cell lines with different PNC prevalence that reflect different level of malignancy. Preliminary methylation results on 2 prostate cell lines demonstrate that the methylation status of MGMT, DKK3 and RARB genes correlates with their expression. Methylation status of TNFRSF10D does not correlate with gene expression data therefore another reference gene will be chosen to re-evaluate. Additional methylation analysis for another prostate cancer cell line PC3M and control fibroblast will be performed in the future.



## PS176

### USAGE OF MIB 1 MONOCLONAL ANTIBODIES IN HISTOPATHOLOGY OF NON-HODGKIN LYMPHOMA

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#### AIM

The aim of this study was to evaluate the percent of MIB-1 positive cells in non-Hodgkin's lymphoma by type of DLBC and FL in patients of different age.

#### INTRODUCTION

Non-Hodgkin lymphomas are malignant lymphocyte tumors, extremely heterogeneous from the standpoint of histological subtypes. Any group, of this lymphoid tumors, can manifest at any age, often manifesting with enlarged lymph nodes, fever and weight loss. MIB 1 is a monoclonal antibody for Ki-67 as antigen. It has great affinity for Ki-67 nuclear antigen and it is used to detect Ki-67 antigen in cells.

#### METHODS

In the aim of this study was used a group of 10 patients with diagnose of non-Hodgkin's lymphoma (7 men and 3 women). The study was conducted on samples collected at the Center for Pathology, Clinical Center in Nis, in a period from 2006. to 2010. year. Primary antibody used in this paper was MIB 1. Stained preparations were analyzed using a Nikon Eclipse 50 microscope. Determination of MIB 1 positive cells number was performed using a computer program ImageJ, plugin Point Picker.

#### RESULTS

Of the ten patients, five of them were diagnosed as diffuse large B cell type of non-Hodgkin lymphoma (DLBC); the other five was diagnosed as follicular lymphoma (FL). The number of MIB 1 positive cells in FL varied from 17 to 23 per hundred cells. In non-Hodgkin DLBC lymphoma, number of MIB 1 positive cells varied in the range of 36 to 40 per hundred cells.

#### CONCLUSION

MIB 1 is useful in determining the malignant potential and proliferation index of the cells in malignant process. The incidence of diseases such as DLBC and FL was different at different sexes. Among male respondents were noted increased frequency of non-Hodgkin lymphoma type DLBC (57%), while for female gender were more frequent follicular lymphoma (67%).



**PS180****p15, p16, p53 AND DAPK GENES METHYLATION STATUS IN MYELODYSPLASTIC SYNDROME**

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**AIM**

Our aim was to investigate the DNA methylation status of p15, p16, p53 and DAPK genes in Myelodysplastic Syndrome (MDS) patients at diagnosis in bone marrow aspirate and compare the methylation status of bone marrow with peripheral blood.

**INTRODUCTION**

MDS are a heterogeneous group of clonal hematopoietic stem-cell disorders characterized by ineffective hematopoiesis, peripheral-blood cytopenias, and increased probability of leukemic transformation. Although MDS pathogenesis is not completely understood, deregulated epigenetic mechanisms are likely involved. DNA methylation is one of the epigenetics processes more frequently studied and several genes have been shown to be transcriptionally silenced in association with promoter methylation. Aberrant methylation of gene promoter region is responsible for inappropriate gene silencing, namely tumor suppressor genes, and it has been associated with cancer initiation and progression.

**METHODS**

The methylation status of p15, p16, p53 and DAPK genes were analyzed in bone marrow and peripheral blood cells of 40 patients with de novo MDS, collected at diagnosis. Genomic DNA was isolated by standard protocols and modified using sodium bisulfite. The MS-PCR for gene promoter methylation was performed using two sets of primers, one for methylated DNA and other for unmethylated DNA. The patient group median age was 74 years (22-89), gender M/F=22/18, WHO subtypes: RCMD (37%), RA (17%), RAEB-1 (6%), RAEB-2 (20%), 5q- syndrome (3%), CMML (11%), and IPSS: low (27%), intermediate-1 (55%) and

intermediate-2 (18%).

## RESULTS

Overall, 65% of MDS patients presented at least one methylated gene in BM samples (RCMD: 23%, RA: 100%, RAEB-2: 29%, CMML: 50%) and 20% presented two or more methylated genes (RCMD: 77%, RA: 50%, RAEB-2: 0%, CMML: 0%). Moreover, 65% of MDS patients presented DAPK gene methylated (RCMD: 67%, CMML: 25%), 44% presented p15 gene methylated (RCMD: 46%, RA: 83%, RAEB-2: 14%, CMML: 25%), 38% presented p16 gene methylated (RCMD: 50%, RA: 67%, RAEB-2: 17%, CMML: 0%) and none of patients studied presented p53 gene methylation. We also observed a predominance of methylation in low risk patients, since 89% and 28% patients with low and Int-1 IPSS, respectively, presented at least one methylated gene of and none of Int-2 patients studied presented methylated genes. Besides that, we only observed 2 out of 14 (14%) samples with discrepant results in DAPK methylation between BM aspirate and PB. However, the discrepancies in p15 gene were 3 out of 13 (23%).

## CONCLUSION

Our results show that aberrant methylation of p15, p16 and DAPK genes seems to be a common event in MDS patients, especially in low risk patients. Moreover, we observed a correlation between methylation patterns of DAPK gene between peripheral blood and in bone marrow aspirate. Although DNA methylation patterns measured in peripheral blood have great potential to be useful and informative biomarkers of cancer risk and prognosis, large systematic and prospective studies will be needed.

## PS184

**THE ROLE OF VISMODEGIB IN HEMATOLOGICAL NEOPLASIAS TREATMENT**

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## AIM

The main objective of this work is to evaluate the therapeutic efficacy of the hedgehog inhibitor, vismodegib, in hematological neoplasias cell lines in culture.

## INTRODUCTION

Hematological neoplasias development is regarded as a multistep process that is orchestrated by genetic and/or epigenetic mechanisms that drive the transformation of normal human hematopoietic stem/progenitor cells. On this way, Hedgehog (Hh) conserved embryonic signaling pathway, critical for stem cell self-renewal and differentiation in hematopoiesis, has been implicated in the pathogenesis of several hematological malignancies. Take into account, the identification of targeted inhibitors of Hh pathway may constitute a new successfully therapeutic strategy in hematological malignancies.

## METHODS

For this purpose we maintained in culture CEM (Acute Lymphoblastic Leukemia cell line), HL-60 (Promyelocytic Leukemia cell line), K-562 (Chronic Myeloid Leukemia/erythroleukemia cell line) and FARAGE (Diffuse Large B-Cell Lymphoma cell line) cells and tested the effect of different concentrations of vismodegib (GDC-0449). Cell viability was assessed by the trypan blue and alamar blue assays and cell death by Optical Microscopy (May-Grunwald staining) and flow cytometry (FC) using the Annexin V/Propidium Iodide (PI) double staining. Some of the mechanisms involved as BAX/BCL-2, caspases, p53 and cyclin D1 expression levels were also evaluated by FC using specific monoclonal antibodies. Cell cycle arrest was also assessed by FC using PI solution.

## RESULTS

Our results showed that vismodegib induces antiproliferative and cytotoxic effects in a dose, time, administration schedule and cell type dependent manner. The half maximal inhibitory concentration (IC50) at 48h is 75  $\mu$ M, 100  $\mu$ M and between 100–150  $\mu$ M, respectively for HL-60, CEM and K-562 cell lines. On the other hand, in FARAGE cells the IC50 was not reached. This compound induces cell death mainly by

apoptosis in agreement with the observed increase in caspases levels and BAX/BCL-2 ratio and the decrease of mitochondrial membrane potential. Moreover, vismodegib induces antiproliferative effects through cell cycle arrest in S phase which may be correlated with the decrease in p53 and cyclin D1 levels.

### CONCLUSION

In conclusion, our study suggests that vismodegib (GDC-0449) may constitute a new potential targeted therapeutic approach in hematological neoplasias, namely in acute leukemias.

This work was supported by Center of Investigation in Environment Genetics and Oncobiology (CIMAGO).



## PS9

# **INHIBITION OF METALLOPROTEINASES AS A NEW THERAPEUTIC APPROACH IN ACUTE PROMYELOCYTIC LEUKEMIA**

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## **AIM**

The aim of this study was to evaluate the therapeutic potential of Batimastat (BB-94), a matrix metalloproteinases inhibitor, in acute promyelocytic leukemia in vitro.

## **INTRODUCTION**

Acute promyelocytic leukemia (APL) is characterized by abnormal accumulation of myeloid precursors blocked at the promyelocytic stage of maturation in the bone marrow. The majority of APL cases are associated with the chromosomal translocation t(15;17) that encodes the fusion protein PML-RAR $\alpha$ . The matrix metalloproteinases (MMPs) are an important player in leukemic microenvironment, since these proteins can degrade all the protein components of the extracellular matrix. Since some patients fail or relapse after APL conventional therapies, the inhibition of MMPs activity may constitute a new therapeutic strategy for this disease.

## **METHODS**

For this purpose, we used two APL cell lines, the NB-4 cells, with the t(15;17) translocation, and the HL-60 cells, without this translocation. Both cell lines were cultured in absence and presence of different concentrations of Batimastat (BB-94) ranged from 0,1  $\mu$ M to 10  $\mu$ M, in a daily or single dose administration. To evaluate the effect of this inhibitor on cell viability and cell density we used the Trypan Blue Assay. Cell death was determined by optical microscopy (May-Grunwald Giemsa staining), and by flow cytometry (FC) using the Annexin V and Propidium Iodide double staining. It was also evaluated the activation of caspases using the Apostat probe.

## **RESULTS**

Our results showed that BB-94 reduces cell viability and proliferation in both cell lines in a time, dose and cell line characteristics dependent manner. We found that the half maximal inhibitory concentration (IC50) at 48 hours of exposure was, approximately, 7,5  $\mu$ M for HL-60 and 2,5  $\mu$ M for NB-4. Besides that, the daily administration schedule seems to be more effective in the reduction of cell viability and proliferation when compared to the same doses in single administration. BB-94 induced cell death by apoptosis with activation

of caspases, in a dose-dependent manner.v

## CONCLUSION

In conclusion, our results suggest that BB-94 is a potential new targeted therapy in APL treatment, being more effective in the presence of the t(15;17) and on a daily administration schedule, which could be advantageous in vivo since it could induce less systemic toxicity.

This work was supported by Center of Investigation in Environment Genetics and Oncobiology (CIMAGO).



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MUNEER AL-HUSSEINI, MUAYAD ABDULAZIZ ALZUABI, ZEINAB HASSAN AWAD, DIAA MOHAMMED HUSSEIN, OMNIA SHAFEEK KADURA, EBTESAM ALAA EL-SHENNAWY, HAMDY M. ALY M.D., Ph.D

## PS24

### **CORONALLY ADVANCED FLAP PROCEDURE FOR MULTIPLE RECESSIONS WITH MINIMAL SURGICAL INCISIONS**

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AIM

Cover the root exposed surfaces of the teeth 22,23,24 with advanced coronally advanced flap.

#### **INTRODUCTION**

The lining mucosa is elastic, a mucosal flap raised beyond the mucogingival junction, can be stretched in coronal direction to cover exposed root surfaces of the teeth 22,23,24.

#### **METHODS**

The coronally advanced flap procedure is initiated with a beveled intrasulcular incision along the edge of the recession defect. The papilla areas are de-epitalized to allow anchorage of the flap coronal to the CEJ. First the flap is with split-thickness mesial and distal to the recession, connected with intracrevicular incision. Apical to the receded soft tissue margin on the facial aspect of the tooth, a full thickness of the tissue flap to be used for root coverage. Apical of the mucogingival line, the elevation is continued as full-thickness until it is possible to passively move the mucosal graft laterally to the recipient site.

#### **RESULTS**

We succeed to cover the exposure vestibular root surface of the teeth 22,23,24 without disturbing the gingival esthetic.

#### **CONCLUSION**

With this technique we received full root coverage, with coronally advanced flap! The esthetic increased and the sensitivity of the root decreased. This procedure can be used for root coverage of a single tooth, as well as multiple teeth.

## PS47

**METABOLIC CHANGES AFTER SIMULTANEOUS PANCREAS- KIDNEY TRANSPLANTATION**

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AIM

In our study we compared the metabolic (carbohydrate and lipid metabolism) parameters in patients after simultaneous pancreas-kidney transplantation with those of patients who underwent kidney alone transplantation and with those of a healthy control group.

**INTRODUCTION**

Simultaneous pancreas-kidney transplantation started at the Department of Transplantation and Surgery, Semmelweis University, Budapest, Hungary eight years ago. Conforming to the principles of transplantation in Hungary only patients suffering from type 1 diabetes with end stage kidney failure could undergo this intervention.

**METHODS**

We have studied the data of 18 patients who have had Simultaneous Pancreas-Kidney transplantation. The transplantation took place 10 to 89 months before our study started. We have studied the patients' metabolic (carbohydrate and lipid metabolism) parameters (HbA1c; baseline blood sugar; insulin; C-peptide; total and LDL-cholesterol; triglycerides levels) retrospectively at zero time and after the patients were given a standard glucose dose (75g OGTT). We used the Kruskal-Wallis and the Dunn post hoc test to compare the results.

**RESULTS**

The average HbA1c value (median; lower-higher quartile) in SPK patients was 5,55 (5,30 - 6,00) %, a value in the normal range, which is significantly lower than that of the patients in the „Kidney Alone transplantation” group (7,60 (6,95 - 8,00)%). Checking SPK patients' baseline blood sugar [5,15 (4.55 - 5.83) mmol/l], their insulin level [13,90 (8,23-19,41) uE/ml] and C-peptid level ( $2.36 \pm 1.12$  pg/ml) we found that all these values stayed in the normal range. Two hours after these patients were given a standard glucose dose their blood sugar level was 5,20 (4,15-6,23)mmol/l while their insulin level was 32,96 (23,46-55,04)uE/ml. Total and LDL-cholesterol levels were slightly elevated:  $5.42 \pm 1.16$  and  $2.76 \pm 0.89$  mmol/l respectively, while the triglyceride level was also in the normal range:  $1.23 \pm 0.70$  mmol/l. On the other hand, the baseline blood sugar 7,50 (6,90-7,95)mmol/l was elevated in the “Kidney Alone transplantation” group.

**CONCLUSION**

The results show that 10 to 89 months after SPK transplantation beta cell function is maintained, carbohydrate metabolic parameters stay in the normal range and satisfactory reaction occurs after glucose stimulus. These patients have insulin resistance but the graft can compensate for it. Metabolic parameters with patients who have had „kidney alone transplantation” proved to be worse and were in the pathological range. Based on these results we can state that in type 1 diabetic patients who developed end stage kidney disease a simultaneous kidney and pancreas transplantation should be done because by this they are cured

# YES GUIDE BOOK

from both diabetes and uremia.





## PS124

# **PREDICTING CARDIOTOXICITY: FINDING ECHOCARDIOGRAPHIC PROGNOSTIC MARKERS IN A BREAST CANCER PATIENT POPULATION**

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## AIM

Oncological treatments of breast cancer (BC) patients (pts) make them prone to cardiotoxicity (CTX), with great implications in their therapy and prognosis. We aim to identify echocardiographic (echo) predictors of susceptibility for left ventricular (LV) dysfunction and adverse remodeling, improving the management of these pts.

## INTRODUCTION

The increase in the survival rate of BC pts was accompanied by a rise in CTX, which can compromise the effectiveness of cancer therapy. Thus, early detection of subclinical cardiac damage may allow better interventions.

Clinical examination and serial echo LV ejection fraction (EF) measurements are now used to assess the CTX of chemotherapy (CT). Still, a decline in LVEF represents a relatively late stage of cardiac dysfunction, which is an important limitation. New methodologies for the echo assessment of LV function, as myocardial deformation (strain, strain rate and speckle-tracking) and 3D echocardiography, can be sensitive tools to detect myocardial dysfunction before changes in LVEF are evident, fulfilling this urging need for early detection.

## METHODS

Prospective study of 40 BC pts naive to CT and without structural heart disease. We performed clinical and echo evaluation before and 1, 3 and 6 months after CT administration, including assessment of LVEF by 2D and 3D echocardiography and myocardial deformation by speckle-tracking. Diastolic function was studied by conventional Doppler, tissue velocity imaging and 2D strain using speckle-tracking. Unfavorable LV remodeling was defined as a 10% increase in LV end-systolic volume and a reduction  $\geq 5\%$  was considered a decline in LVEF, when the variability of the measurements was under these cut-offs.

## RESULTS

We included 40 women,  $53 \pm 15$  years. 33% had hypertension, 26% dyslipidaemia, 15% diabetes, 10% obesity and 10% smoking habits. All pts were treated with anthracyclines and cyclophosphamide was used in 95%.

During follow-up, peak E velocity ( $p=0,055$ ) and E/A ratio ( $p=0,060$ ) tended to decrease. We found significant reductions in E' velocity ( $p=0,037$ ), E'/A' ratio ( $p=0,007$ ), early peak diastolic strain rate ( $p=0,014$ ) and an increase in E/E' ratio ( $p=0,035$ ).

Although in normal range, LV systolic parameters showed a significant reduction (LVEF 2D  $p=0,003$ ; LVEF 3D  $p=0,023$ ; LV end-systolic volume  $p=0,019$ ; LV global strain  $p=0,013$ ). 20% of pts (8 pts) exhibited a decline in LVEF and 28% (11 pts) had unfavorable LV remodeling at 6 months of follow-up. End-systolic volume variation from baseline to 6 months inversely related to baseline E' velocity ( $p=0,022$ ), E'/A' ratio ( $p=0,023$ ), early peak diastolic strain rate ( $p=0,006$ ) and directly related to late peak diastolic strain rate ( $p=0,006$ ). Pts with a decline in LVEF during follow-up had significantly lower baseline LVEF, although within normal range ( $p=0,015$ ). They also had lower baseline early peak diastolic strain rate ( $p=0,006$ ).

### CONCLUSION

These results suggest that baseline LVEF and diastolic strain rate may predict adverse remodeling after CT in BC pts.

**PS140****COMPARATIVE EVALUATION OF ZINC OXIDE EUGENOL VERSUS GELATIN SPONGE SOAKED IN PLASMA RICH IN GROWTH FACTOR IN THE TREATMENT OF DRY SOCKET**

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**AIM**

The aim of this study was to report a comparison between the zinc oxide eugenol dressing and plasma rich in growth factor (PRGF) with gelatin sponge in the treatment of dry socket

**INTRODUCTION**

Management of dry socket is of great concern for all the dental clinicians due to severe pain along with frequent visits of patient to the hospital. The incidence is 3-5% in non-surgical extraction and up to 15% in impacted third molar extraction socket. Dry socket generally presents with either totally empty or partly covered with grayish-yellow membrane of necrotic tissue. Plasma rich in growth factor (PRGF) obtained from autologous blood is used to deliver growth factors in high concentrations to the site of bone defect. So, we have used PRGF along with gelatin sponge to promote healing and compared it with the traditional treatment of zinc oxide eugenol dressing.

**METHODS**

This study comprised of 45 patients of dry socket in the span of 1 year. After the inclusion of patient into study they were attributed into any one group out of three, one by one, i.e., 1 st patient goes into group A then 2 nd patient goes into group B and 3 rd patient goes to group C and repeating the same until each group contains 15 patients each. Selection was exclusive of consideration of sex and age.

Patients in group A were treated with plasma rich in growth factor with gelatin sponge placed in the socket. Observation was noted on 1 st, 2 nd, 3 rd, 7 th, and 15 th days postoperatively for pain and healing. Zinc oxide eugenol dressing was done in group B cases after proper cleaning and irrigation of the socket without local anesthesia. Observation was noted on 1 st, 2 nd, 3 rd, 7 th and 15 th days postoperatively for pain and healing.

In group C, i.e., control group, patients were treated only by irrigation with saline without any other manipulation of the socket or any medicament.

**RESULTS**

The total number of patients included in this study was 45, which includes 26 females and 19 males. There were significant differences in treatment outcomes in different groups. It shows pain reduction is more rapid in group B than in groups A and C from day 1 to day 7 but the change is non-significant at day 15 in all the groups. Healing is faster in group A than in group B at day 1, day 2, day 3, day 7, and it was significant; whereas at day 15, change is non-significant in both the groups. Group C lagged behind in complete healing still after 15 days.

## CONCLUSION

The combination of gelatin sponge along with PRGF seems to accelerate socket healing due to the growth factors incorporated in the PRGF and scaffold forming capability of gelatin sponge.

However, a long-term randomized study with bigger sample size and control is required to determine the effectiveness of PRGF along with gelatin sponge. This is a first endeavor of this kind and is expected to stimulate further exploration into the deeper aspects of advantages of PRGF along with gelatin sponge in the healing of dry socket.



## PS168

# COMPARISON OF CHANGES IN LIPID PROFILE AFTER ROUX-EN-Y GASTRIC BYPASS AND LAPAROSCOPIC SLEEVE GASTRECTOMY

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AIM

The purpose of this study is to compare the influence of RYGB (Roux-en-Y Gastric Bypass) and LSG (Laparoscopic Sleeve Gastrectomy) on changes in lipid profile in bariatric patients without hypolipidemic drugs exposure.

## INTRODUCTION

Lipid disorders are an integral part of the obesity. Bariatric surgery beyond reducing obesity has a positive impact on comorbidities including lipid disorders. Nowadays, the most popular bariatric intervention is RYGB. Due to the fact that LSG is simpler type of intervention, is becoming more common.

## METHODS

Data of 91 patients operated between 2008 and 2011 were retrospective analyzed. To research qualified 67 (25 men, 42 women) patients who underwent RYGB and 24 (8 men, 16 women) patients who operated using LSG. Patients were followed up before operation, and in 3th and 6th month after intervention. We measured: triglyceride (TG), total cholesterol (TC), high-density lipoprotein (HDL) and low-density lipoprotein (LDL). The data were analyzed using SAS 9.2 - T TEST, General Linear Model, Fisher's exact test were applied.

## RESULTS

The mean age of patients qualified to LSG was 45,2 ( $\pm 11$ ) while in the group of patients who underwent RYGB it was 40,6 ( $\pm 10$ ) years old. The average BMI before surgery was 45,2 ( $\pm 6$ ) in LSG-group and 49,9 ( $\pm 6$ ) in RYGB-group ( $p < 0,05$ ). Level of LDL decreased from 99,1 ( $\pm 20$ ) mg/dL to 69,5 ( $\pm 9$ ) mg/dL at 6th month after RYGB ( $p < 0,05$ ) while in patients after LSG it remained in stable level. TC decreased from 185 ( $\pm 30$ ) mg/dL to 181,5 ( $\pm 31$ ) mg/dL at 6th month after LSG and decreased from 176,3 ( $\pm 29$ ) mg/dL to 139,1 ( $\pm 20,1$ ) mg/dL at 6th month after RYGB ( $p < 0,05$ ). TG level changes in time ( $p < 0,05$ ). It decreased from 149,7 ( $\pm 60$ ) mg/dL to 104,5 ( $\pm 35$ ) mg/dL at 6th month after LSG and decreased from 161,6 (69) mg/dL to 97 ( $\pm 52$ ) mg/dL at 6th month after RYGB. Level of HDL increased after LSG from 47,9 ( $\pm 12$ ) mg/dL to 48,3 ( $\pm 15$ ) mg/dL and increased from 43,6 ( $\pm 11$ ) mg/dL to 44,3 ( $\pm 13$ ) mg/dL at 6th month after RYGB.

## CONCLUSION

Patients with higher BMI are operated using RYGB. The findings of the study proved that RYGB has more beneficial effect on lipid profile in obese patients without hypolipidemic drugs exposure. Statistically significance improve were observed in LDL, HDL and TG.

## PS174

### PATIENT SATISFACTION WITH ANESTHESIA CARE IN A GENERAL HOSPITAL

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#### AIM

Transcultural adaptation of a patient satisfaction with anesthesia questionnaire and its application in a teaching general hospital in Portugal.

#### INTRODUCTION

Satisfaction is frequently portrayed in the literature as a new indicator of healthcare quality. It correlates with patient behavior and beliefs, namely in what concerns treatment and follow-up adherence. In the case of anesthesiology, satisfaction surveys arose from the necessity of establishing new measures of care. The satisfaction level with health care reflects the quality of a health system in the patient's point of view. "The Heidelberg Peri-anaesthetic Questionnaire" allows an evaluation of dissatisfaction with anesthesia care.

#### METHODS

The questionnaire was translated and tested based on psychometric quality criteria in a sample of 107 patients submitted to elective surgery in Hospital de São João. The global satisfaction and the satisfaction for each dimension of care were calculated. The differences between patients with different levels of satisfaction were analyzed and the influence of potential confounding factors was tested.

#### RESULTS

The Portuguese version of the questionnaire has 32 items distributed in three dimensions of care: "staff", "discomfort" and "fear". The mean values of satisfaction for each dimension were 83.4%; 66.8% e 65.9%, respectively. The internal consistence was demonstrated by an alpha coefficient of 0.70 for the sum score and the alpha coefficient ranged from 0.776 to 0.875 in the three dimensions. In the multivariate analysis, significant influence of gender in the "discomfort" dimension was found. Dissatisfied patients had a median satisfaction (interquartile range [range]) of 61% (55-67% [40,70]) and the satisfied patients a median of 91% (88-95 [85,99]). The two groups are different in the three dimensions, with a minor difference in "staff".

#### CONCLUSION

Dissatisfaction with care mostly reflected on the low score of "discomfort" and "fear" dimensions of care. The domain "staff", which includes the area of care related to the doctor-patient interaction(s), had the higher level of satisfaction

## PS108

**DOES THE LEVEL OF HEMOGLOBIN REACHED AFTER RED BLOOD CELL TRANSFUSION IN PATIENTS WITH ACUTE UPPER GASTROINTESTINAL BLEEDING HAVE AN INFLUENCE ON THE OUTCOMES?**

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**AIM**

The aim of our study was to compare outcomes of patients with upper gastrointestinal bleeding requiring red blood cells transfusion depending on level of hemoglobin reached after transfusion.

**INTRODUCTION**

Many studies investigate the threshold of hemoglobin (Hb) for transfusion of red blood cells (RBC) in patients with acute upper gastrointestinal bleeding (UGIB) and there is a tendency to introduce restrictive transfusion strategy. However, the threshold of hemoglobin which should be reached after transfusion is still controversial. Many patients receive routine amount of RBC units regardless the Hb level before and after transfusion. Proper management of blood products is essential with regard to possible side-effects associated with their administrations and still insufficient amount available, especially during holidays.

**METHODS**

Medical records of 253 patients (66,4% males) admitted to 3rd Department of General Surgery Jagiellonian University Medical College in Cracow, Poland between January 2009 and December 2012 with acute upper gastrointestinal bleeding were obtained retrospectively. Mean age of the patients was  $63,8 \pm 17,5$  (min. 22, max. 101) years. 82% of patients required RBC transfusion during hospitalization. Those patients were divided into 2 groups depending on level of hemoglobin after transfusion: group 1: Hb  $>10$  g/dl and group 2: Hb  $<10$  g/dl.

**RESULTS**

There were no significant differences between the groups regarding age, gender and presence of comorbidities. Patients in group 1 had statistically lower Hb level at admission (mean. 7,66 g/dl) vs. group 2 (mean. 8,84 g/dl,  $p=0,017$ ) but there were no differences between the groups in number of transfused units of RBC and fresh frozen plasma (mean. 4,4 vs. 3,7 and 2,5 vs. 2,1 respectively). Mortality in group 2 was significantly higher 31,25% vs. 8,57% in group 1 ( $p=0,000$ ). Hemoglobin level below 10 g/dl after transfusion was associated with more frequent admission to Intensive Care Unit (30,21% vs. 14,15%  $p=0,006$ ) and presence of complications during hospitalization (38,54% vs. 20,19%  $p=0,004$ ) as well.

**CONCLUSION**

The outcomes were significantly better in the group of patients who reached  $>10$  g/dl Hb after RBC transfusion. It suggests that patients should not be transfused with routine number of RBC units and the decision whether patient requires further transfusions should be made based on results of control complete

blood count. We suggest that  $Hb > 10$  g/dl is a safe threshold to withhold RBC transfusions in patients with acute upper gastrointestinal bleeding.





## PS183

**INFLUENCE OF ANTIPLATELET THERAPY ON THE STAGE OF COLORECTAL CANCER AT THE MOMENT OF DIAGNOSIS ——— BLESSING IN DISGUISE?**

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**AIM**

The aim of our study was to evaluate whether antiplatelet treatment, a popular medication among elderly patients with concomitant coronary or peripheral arterial disease, has an influence on an earlier stage diagnosis of colorectal cancer (CRC).

**INTRODUCTION**

Antiplatelet drugs have an established place in the prevention of vascular events in a variety of clinical conditions, such as myocardial infarction, stroke and cardiovascular death. In high-risk patients, such as those with post-acute myocardial infarction, ischemic stroke or transient ischaemic attack, peripheral arterial occlusive disease or atrial fibrillation, antiplatelet treatment may significantly reduce the risk of a serious fatal cardiovascular event. However, one common side effect of this drug category is the susceptibility to bleeding. On the other hand, lower gastrointestinal bleeding, either chronic or acute, may be the presenting symptom of CRC that usually dictates the endoscopic work-up.

**METHODS**

Medical records of 137 patients (62% male) with colorectal cancer in average age of 68,4+/-11 (38-96) years old with colorectal cancer admitted to 3rd Department of General Surgery in Cracow in 2006 and 2007 were obtained. The main inclusion criteria was the possibility to obtain results of histopathological examination and medications taken at the moment of admission. Statistical analysis included demographic data, type of admission, medications taken and histopathological results. 81 patients met the criteria and were subsequently divided into 2 groups: treated with antiplatelet drugs (17%) and not treated with platelet drugs (83%).

**RESULTS**

The group with antiplatelet therapy was significantly older than the other one (median age 75,5 vs. 70;  $p=0.029$ ). There were no differences regarding gender, histological type and grading between the groups. The staging of CRC was significantly lower in the group on antiplatelet therapy compared to the group without such therapy: I stage - 35,7% vs. 9%, II ——— 14,3% vs. 29,9%, III ——— 52,2% vs. 35,7%, IV ——— 9% vs. 14,3 ( $p=0,04$ ), respectively. Patients receiving antiplatelet drugs had more frequently suffered from cardiac comorbidities ——— 94,4% vs. 57,1% ( $p=0,003$ ) and were more often admitted in the emergency setting - 66,7% vs. 35,7% ( $p=0,01$ ). There were no differences between the groups regarding presence of the symptoms such as bleeding, anemia, pain or changes in bowel habits.

**CONCLUSION**

Antiplatelet drugs may lead to an earlier stage diagnosis of CRC, which is crucial in the course of treatment as it is highly treatable in its early stage. Patients on the antiplatelet therapy presumably start to bleed from the tumor earlier than those without such therapy. The adverse effect of bleeding that is justifiably attached to this drug category seems to have a favorable impact on the staging characteristics of an existent CRC.

## PS122

**NEOADJUVANT THERAPY AND LIVER TRANSPLANTATION FOR HILAR CHOLANGIOCARCINOMA: IS PRETREATMENT PATHOLOGICAL CONFIRMATION OF DIAGNOSIS NECESSARY?**

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**AIM**

Aimed to determine the need for pathological confirmation of cholangiocarcinoma before treatment with primary sclerosing cholangitis and those with de novo cholangiocarcinoma

**INTRODUCTION**

Hilar cholangiocarcinoma is a devastating disease, which may arise in the setting of chronic liver disease such as primary sclerosing cholangitis. In this study, we aimed to determine the need for pathological confirmation of cholangiocarcinoma before treatment with primary sclerosing cholangitis and those with de novo cholangiocarcinoma.

**METHODS**

215 patients with cholangiocarcinoma began neoadjuvant therapy in anticipation of liver transplantation. The survival rates of patients who had pretreatment pathological confirmation are compared with who had not, and calculated by Kaplan-Meier method.

**RESULTS**

Two hundred and fifteen patients received neoadjuvant therapy between 1992 and 2011. One hundred and eighty-two patients underwent operative staging and 38 (21%) had findings that precluded transplantation. Pathological confirmation of CCA before therapy was achieved in 45 of 87 (52%) PSC patients and 22 of 49 (45%) de novo patients who underwent transplantation. Pretreatment pathological confirmation was associated with significantly worse 5-year survival after start of therapy for PSC patients (50% vs 80%;  $p = 0.001$ ), but not for de novo patients (39% vs 48%;  $p = 0.27$ ). Pretreatment pathological confirmation was associated with worse 5-year survival after transplantation for PSC patients (66% vs 92%;  $p = 0.01$ ), but not for de novo patients (63% vs 65%;  $p = 0.71$ ).

**CONCLUSION**

Rates of residual CCA in liver explants and recurrences after transplantation are comparable for patients with and without pretreatment pathological confirmation of CCA and attest to the accuracy of clinical diagnostic criteria. Pretreatment pathological confirmation of CCA is desirable but should not be a requirement for treatment.

## PS128

### POSTOPERATIVE STROKE IS LESS FREQUENT AFTER OFF-PUMP CABG COMPARED TO ON-PUMP SURGERY

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AIM

The aim of the study was to compare the two methods of CABG surgery and analyze short time postoperative results of off-pump and on-pump CABG one in order to decide which method is friendlier for convalescence.

#### INTRODUCTION

Coronary artery bypass grafting is a procedure which improve hear functions by diverting the flow of blood around a section of a blocked artery. The two techniques are available to perform this surgery – on-pump and off-pump. First one is connected with using extracorporeal circulation, whereas the second is performed on beating heart. Both of them are associated with different type of postoperative complications.

#### METHODS

The retrospective study was based on clinical results of 131 patients who underwent CABG surgery. There were two group: the first group (A) consisted of 76 people after off – pump procedure, whereas the second one included 55 patients after on-pump surgery. Data concerning surgery, clinical results and hospitalization were gathered from medical records. Statistical analysis were performed using STATISTICA package for Windows version 10 (StatSoft Polska, Kraków) and the level of significance was set at  $p < 0.05$ .

#### RESULTS

There was no statistically important difference in demographic features between A and B. Statistical significances between A vs B were proved in relation to: postoperative troponin I mean value –  $2.15 \pm 2.49$  in A vs  $3.90 \pm 4.21$  in B ( $p = 0.01$ ), transfusion of packed red blood cells (PRBCs) units average amount –  $2.53 \pm 1.59$  in A vs  $3.35 \pm 1.87$  in B ( $p = 0.00$ ). There were no differences between two groups in mean value of postoperative hemoglobin and total hospitalization time. Furthermore stroke (or neurologic deficit) and post-operative LOS were also less frequent in OPCAB patients.

#### CONCLUSION

Off pump surgery is less harmful for myocardium in comparison to on-pump one. Procedures without CPB could be considered not only in higher risk patients for post-operative neurologic dysfunction or organ failure but also for lower risk patients in similar age. In the first group less PRBCs units are administrated what reduce immunization effects and other complications. The time of hospitalization after both methods of CABG surgery is similar which means that reduced perioperative myocardial damage after OPCAB had no final influence on total hospitalization length



## PS29

**THE MORPHOLOGICAL CHANGES IN THE RABBIT CORNEA IN EXPERIMENTAL CORNEAL WOUND HEALING, WITH MONITORING OF THE CORNEAL ELECTROLYTE CONTENTS WITH AN ENERGY DISPERSIVE X-RAY ANALYZER (EDAX).**

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AIM

1- To investigate the structure and organization of corneal epithelium during the healing process of rabbit corneal wounds, with monitoring of the corneal electrolyte contents with (EDAX). 2- To screen corneal cellular changes for apoptosis and proliferation during healing process.

### INTRODUCTION

Ulcers and erosions of the corneal epithelium, as well as delays in resurfacing of the cornea after wounding, are major causes of ocular morbidity and visual loss. Chemical burns of eye presents a major therapeutic challenge to the ophthalmologist. Corneal alkali burns represent between 7% and 10% of eye injuries corneal.

### METHODS

30 New Zealand rabbits weighing 2.5 kg were used in these studies. An alkali wound of the cornea was performed in the right eye of with round filter paper, 5.5 mm in diameter, which were soaked in 0.5 mol/L NaOH for 5 seconds and then were placed centrally on the cornea for 60 seconds. The left eyes will serve as controls. The corneas (normal ulcerated and healed (epithelialized) were harvested at various time points ( 0 ,day one , 3 days, 7 days, 14 days of corneal injury and processed for examination with light and scanning electron microscopy. with monitoring of the corneal electrolyte contents with (EDAX).

### RESULTS

Inflammatory response with massive inflammatory cell infiltrates mainly leukocytes. Moreover, progressive increase in basal corneal epithelial cell proliferative activity both in limbal region and leading corneal ulcer edge, stromal keratocytes and endothelial capillaries cells was observed. Labeling for apoptosis was found only on the epithelial surface of normal cornea and not in deeper layers. After alkali injury few positive deeper epithelial cell were seen .In addition, stromal cells apoptosis was present in all the alkali-burned corneas. Observable alterations of mineral concentrations in the rabbit cornea after alkali injury burns.

### CONCLUSION

Basal corneal epithelial cell proliferative activity starts earlier after 24hour of alkali injury, and was headed by massive leukocytes infiltrate in the stroma and within epithelial cells. PCNA was expressed in the vascular endothelium .In present investigations; we found alterations of mineral concentrations in the rabbit cornea both in epithelial and collagen contents after alkali injury burns. Molybdenum is an essential trace element was found to increase during the healing process of corneal wound injury.