magnus Group

2nd International Conference on

# ONCOLOGY AND RADIOLOGY

SEPTEMBER 17-19, 2018
ROME, ITALY

ICOR 2018 https://icorad.com/

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## VENUE

HOLIDAY INN ROME AURELIA
VIA AURELIA, KM 8.400, 00165
ROME, ITALY

*Theme: Cancer Free World - Possible or Not*

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ICOR 2018

BOOK OF ABSTRACTS

2nd International Conference on

# Oncology and Radiology

*Theme:*

*Cancer Free World - Possible or Not*

September 17-19, 2018

Rome, Italy

# INDEX

***Annika Lindstrom***
CKF Dalarna, Uppsala University, Sweden

***Bahadir Batar***
Namik Kemal University Medical School, Turkey

***Cagri Oner***
Maltepe University
Turkey

***Chae Ri Park***
Asan Medical Center (AMC)
Korea, Republic of

***Chiu Sai Yiu Richard***
Hong Kong Baptist Hospital
Hong Kong

***Elizabeth Franzmann***
Vigilant Biosciences
USA

***Erwin Danil Yulian***
University of Indonesia
Indonesia

***Eva Wegner***
Prince of Wales Hospital
Australia

***Francesco Giovinazzo***
University Hospital of Southampton NHS Foundation Trust
UK

***Francesco Izzo***
National Cancer Institute of Naples
Italy

***Giulia Zumbo***
Southampton General Hospital
UK

***Ivana Jovcevska***
University of Ljubljana
Slovenia

***Jalil Ur Rehman***
Baluchistan University of Information Technology Engineering , Managements and Science
Pakistan

***Jerome Paillassa***
Centre Hospitalier Universitaire d'Angers
France

***Joo Hee Yoon***
The Catholic University of Korea
Korea, Republic of

***Jose Carlos dos Santos***
Universitatsklinikum Heidelberg
Germany

***Jozef Sabol***
Department of Crisia Management, PACR
Czech Republic

***Lucio Miele***
Louisiana State University Health Sciences Center
USA

***Marina De Rosa***
University of Naples Federico II
Italy

***Mark S. Parker***
VCU Medical Center
USA

***Martina Seifrtova***
Charles University
Czech Republic

***Maryla Stelmach***
Epworth Hospital
Australia

***Myron R. Szewczuk***
Queen's University
Canada

***Neeraj Jain***
Sri Guru Ram Das University of Health Sciences
India

***Ocung Guido***
Makerere University
Uganda

***Rossana Berardi***
Universita Politecnica delle Marche
Italy

***Surajit Pathak***
Chettinad Academy of Research and Education
India

***Tamara Lah Turnsek***
National Institute of Biology
Slovenia

***Victoria Seewaldt***
City of Hope Comprehensive Cancer Center
USA

***Wanda Stelmach***
Northern Health
Australia

***Wassil Nowicky***
Ukrainian Anti-Cancer Institute
Austria

***Yajue Huang***
Mayo Clinic
United States

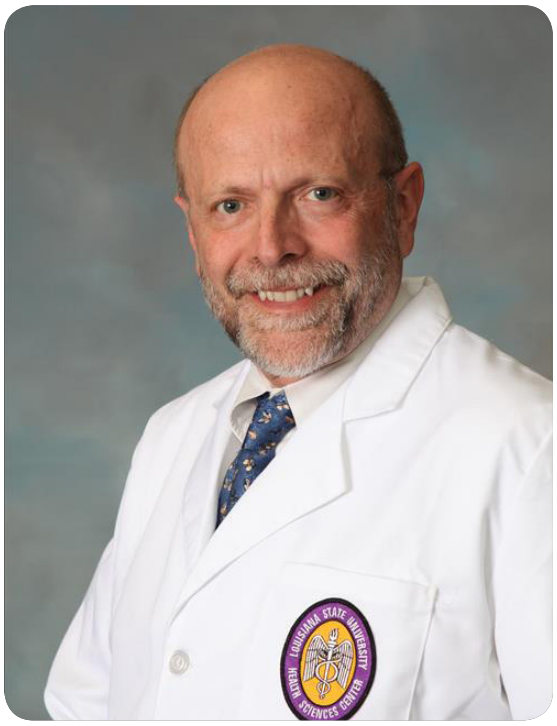
***Yaoru Huang***
Taipei Medical University Hospital
Taiwan

***Youn Kyoung Jeong***
Korea Institute of Radiological & Medical Sciences
Korea, Republic of

***Joshua D. Palmer***
Ohio State University Wexner Medical Center
United States

*Thank You All...*

# Welcome Message



On behalf of the Scientific Committee and the Magnus Group, we cordially invite you to attend the Second International Conference on Oncology and Radiology (ICOR), to be held between September 17 and 19, 2018 at the Holiday Inn Rome Aurelia, Rome, Italy.

Medical and radiation oncology are undergoing rapid changes, powered by scientific advances in fields like genomics, metabolomics, molecular diagnostics, imaging, nanotechnology, immunotherapy and virotherapy. As a result, oncology research and clinical practice have become team-based, multidisciplinary endeavors.

ICOR 2018 will offer a unique opportunity for academic and industry investigators and clinicians to share innovative research ideas, build new collaborative relationships and learn about ongoing research by leading groups from Europe, North America and Asia. The conference setting is ideal to facilitate informal interactions and promote interdisciplinary collaboration.

We look forward to seeing you in Rome!

**Lucio Miele, MD, PhD**
Cancer Crusaders Endowed Professor and
Chair, Department of Genetics,
Louisiana State University Health Sciences Center, New Orleans, USA

# Welcome Message

I am truly honored and delighted to take this opportunity to welcome delegates from all around the world to ICOR 2018.

It will be a great conference for sharing the latest insights of academic and industrial research as well as to experience the unique environment of Rome, a city which has been at the heart of the artistic, cultural, and scientific development since many centuries.
We have an exciting program at this conference that will allow members to make and renew friendships and extend networks, and jointly explore current and future research directions.
We hope that you will have a productive and fun-filled time at this very special conference.

We thank you for your participation and look forward to seeing you in Rome, the capital of my Country Italy!

Sincerely,

**Rossana Berardi**
Professor of Medical Oncology
Director of Medical Oncology
Università Politecnica delle Marche
Ancona - Italy

# Welcome Message

I'd like personally to welcome each of you to 2nd International Conference on Oncology and Radiology during September 17-19, 2018 in Rome, Italy.

ICOR 2018 will provide a wonderful forum for you to refresh your knowledge base and ex-plore the innovations in Cancer Nanotechnology, Radiation Oncology, Sample Quality Mat-ters for Clinical Research, MicroRNA and Cancer, Cancer Biology, Cancer Screening & Di-agnosis, Advances In Cancer Research And Treatment, Managing Cancer Care & Patient Support, SNP And Cancer, Cancer Epidemiology, Oncolytic Virus And Cancer, Cancer Causes & Risk Factors, Organ Specific Cancer ,Cancer Pathology And Genetics, Nutrition And Metabolism, Surgical And Clinical Oncology, Clinical and Medical Case Reports, etc.

The Conference will strive to offer plenty of networking opportunities, providing you with the opportunity to meet and interact with the leading scientists and researchers, speakers, to help enhance professional skills and meet personal educational goal as well as friends and colleagues, different sponsors and exhibitors.

I'd like to thank each of you for attending our conference and bringing your expertise to our gathering. You all, as Conference Speakers, have the vision, the knowledge, the wherewithal and the experience to help us pave our way into the future. You are truly our greatest asset today and tomorrow, and we could not accomplish what we do without your support and encouragement. My personal respect and thanks go out to all of you.

We thank you for your participation and look forward to seeing you in Rome, Italy

**Dr. Wassil Nowicky**
Ukrainian Anti-Cancer Institute, Vienna, Austria

# Welcome Message

Dear Participants!

On behalf of the Organizing Committee I am welcoming you on the 2nd International Conference on Oncology and Radiology in Rome!

The Conference is designed to facilitate the sharing of knowledge and experience of researchers, young scientists, academicians, and on the other hand oncologists and participants from the business sector.

Since the introduction of radiology into oncology, immense achievements have been made in terms of improved irradiation technologies, focusing on of tumour cells on one hand and on the other on applications of adjuvant therapies, concomitantly targeting tumour microenvironment.

Our slogan “Cancer Free World - Possible or Not ” will stimulate “out of the box” thinking on problems, caused by global environmental pollution, resulting among others in higher incidence of cancer that in spite of decreased mortality ins some cancers, still gives rise to increased cancer incidence.

Nowadays, we know that conquering cancer in not only the task of scientist and dedicated surgeons, radiologists and oncologists, but needs to be supported by substantial funding that cannot be provided by public sector alone, so we thank the sponsors for their continuous support.

**Tamara Lah Turnšek**
Scientific Councilor ar National Institute of Biology
Professor Faculty of Chemistry and Chemical Engineering University of Ljubljana
Ljubljana, Slovenia

# keynote speakers

***Lucio Miele***
Louisiana State University
Health Sciences Center
USA

***Rossana Berardi***
Universita Politecnica
delle Marche
Italy

***Wassil Nowicky***
Ukrainian Anti-Cancer
Institute, Austria

***Tamara Lah Turnsek***
National Institute of Biology
Slovenia

***Elizabeth Franzmann***
Vigilant Biosciences
USA

***Jozef Sabol***
Department of Crisia
Management, PACR, Czech
Republic

# *About* MAGNUS GROUP

Magnus Group (MG) is initiated to meet a need and to pursue collective goals of the scientific community specifically focusing in the field of Sciences, Engineering and technology to endorse exchanging of the ideas & knowledge which facilitate the collaboration between the scientists, academicians and researchers of same field or interdisciplinary research. Magnus group is proficient in organizing conferences, meetings, seminars and workshops with the ingenious and peerless speakers throughout the world providing you and your organization with broad range of networking opportunities to globalize your research and create your own identity. Our conference and workshops can be well titled as 'ocean of knowledge' where you can sail your boat and pick the pearls, leading the way for innovative research and strategies empowering the strength by overwhelming the complications associated with in the respective fields.

Participation from 80 different countries and 688 different Universities have contributed to the success of our conferences. Our first International Conference was organized on Oncology and Radiology (ICOR) in Dubai, UAE. Our conferences usually run for 2-3 days completely covering Keynote & Oral sessions along with workshops and poster presentations. Our organization runs promptly with dedicated and proficient employees' managing different conferences throughout the world, without compromising service and quality.

# *About* ICOR 2018

ICOR 2018, planned to achieve the knowledge transfer of highly updated and relevant information to a broad audience in oncology radiology and related specialists in the field. It can be achieved by scheduled scientific sessions, keynote presentations by renowned scientists, and poster sessions at this radiation oncology conference, which promises to deliver something for everyone involved in cancer research or practice.

Oncology and Radiology conference explores the entire scope of cancer with earlier and contemporary work and provides a critical review of the present state of the subject. Our expert honorary speakers will provide you with the most clinically up-to-date relevant information, you'll leave better educated and more invigorated than you thought possible.

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DAY 1

KEYNOTE FORUM

2nd International Conference on

# Oncology and Radiology

SEPTEMBER 17-19, 2018
ROME, ITALY

## Biography

Dr. Miele is the Cancer Crusaders Professor of Cancer Research and Chair of the Department of Genetics, School of Medicine, at the Louisiana State University Health Sciences Center, New Orleans, Louisiana. Among other leadership roles, he is the LSUHSC site Principal Investigator for the NIH's "All of Us" Precision Medicine Initiative. Dr. Miele has authored over 220 peer-reviewed publications in biomedical journals to date. He regularly chairs scientific grant review panels for NIH, NCI, NCATS, the DOD and research funding agencies from European and Asian countries. He serves as Editor or Associate Editor of several biomedical journals, and has consulted for pharmaceutical and biotechnology companies regarding oncology drug development.

# Precision medicine in cancer treatment and prevention

## Lucio Miele, M.D., Ph.D.

Louisiana State University Health Sciences Center, USA

Recent advances in our understanding of cancer biology and genetics have led to the development of numerous genomic tests exploring somatic and germline mutational profiles as well as gene expression signatures for clinical use. Somatic mutation panels and gene expression signatures are potentially useful to guide cancer treatment, to estimate the risk of recurrence of individual cancers and to screen patients for eligibility to "basket" and "umbrella" oncology clinical trials. Germline tests are increasingly useful to quantify individual risk of malignancy, particularly in patients with informative family histories. Recent success stories have highlighted the power of genomics to inform clinical decisions. The first FDA approval of an anti-neoplastic agent (pembrolizumab) based exclusively on the genomic profile of tumors rather than on tumor site or histology was a landmark in oncology, and very likely the first of many such approvals. The results of large clinical trials like GeparSixto, MINDACT and TAILORx have demonstrated that gene expression signatures can successfully predict the likelihood of complete pathological remission (cPR) in triple-negative and Her2-enriched breast cancers and identify patients who do not require chemotherapy. Virtually every malignancy is now classified into molecular rather than merely histological subtypes, and these subtypes often have strikingly different outcomes. "Liquid biopsies" hold the promise of highly sensitive detection of recurrence and mutational profiling of emerging cancer clones.

That said, the field of cancer precision medicine is still in its infancy, and significant challenges remain. Most of the data on which outcome predictions are based derives from European or European-American patients, and is not validated in populations of diverse ancestry. Our own research has shown significant differences in gene expression profiles of breast cancers based on ancestry. For somatic mutation panels, tumor heterogeneity remains a potential confounder. Clonal evolution under therapy-induced selection leads to the emergence of clones with novel driver mutations. Hence, a mutational profile obtained from a surgical specimen in an untreated patient may or may not reflect the molecular portrait of the tumor after multiple cycles of chemo- radio- or targeted therapy. One might argue that longitudinal molecular follow-up of cancers coupled with adaptive treatment strategies will become necessary to obtain the most useful information for patient management. Additionally, novel variants in genes of potential biological importance pose an interpretation challenge. Bioinformatics research is improving tools to predict the biological impact of newly identified mutations in coding as well as non-coding regions of the genome, but these are not yet used in the clinic. That means that variants that may affect tumor response but are not well characterized and included in large databases (e.g., COSMIC) are often classified as "Variants of Unknown Significance" (VUS). The sensitivity of liquid biopsies is influenced by tumor location, tumor burden, background, non-pathogenic mutations in leukocytes and depth of sequencing. Finally, the speed of data interpretation and reporting must be increased if clinical decisions are to be made "in real time" in response to molecular tests.

From the standpoint of germline genetic risk, outside the well-known group of genes with high penetrance and large effects on risk (e.g., BRCA1/2, PTEN, TP53, PALB2 etc.), the main challenge is the large number and cooperativity of genes with relatively small effects on cancer risk. Individually, many of the genes recently identified have small effects on relative risk. However, these effects may be clinically meaningful when integrated with other information, such as clinicopathological, lifestyle, environmental and socioeconomic factors. "Big data" analytics on large, multidimensional datasets such as the ones expected from the American Cancer Society's Cancer Prevention 3 or the National Institute of Health's "All of Us" Precision Medicine initiative will undoubtedly produce breakthroughs in the next few years.

In summary, the future of cancer precision medicine and prevention is bright, but the field will require considerable additional clinical, molecular and epidemiological research to reach its full potential to improve our management of cancer at the individual and population levels.

**Audience Take Away:**

- Clinicians in the audience will be offered an up-to-date picture of the state of the art in cancer precision medicine, which will inform their use of precision medicine in their practices.
- Researchers in the audience will be informed on the most pressing knowledge gaps that must be addressed through clinical and translational research.
- Teachers in the audience will be offered a conceptual framework for teaching medical and life science trainees (students, residents, fellows), informing their trainees on the present and future of precision oncology.
- Public health investigators in the audience will be presented with a multi-disciplinary picture of how cutting edge molecular genetics can and should be integrated with population level data to improve our understanding of cancer risk factors.

## Biography

Dr. Elizabeth Franzmann, M.D. is certified by the American Board of Otolaryngology specializing in otolaryngology and head and neck surgery as an Associate Professor of Otolaryngology at the University of Miami Miller School of Medicine. Dr. Franzmann serves as the Scientific Founder and Chief Scientific Officer of Vigilant Biosciences. Her innovative clinical research on selective salivary biomarkers for head and neck squamous cell carcinoma serves as the foundation for Vigilant Biosciences' product line.

Dr. Franzmann's work has been funded by foundations as well as state and federal agencies with the resulting research published in numerous, well-respected, and peer-reviewed journals. Dr. Franzmann has been recognized as one of the "Best Doctors in America," an honor that reflects fellow physicians considering her to be one of the most skilled in her field and most qualified for reviewing complex medical conditions. Dr. Franzmann received her Bachelor of Science and Doctorate of Medicine at the University of California, Los Angeles.

# Performance of an optimized oral rinse point-of-care assay to aid in the diagnosis of oral cancer

## Elizabeth Franzmann, M.D.

Vigilant Biosciences, USA

Head and neck squamous cell carcinoma (HNSCC) is the 6th most common cause of cancer mortality. The ability to detect HNSCC an earlier stage could have significant impact on overall outcome. Previous studies demonstrated that a point-of-care (POC) lateral flow assay and an ELISA LAB test measuring CD44 and total protein (TP) aid in the diagnostic process for HNSCC. We sought to better understand the performance of the POC assay in a case control study.

**Audience Take Away:**

- Current screening for oral and oropharyngeal cancer is insufficient. With the worldwide 5-year survival rate of only 50% due to delayed intervention and with more than half of diagnoses at stage III and stage IV, there is a need for improved screening. Early diagnosis can double the chance of survival and save healthcare systems billions through earlier intervention. Earlier detection at stage I and II yields survival rates up to 80%-90%. There is an accurate, non-invasive and cost-effective solution for patients, ENTs, H&N surgeons, oncologists, oral pathologists, primary care physicians, dentists, nurses and hygienists to aid in the early detection even before lesions become visible.

## Biography

Rossana Berardi, MD, Director of Department of Medical Oncology, Director of the Postgraduate School of Oncology, Head of "Genetic Cancer" Laboratory, Deputy Director of Department of Clinical and Molecular Science and coordinator of the Hospital Breast Unit at Università Politecnica of Marche Region – Ospedali Riuniti of Ancona, Italy. She is author of more than 200 manuscripts in peer-reviewed journals and of more than 100 abstracts, speaker at national and international meetings and involved in advisory boards expecially chest tumours, neuroendocrine tumours, SIADH and on clinical and translational research.

# Immunotherapy in lung cancer patients: Benefits and costs

**Berardi R, M.D.**

Università Politecnica delle Marche, Ospedali Riuniti di Ancona, Ancona, Italy.

Lung cancer is the leading cause of tumour-related death, in both sexes. Non-small cell lung cancer (NSCLC) represents the most frequent histological subtype including adenocarcinoma and squamous cell carcinoma.

In the past decades, despite the development of new treatment options, five- and ten-years survival rates showed just little improvement and prognosis remained poor.

Platinum-based chemotherapy represented the standard I line treatment for advanced disease, when histological testing showed no targetable genomic aberrations such as epidermal growth factor receptor (EGFR) mutations, anaplastic lymphoma kinase (ALK) or ROS1 translocation or rearrangements and taxane-based chemotherapy was the best treatment options in second line, archiving a median overall survival (OS) of few months.

The advent of immunotherapy has eventually changed outcomes of patients affected by NSCLC providing new and promising weapons.

In particular, several agents modulating PD-1/PDL-1 pathway, demonstrated significant efficacy in prolonging NSCLC patients' survival.

Nivolumab, a PD-1 inhibitor, demonstrated to reduce by 40% the risk of death in NSCLC patients selected by histology, (Checkmate 017, for squamous carcinoma and Checkmate 057 for non-squamous carcinoma) in second line treatment, independently of PD-L1 expression.

Pembrolizumab in monotherapy, another PD-1 inhibitor, reached survival improvement in NSCLC patients with positive PD-L1 expression, independently of histotype, both in first line for strong positive patients (Keynote 024) and in second line (Keynote 010). Recently Keynote-189 study, underlined a reduction of risk of death by 41% in non-squamous NSCLC patients treated with pembrolizumab in combination to platinum-based chemotherapy, independently of PD-L1 expression.

Two PD-L1 inhibitor have also been recently approved: atezolizumab in second line treatment independently of histotype and PD-L1 expression (OAK trial) and durvalumab for patients with stage III NSCLC whose disease did not progress after concomitant chemo-radiation therapy (PACIFIC trial), reaching a 18-month progression-free survival rate of 44.2% versus 27.0%

On one hand, the outbreak of immunotherapy in NSCLC has revolutionized treatment and outcomes of NSCLC patients, encouraging research to proceed. On the other hand this new therapeutic frontier brought along a full baggage of unresolved questions.

Despite the extraordinary efficacy of immunotherapy, only a fraction of patients actually benefits of such treatments and predictive factors to aid clinicians' decision-making are still lacking. Identifying the right patient is becoming more and more important as new drugs are approved and combined treatments are under investigation. To achieve a true personalized medicine, focus has been pointed on molecular biomarkers that can predict a response to immune checkpoints.

Moreover, immunotherapy functions through the regulation of immune system, causing a new landscape of adverse events. Immune-mediated adverse events include a range of dermatologic, pulmonary, gastrointestinal, endocrine, and hepatic toxicity. Multidisciplinary approach is extremely useful to face this new challenge in order to hasten diagnosis and prevent high-grade toxicity.

The efficacy of innovative treatments is noteworthy, but their price is highly expensive. The continuous rise of cancer care costs (with the important contribute of immunotherapy in NSCLC) is becoming a real issue and it is to wonder until when health care systems will be able to afford it.

**Audience Take Away:**

- The presentation aims to deliver clear and updated information about immunotherapy in NSCLC underlining its outstanding efficacy and illustrating the new challenges brought by this new modality of treatment. A special focus will be given on costs and on sustainability issues.
- The immunotherapeutic landscape in NSCLC treatment will be presented to the audience in order to provide useful information needed to face NSCLC patients care. The new challenges that entered oncologic fields along with immunotherapy will be also discussed.
- The importance of a personalized medicine in NSCLC will be explained and the need of predictive biomarkers will be highlighted, delivering to the audience new and innovative research topics.
- The immune-related toxicity and strategies to treat it will be also discussed.
- The raising costs of cancer care, especially when involving immunotherapy will be presented to the audience in order to design hypothetical approaches to face them.
- Patient selection for immunotherapy in lung cancer still remains a hot topic. Benefits, potential biomarkers and treatment costs also in terms of toxicity will be discussed and the presentation will provide practical solutions to these problems.

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# DAY 1

## SPEAKERS

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# Lung cancer screening: Simplifying the shared decision making process

**Mark S. Parker, M.D., F.A.C.R.**
Professor, Diagnostic Radiology and Internal Medicine
Director, Thoracic Imaging Division
Director, Lung Cancer Screening Program
VCU Medical Center, Richmond, Virginia, USA

Lung cancer is the leading cause of cancer death among both men and women, not only in the U.S., but worldwide. For decades, lung cancer was the sole cancer among the top four deadliest cancers without an evidence-based screening method for decreasing mortality. This changed November 2011, when the National Lung Screening Trial (NLST) results showed annual low-dose CT screening was more efficacious in reducing deaths in high-risk persons than radiography. An ever-increasing number of societies and organizations now endorse LDCT for the early detection of lung cancer. More recently, the United States Preventive Services Task Force (USPSTF) and Centers for Medicare and Medicaid Services (CMS) endorsed LDCT screening in eligible persons. Most third party payers have adopted this same stance. Under CMS guidelines, healthcare providers must counsel and document mutual participation between themselves and prospective screenees in a shared decision-making (SDM) visit prior to ordering a screen. During the visit, providers must assess screenee eligibility, document current and or past cigarette use, and discuss benefits and potential harms of LDCT screening including: false positive and over-diagnosis rates and radiation dose exposure. This information must be documented in the screenee's medical record.

Due to the rapid evolution of lung screening CT, many providers and radiologists alike are uncertain of the current eligibility criteria. Likewise, many are not comfortably equipped to discuss the benefits and potential harms associated with screening, which often translates into inconsistent or inaccurate conveyance of critical information. We present our simplified approach to discussing the key elements of SDM with potential screenees as used in our patient-centric lung-screening clinic. A model we hope other centers may find useful and adopt.

## Biography

Mark S. Parker, M.D is a Professor of Radiology and Internal Medicine, Thoracic Imaging Director, and Director of the Lung Cancer Screening Program at VCU Health, Richmond, Virginia. He received his medical school and diagnostic radiology training at Eastern Virginia Medical School and thoracic disease fellowship training at Vanderbilt University Medical Center. Dr. Parker became Thoracic Imaging Director at VCU Health in 2009. In 2015, he was inducted as a Fellow in the American College of Radiology (ACR). He served as an American Board of Radiology (ABR) examiner and as Technical Expert and Key Informant for the Agency for Healthcare Research and Quality (AHRQ); Evidence-Based Practice Center Systematic Review Protocol Project for the recent Imaging Guidelines on the Pretreatment Staging of Small Cell Lung Cancer. Dr. Parker has written two thoracic imaging core textbooks and is lead author on a recently released Lung Cancer Screening textbook. He was instrumental in developing one of the first lung screening programs in Virginia, a center recognized by the ACR and Lung Cancer Alliance as a screening center of excellence.

# The interface of breast cancer and diabetes: Practical options to manage weight gain in women at high-risk for breast cancer

**Victoria Seewaldt[1]*, Lisa Yee[1], Jerneja Tomsic[1], Terry Hyslop[2], Joseph Geradts[1], Jeannine McCune[1], David Ann[1], Dustin Schones[1]**

[1]City of Hope Comprehensive Cancer Center, USA

[2]Duke University, USA

Although diabetes, obesity, and breast are distinct diseases, they do not occur in isolation. At our City of Hope Clinics, many of our premenopausal patients who are at risk for breast cancer also have pre-diabetes (insulin resistance).

Insulin resistance occurs when cells stop responding to insulin. Every time a woman with insulin-resistance eats, serum insulin spikes to 5-10 times normal (hyperinsulinemia). Insulin stimulates hunger and prevents the body from breaking down fat. For this reason, diet and exercise alone is rarely effective in promoting weight loss in women who are insulin-resistant.

Up until recently, women with insulin-resistance were rarely identified or treated. Now the current American Diabetes Association Guidelines (2014) recommend both the identification and treatment of pre-diabetes. Current guidelines recommend the use of metformin for treatment of pre-diabetes and reduction of circulating insulin.

Recent research provides evidence that insulin drives signaling pathways that define the aggressive biology of estrogen-receptor negative breast cancer (such as Akt/mTor and Wnt). For this reason, there is significant concern that high-insulin/pre-diabetes may be harmful to women at high-risk for breast cancer. Metformin is known to reduce circulating insulin. As a result, there are numerous clinical trials in progress to test the ability of metformin to prevent breast cancers.

Here we will present a practical set of options for identifying women who are pre-diabetic and providing potential risk reduction options that fall within standard of care guidelines.

**Audience Take Away:**

- Women at risk for breast cancer are many times at risk for diabetes. Here we will discuss potential ways by which pre-diabetes breast cancer risk.
- Discuss why women who are pre-diabetic cannot lose weight (aka why diet and exercise are not enough).
- Discuss potential options that fall within standard clinical guidelines for managing women who have both breast cancer and diabetes risk.

## Biography

Victoria L. Seewaldt, M.D., is the Ruth Ziegler Professor and Chair of the Department of Population Science at City of Hope and Associate Cancer Center Director. Dr. Seewaldt serves on the United States National Institute Board of Scientific Advisors. Dr. Seewaldt leads a lab to community translational research program at City of Hope to promote risk assessment and early detection. Biomarkers identified in the laboratory are tested as predictors of short-term breast cancer risk in the high-risk women who participate in Dr. Seewaldt's clinical trials. Dr. Seewaldt has had continuous R01 funding for the past 14 years and was recently awarded a U01 grant to test whether combined imagining and metabolic biomarkers can provide early detection of aggressive breast cancers. Clinically, Dr. Seewaldt aims to empower women who are at risk for breast cancer and be full partners in developing wellness strategies that promote full person health.

# Prevalence of HPV and HPV-related dysplasia in elderly women

**Annika Lindstrom MD, PhD**
Orebro University, Uppsala University, Sweden

Despite a high incidence of cervical cancer (CC) in women over the age of 60, elderly women are not included in the screening programs for cervical cancer prevention. In Sweden, about 30% of CC cases occur in women over 60 and the mortality rate is about 70% in this age group. Cervical cancer in women above the age of 65 is usually discovered at advanced stages and the prognosis is poor. During the past century, the average life expectancy for women has increased, and many women over 65 are healthy, continue to work, and have an active sex life. There are few studies on HPV prevalence in elderly women. We found an HPV prevalence of about 4 % in this age group and HPV clearance between HPV test one and two was about 40% when the second HPV test was done. It is clear that persistent cervical HPV infection is common in this age group and that the vast majority have cervical dysplasia diagnosed by histology. Among women with two HPV positive tests there was a high prevalence of high grade intraepithelial neoplasia (HSIL) diagnosed by histology, which motivates screening to continue at older ages. In post-menopausal women, due to hormonal changes, the transformation zone where precursor lesions develop, is situated in the cervical canal and is therefore not accessible for proper examination and sampling. As a consequence Pap smear for conventional cytology or liquid based cytology (LBC), has a low sensitivity and diagnostic surveillance with colposcopy for biopsy has little value. It is clear that cytologically-based screening is not meaningful in this age group due to the low sensitivity of this method. The next step would be to introduce repeat HPV testing as a screening method and to find algorithms for sampling strategies such as self-sampling, test intervals and treatment options. Our results can serve as motivation to conduct studies focusing on older women also, in order to effectively reduce the prevalence of cervical cancer in this age group.

**Audience Take Away:**

- Cervical cancer occurs in older women not included in screening programs and the mortality in cervical cancer is higher in older women. Cervical cancer can be prevented in older women.
- A significant proportion of elderly women were found to have a persistent cervical HPV infection. Among them there was a high prevalence of dysplasia diagnosed by histology which motivates screening to continue at older ages.
- The repeat HPV test showed high sensitivity and specificity in detecting CIN in elderly women, while cytology showed extremely low sensitivity.
- Self-sampling at home for HPV-testing was well accepted among elderly women.
- Cytologically-based screening is not meaningful in this age group due to the low sensitivity of this method.
- Future research on the prevalence of HPV and dysplasia in elderly women, intervals between screening and health economy analysis are needed to and eventually include older women in screening.

## Biography

Senior consultant obstetrics and gynecology 50% Postdoc 50% Center for Clinical research Dalarna, Uppsala University, Clinical Research Center, Faculty of Medicine and Health, Orebro University Sweden. Earlier work in hospitals in gynecology Falun and Gavle, and gynecologic oncology Akademiska sjukhuset, Uppsala , Sweden and Radiumhospitalet, Oslo Norway. Doctoral thesis: Prognostic factors for squamous cell cervical cancer, tumor markers, hormones, smoking and S-phase fraction, Umea University, Sweden 2010. Present research in cervical cancer prevention in elderly women and Urethral Pain Syndrome in women.

# Electrochemotherapy as a new approach on pancreatic cancer and on liver metastases

**Francesco Izzo* MD, Raffaele Palaia MD, Vittorio Albino MD, Salvatore Tafuto MD, Roberta Fusco Ing, Antonella Petrillo MD, Vincenza Granata MD**
National Cancer Institute of Naples, IRCCS "G. Pascale" Foundation, Naples Italy

Electrochemotherapy is a local non-thermal treatment for cancer ablation. Currently, many studies and case report have investigated the differences in effectiveness of electrochemotherapy with respect to tumor type, chemotherapeutic drug, and route of drug administration. ESOPE trial validated standard operating procedures [SOP] for ECT using the Cliniporator device and demonstrated that ECT is a simple, highly efficacious, and cost-effective treatment of cutaneous and subcutaneous nodules from different primary tumors for cutaneous or superficial lesions. This presentation has the purpose to summarize current knowledge about clinical effectiveness of electrochemotherapy and future prospects regarding its use on pancreatic cancer and liver metastasis.

**Audience Take Away:**

- Presentation will summarize current knowledge about clinical effectiveness of electrochemotherapy
- Will explain the new indications of ECT in unresectable pancreatic and liver tumors
- Will suggest new application of ECT as neoadjuvant setting

## Biography

Dr Izzo is Director and Chief of the Hepatobiliary and Pancreatic Unit, within the Department of Surgical Oncology at the National Cancer Institute of Naples. His clinical practice and research focuses on new surgical oncology treatments and he has been a pioneer in designing improved techniques for surgical removal of hepatic tumours and direct tumour injection therapies. Additionally, Dr Izzo is Principal Investigator of a number of national and international protocols in this field and has authored or co-authored more than 220 publications and 18 book chapters relating to the treatment of patients with HPB tumours. Total Impact Factor: 638,003 ; H-INDEX: 35; Sum of the times citated: 7.017; Database utilized: SCOPUS for H-Index and Bibliosan for IF.

# Monitoring of antifungal therapy using $^{18}$FDG-PET/CT in patients with acute leukemia: 2 case reports

**Jérôme Paillassa[1]*, Pacôme Fosse[2], Corentin Orvain[1-3], Pierre Abgueguen[4], Marie-Christine Rousselet[5], Myriam Ammi[6], Jonathan Farhi[1], Mathilde Hunault-Berger[1], Franck Lacoeuille[2-3], Aline Tanguy-Schmidt[1-3]**

[1]Service des Maladies du Sang, CHU Angers, Angers, France [2] Service de Médecine Nucléaire et de Biophysique, CHU Angers, Angers, France [3] CRCINA, INSERM, Université de Nantes, Université d'Angers, Angers, France [4]Service de Maladies Infectieuses et Tropicales, CHU Angers, Angers, France [5]Département de Pathologie cellulaire et tissulaire, CHU Angers, Angers, France [6]Service de Chirurgie Vasculaire et Thoracique, CHU Angers, Angers, France

CASE 1: A 65-year old man was diagnosed with acute myeloblastic leukemia (AML) and was treated with an intensive chemotherapeutic regimen. During induction phase, the patient developed pulmonary mucormycosis. This diagnosis was made thanks to CT scan and bronchoalveolar lavage. An antifungal therapy (AFT) with liposomal amphotericin B and posaconazole was started. After 4 months of AFT, a second CT scan was realized showing a residual lung lesion. This lesion was excavated and localized in the superior lobe of the left lung (24x14x15 mm). A $^{18}$FDG-PET/CT did not show any metabolic activity of this lesion (Suv max 1.2), highlighting that it was residual and allowing the end of AFT. A surgical resection of this lesion was performed. Interestingly, its histological exam did not show any fungus but cicatricial lesion with fibrosis. Unfortunately, the patient relapsed of the AML and died.

**CASE 2:** A 28-year old man was diagnosed as having a B-cell acute lymphoblastic leukemia (ALL) CD20+ Ph1- and received intensive chemotherapy. During the treatment, the patient displayed a multisystemic invasive fungal disease (IFD) involving lungs, liver, lymph nodes, spleen and kidneys. The histological exam of a hepatic abscess and a lymph node found mold elements, but they were too altered to make a more precise diagnosis. An AFT with liposomal amphotericin B and posaconazole was started. $^{18}$FDG-PET/CTs were performed at 5, 6 and 14 months of AFT in order to monitor its efficacy. The first one shew multiple hypermetabolic foci; all of them disappeared on the last one. Thanks to that, AFT was stopped after 19 months without recurrence of IFD.

**DISCUSSION:** About 50-70% of febrile neutropenias are considered as « fevers of unknown origin » (FUO). A growing number of studies highlight the role of $^{18}$FDG-PET/CT in the diagnosis of IFD in neutropenic and non-neutropenic patients. Moreover, recent studies also show a role of this imaging in the therapeutic monitoring of neutropenic and non-neutropenic patients with IFD. Therefore, in the future, $^{18}$FDG-PET/CT could be used in hematology, both in the neutropenic and non-neutropenic settings, in order to reduce the duration of AFT which may be toxic and expensive.

**Audience Take Away:**

- Understanding the usefulness of $^{18}$FDG-PET/CT in the diagnosis and therapeutic monitoring of IFD in hematology.
- Encouraging the audience to use $^{18}$FDG-PET/CT in this setting in order to reduce the duration of AFT, allowing a less toxic and less expensive treatment of IFD in hematology.
- Encouraging the audience to include such patients in prospective clinical trials evaluating the role of $^{18}$FDG-PET/CT in the diagnosis and therapeutic monitoring of IFD in hematology.

## Biography

Resident in clinical hematology, Centre Hospitalier Universitaire d'Angers, Angers, FRANCE since 2013 Student at unit 978, Institut National de la Santé et de la Recherche Médicale (INSERM) : "Adaptators of signalling in hematology", Université Paris XIII, Bobigny, FRANCE since 2017.

# Stereotatic body radiotherapy for liver metastases: A Single-Institute experience in Taiwan

**Yaoru Huang*, M.D., Wei-Jun Wang, M.D., Lai-Lei Ting, M.D., Jeng-Fong Chiou, M.D., Ph.D.**
Taipei Medical University Hospital, Taiwan

**Purpose:** Stereotactic body radiotherapy (SBRT) has been increasingly used for liver metastases which are unresectable or not suitable for other local therapy. Although burgeoning literature has been discussing SBRT for liver metastases, most SBRT to liver metastases requires fiducial markers and/or air-breath control for organ motion management. These methods are invasive with more complication, limited to favorable patients, and demand more training for both physicians and therapists. Therefore, we report our experience about the outcome and toxicity of SBRT for liver metastases, using respiration correlated CT (4D-CT) and abdominal compressor as organ motion management.

**Materials and Methods:** Between 2009 June to 2017 December, 27 patients with 39 hepatic nodules at our institution, after multidisciplinary review, received SBRT to their liver metastases, which were not suggested for other local therapy, including resection. Mean diameter for each nodule was 2.37 cm (range: 0.6 ~ 6.0cm) and mean gross tumor volume (GTV) was 22.70ml (range: 3.85 ~ 107.7ml). Prescribed dose ranges 21 to 42Gy in 3 to 6 fractions with 5-7Gy per fraction.

**Results:** None of these 27 patients developed ≥grade 3 side effects during or within 1 month after radiotherapy. For 25, traceable and assessable patients, median follow-up was 14.3 months (range: 3~26 months). Despite all patients continued chemotherapy, 4 patients achieved complete remission (CR) after SBRT while 10 patients had partial response (PR) and 8 patients remained stable disease (SD). In-field progression-free survival (in-field defines as irradiation area) for CR, PR and SD patients were 15.9, 6.9 and 6.4 months while overall survival were 15.9, 18.2 and 8.3 months, respectively.

**Conclusion:** For liver metastases not indicated for operation nor other local therapy, SBRT offers a feasible option for considerable local tumor control. Although our domestic practice was relatively more conservative, this initial single-institute experience might help provide an option for future liver metastases.

**Audience Take Away:**

- The audience shall understand more about clinical benefit of stereotactic body radiotherapy (SBRT) for unresectable liver metastases or inoperable patients.
- For improved technique of organ motion management as 4D-CT with abdominal compressor, which is non-invasive, less selective to patients and more convenient for both physicians and therapists, SBRT could be applied for more patients and more clinical setting.
- SBRT with higher radio-biological effect and vascular damage to tumor circulation, little has investigated on comparing clinical result between SBRT and traditional radiotherapy. Here we will raise some initial, interim experience for interested participants to expand their related research.

## Biography

Dr. Yaoru Huang received his medical degree in 2009 at Taipei Medical University, Taiwan and finished the specialty training of radiation oncology in 2015 and hospice and palliative care in 2016, in Taipei Medical University Hospital. After summer fellowship in Cancer Prevention in 2016 at National Cancer Institute, National Institute of Health, USA, Dr. Huang is the attending physician in both department of Radiation Oncology and department of Hospice and Palliative Care, TMUH. Meanwhile, he is also a Ph.D. student at Graduate Institute of Biomedical Material and Tissue Engineering, Taipei Medical University. Currently, his research and clinical interest focus on stereotactic body radiotherapy and concurrent radiotherapy with chemotherapy, target therapy or immunotherapy, as well as palliative radiotherapy.

# The role of selective intraaterial and intravitreal chemotherapy in organ-preserving treatment of the children with an intraocular retinoblastoma

**I. Pogrebnyakov[1]*, B. Dolgushin[1], T. Ushakova[2], I.Trofimov[1], A. Kukushkin[1], E. Virshke[1], O. Gorovtsova[2], Y. Serov[2], A. Yarovoy[3], S. Saakyan[4], V. Polyakov[2]**

[1]. SRI of clinical and experimental radiology of N.N.Blokhin CRC, Moscow, Russian Federation
[2]. SRI of pediatric oncology and hematology of N.N.Blokhin CRC, Moscow, Russian Federation
[3]. S.Fyodorov Eye Microsurgery Complex, Moscow, Russian Federation
[4]. Moscow Helmholtz Research Institute of Eye Diseases, Moscow, Russian Federation

**The aim of the research:** Improving of organ-preserving treatment results of the children with an intraocular retinoblastoma (IRB) with local selective intra-arterial (IAC) and intravitreal (IViC) chemotherapy methods.

**Materials and methods:** The research included treatment results of 110 children (129 eyes) in N.N.Blokhin Cancer Research Center of Oncology with one - and a bilateral retinoblastoma from 2011 to 2017. All patients/eyes were divided into 2 groups. The first group (combined therapy) included 99 children/116 eyes where IAC±IViC were carried out due to insufficient efficiency of earlier treatment of RB refractory forms (n=32) and according to the multicenter protocol of an retinoblastoma C and D groups treatment (n=84). The 2nd group of IAC±IViC monotherapy included 11 patients/13 eyes with initially identified one - and bilateral IRB where the local chemotherapy (IAC±IViC) was the first treatment stage.

**Results:** In the first group 95 of 114 eyes were retained. One patient with a bilateral lesion left the study. The salvage of eyes by Kaplan-Meier was reached in 94,5% in 1 year, 88,5% in 2 years, 86,5% in 3 years, 82,9% in 4 years and 75,0% from 4th to 6th years. Patients were followed up to 30,3±16,81 month, and 23,74 ±12,45 months was the recurrence-free period. In group of IAC±IViC monotherapy 11 of 12 eyes were retained. One patient with bilateral form left the study due to the presence of a second tumor. The salvage of eyes by Kaplan-Meier was reached in 92,3% in 1 and 2 years. Patients were followed up to 13,5±5,3 months, and 23,74 ±12,45 months was the recurrence-free period.

**Conclusion:** Local chemotherapy is an effective and perspective organ-preserving method. It can be used as a complex therapy part of advanced and refractory IRB forms and as a monotherapy of the primary identified IRB.

# CXCR4 and RANK as a predictor bone metastasis in breast cancer

**Erwin Danil Yulian[1]*, MD.,MBBS. Ph.D., Bajuadji Sudijono[2], MD, MBBS., MHA., Walta Gautama[3], MD., MBBS, Primariadewi Rustamadji[4], MD., MBBS. Ph.D., Ricky Dosan[5], MD.**

[1]Surgical Oncology Division, Department of Surgery, Faculty of Medicine, University of Indonesia, Indonesia
[2]Surgical Oncology Division, Department of Surgery, Koja District Hospital, Indonesia
[3]Surgical Oncology Division, Department of Surgery, Dharmais Cancer Hospital, Indonesia
[4]Department of Anatomical Pathology, Faculty of Medicine, University of Indonesia, Indonesia
[5]Integrated Laboratory, Faculty of Medicine, University of Indonesia, Indonesia

Until recently, among any cancer in women, breast cancer has the highest prevalence and incidence. Bone metastasis is more common than visceral metastasis in breast cancer. Patients with bone metastasis have better overall survival but consume high cost for treatment. Because of that, tumor markers which could act as an early predictor for bone metastasis are needed so early intervention could be given efficiently and increase patient's quality of life.

CXCR4 and RANK have been known for it's role in cancer cell homing to bone. Instead of other biomarkers of bone metastasis, CXCR4 and RANK act in the early cascade of bone metastasis process. CXCR4/SDF-1 axis plays a great role in cell trafficking of many types of human stem cell. RANK/RANKL/OPG axis mediates osteoclastogenesis and bone resorption. In several studies, CXCR4 and RANK are highly expressed in breast cancer and correlate with bone metastasis.

In an observational analytic cross sectional study, CXCR4 and RANK immunohistochemistry were done to 58 breast cancer samples from stage I-IV. Correlation with metastasis, menopausal status, cancer stadium, lymph node involvement, hormonal receptor and HER-2 amplification were analyzed.

Combination of highly expressed CXCR4 and highly expressed RANK had significant correlation with bone metastasis ($p<0.01$). Breast cancer's stadium had significant correlation with combined CXCR4 and RANK expression ($p<0.01$).

Combination of CXCR4 expression and RANK expression could act as a predictor for bone metastasis in breast cancer. Early detection of bone metastasis will have a great implication in patient's quality of life and treatment cost.

**Audience Take Away:**

- Stimulate researchers to study bone metastasis prevention and discover the best protocol for bone metastasis prevention.
- Become a new insight and expand other researchers who have the same interest in metastasis prevention.
- If the best method for bone metastasis prevention is discovered, breast cancer patients would have better quality of life and lower treatment cost.

## Biography

Dr. Erwin Danil Yulian is a Surgical Oncologist from University of Indonesia and frequent speaker at oncological events in Indonesia. For the past 10 years, Dr. Erwin has been researching breast and thyroid cancer.He inspire many of his students to do research in oncology. Since 2016, he has been promoted to be the head of Breast Cancer Research in Indonesian Medical Education and Research Institute (IMERI). Dr. Erwin heads up to the Fellow Program for Surgical Oncology and the Doctoral Program of Medicine at University of Indonesia. His current research and publications focus on metastasis prevention in Breast Cancer.

# Role of 9-Fluorenone in regulation of cancer stem cell properties through direct targeting of a mesenchymal stem cell's marker TAZ

**Surajit Pathak* Ph.D., Madhumala Gopinath M. Phil., Sushmitha Sriramulu M. Sc., Antara Banerjee Ph.D.**
Faculty of Allied Health Sciences, Chettinad Academy of Research and Education, Kelambakkam, India

Cancer stem cells (CSC) generally acquire the features that are related to the normal stem cells. In the study of CSCs, the role of Tafazzin (TAZ) gene has been looked into in the past decade. TAZ serves to be a downstream effector in the Hippo signalling pathway and increased TAZ protein levels have been linked with several other human cancers including breast, thyroid and non-small lung cancer. TAZ has been obtaining importance very recently as studies have shown that it is over expressed in various cancers. The increase in the perception of cell biology, with respect to stem cells, has now led to the isolation of various tissue specific stem cells and identification of stemness properties in cancer cells. This paves way in the identification of several biomarkers that have the ability to convert cancer cells into CSC. TAZ generally plays a main role in clonogenicity (ability to form clones), non-adherent growth in vitro and tumor formation in vivo. The outrageous level of RNA expression of TAZ correlates with the shorter survival among colon cancer patients. Thus, it is only natural, that TAZ is strongly expressed in endothelium rich organs as the mutation of Hippo pathway, in any one of the endothelial organs, can lead to cancer. TAZ, a component of Hippo signalling pathway regulates stemness property when it is transcriptionally active. The post-translational modification of TAZ leads to phosphorylation of TAZ, thus leading to loss of stemness in the stem cells resulting in differentiation. We have studied TAZ directed mesenchymal stem cells regulation by using 9-flourenone (9F) (an inhibitor of TAZ).

**Audience Take Away:**

- TAZ might thereby regulate the cancer stem cells (CSCs) and down regulation of TAZ will be a potential strategy to kill CSCs, which are considered as a causative factor for recurrence following cancer therapy.
- Further, direct targeting of CSCs by liposomal nanoformulated 9-F may be having potential therapeutic outcome.
- CSCs have more folic acid receptor in their cellular surface, so liposomal nanoformulation of 9F, which have higher affinity for folic acids, probably thereby enhance the targeting of TAZ which might in turn reduces the chances of recurrence of cancer cells.
- Additional studies are required to uncover the physiological roles of YAP/TAZ in a broad range of tissue-specific stem cells and various types of mesenchymal stem cells for clinical applications in the field of regenerative medicine.

## Biography

Dr. Surajit Pathak is an Indian born research scientist, advisor and an Associate Professor at CHETTINAD ACADEMY OF RESEARCH AND EDUCATION, Chennai, India who has multiple expertise encompassing endocrinology, cancer biology, stem cell and regenerative medicine. He started his active research in the year 2001 and received his Ph.D. from University of Kalyani, INDIA in 2007. He has a total of 16 years of research experience and 3 years of teaching experience in the respective field. He worked in University of Alabama, USA, University of Padova, Italy and University of Linkoping, Sweden over 10 years with 930 citations. He has got various research grants including Indo-Italian Bilateral project and as well as EMR funded Science and Engineering Research Board (SERB) project, Government of India. He has delivered his speech as invited speaker in various International World Congress meetings at Russia, Monte Carlo and Taiwan. Dr. Pathak has published over 52 papers and filed 6 patents till date.

# Molecular markers in low-grade glioma: Correlative analysis of NRG trials

**Joshua D. Palmer*, MD, Erica Bell, PhD, Arnab Chakravarti, MD, PhD.**
Department of Radiation Oncology, The James Cancer Hospital and Solove Research Institute, Ohio State University Wexner Medical Center

Gliomas are a heterogeneous group of primary tumors and have recently undergone improved classification with molecular markers in the new 2016 WHO classification. I will present the molecular marker data from prospective NRG trials (RTOG 0424 and 9802) performed by the Chakravarti lab. Our data will help improve the prognostic classification of low grade gliomas.

**Audience Take Away:**

- Explain how the audience will be able to use what they learn?
- The audience will learn about the standard of care for low grade gliomas based on RTOG 9802, as well as understand the prognostic significance of MGMT methylation and IDH-1 in low grade gliomas.
- How will this help the audience in their job? Is this research that other faculty could use to expand their research or teaching? Does this provide a practical solution to a problem that could simplify or make a designer's job more efficient? Will it improve the accuracy of a design, or provide new information to assist in a design problem? List all other benefits.
- The presented data helps practicing physicians discuss treatment with patients with low grade glioma and understand the changing landscape of molecular markers for low grade tumors. New studies will continue to use this data to make treatment decisions.

## Biography

Dr. Joshua D. Palmer is an academic radiation oncologist, specializing in central nervous system and pediatric tumors. He has published over 50 peer-reviewed journal articles, abstracts and book chapters related to brain and spine tumors. He has received numerous clinical and research awards including the post-graduate research award from the Alpha Omega Alpha Society to study glioblastoma and the American Society of Clinical Oncology 2015 Conquer Cancer Foundation Oncology Trainee award. He is a Co-PI on two national brain metastasis trials in the RTOG/NRG and ALLIANCE. His research focus includes translational oncology, biomarker discovery, and dietary effect on cancer therapy.

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# Immunocytochemical negativity of HPV L1 proteins in ASCUS or LSIL can predict higher grade CIN

**Joo Hee Yoon*[1], Miyoung Park[1], Sang Il Kim[1], Sung Jong Lee[1], Eun Young Ki[2]**
[1]Department of Obstetrics and Gynecology, St. Vincent's Hospital, College of Medicine, The Catholic University of Korea
[2]Department of Obstetrics and Gynecology, Daejeon St. Mary's Hospital, College of Medicine, The Catholic University of Korea

**Background:** The aim of this study was to evaluate the immunocytochemical expression of human papillomavirus (HPV) L1 capsid protein in patients with atypical squamous cells of unknown significance (ASCUS), and low grade squamous intraepithelial lesions (LSIL) at high risk of HPV infection. We want to investigate the association of HPV L1 capsid protein expression and its clinical significance.

**Materials and Methods:** Between January 2013 and December 2017, we performed immunocytochemistry of HPV L1 protein in cervical cytology samples (49 normal cytology, 70 ASCUS, and 215 LSIL) obtained from 334 patients using the Cytoactiv® HPV L1 screening set. The expression of HPV L1 capsid protein was assessed by using cytology and was compared with the results of histopathological examination of surgical samples.

**Results:** Patients with ASCUS (n=70) or LSIL (n=215) in cervical cytology differently showed negativity for L1 capsid protein when they were diagnosed as ≥ cervical intraepithelial neoplasia (CIN) 2 (ASCUS group: 82.6%, P=00046; LSIL group: 72.2%, P=0.02). The negativity for L1 capsid protein was significantly higher in patients with HPV 16 or 18 infection when they were diagnosed as ≥CIN 2 (P=0.03). The risk of ≥CIN 2 was higher in ASCUS with HPV L1 capsid protein negative group than LSIL or negative group (Odds ratio: 14.7, 95% CI 3.5-64.5, P<0.001). Model comparison analysis revealed that cytology plus HPV capsid protein immunocytochemistry or cytology plus HPV test improved the diagnosis rate compared with cytology alone (AIC: 229.9 vs 236.0 vs 241.0; SC: 245.2 vs 251.3 vs 252.4). After adjustment of age and parity, HPV L1 capsid protein immunocytochemistry negativity (OR 4.16, 95% CI 1.86-9.33, P=0.0005) increased the risk of ≥CIN2 than HPV type 16or 18 infection (OR: 4.04, 95% CI 1.56-40.48, P=0.0042).

**Conclusion:** Our study demonstrates that the negativity of HPV L1 capsid protein in low-grade cytology (i.e., ASCUS and LSIL) is strongly associated with high-grade histopathology diagnoses. Especially, loss of L1 expression in ASCUS could be a potent prognostic marker for the development of CIN.

# Potential chemotherapeutic agent haemanthamine affects the anticancer effect of histone deacetylase inhibitor in ovarian cancer cells

**Martina Seifrtová[a]*, Radim Havelek[a], Lucie Cahlíková[b], Daniela Hulcová[b], Naděžda Mazánková[a], Martin[a] Řezáčová[a]**
[a]Department of Medical Biochemistry, Faculty of Medicine in Hradec Králové, Charles University, Šimkova 870, Hradec Kralove 500 38, Czech Republic
[b]ADINACO Research Group, Department of Pharmaceutical Botany and Ecology, Faculty of Pharmacy, Charles University in Prague, Heyrovského 1203, Hradec Králové 500 05, Czech Republic

Histone deacetylase inhibitors (HDACi) have been found to cause growth arrest and apoptosis of many malignant cells and its antitumor activity has been linked to their ability to induce gene expression through the increased acetylation of histones. In present-day medicine the HDACi are widely used as an anticancer drugs alone or in combination with chemotherapy agents. One of the most studied HDACi is sodium butyrate (NaB). NaB is short-chain fatty acid formed naturally in the colon by fermentation of dietary fibers. NaB exhibits several effects on cells such as inhibition of proliferation and apoptosis. Although NaB has been studied in several human cancer cells, its effect in human ovarian cancer cells and in normal human fibroblasts has yet to be characterized.

Haemanthamine (HA) belongs to the crinine type of alkaloids and represents promising therapeutic agent because of its anticancer activities. The anticancer effect of HA has been proved in a number of different types of cancer cells. In our previous study we have elucidated the anticancer effect of HA in leukemic cell lines. Our results have shown that HA treatment cause the inhibition of proliferation, accumulation of cells preferentially at G1 and G2 phases as well as induction of apoptosis in leukemia cells. However the mechanisms of action of HA are not completely clear and there are no information about its effect in human ovarian cancer cells.

It was reported that HDACi may enhance sensitivity of other anticancer agents, but there are no studies combining naturally occurring compound such as HA with the HDACi. This unknown problem was the main object for the present study, in which we assessed the effect of HA and NaB alone as well as in combination in human ovarian carcinoma cells A2780 and in non-cancerous normal human fibroblasts MRC-5. Sensitization of cells to both compounds was accompanied by activation of proteins regulating cell cycle. HA in combination with NaB increased acetylation of histones and decreased activation of check-point kinases and $p21^{WAF1/Cip1}$ in comparison to treatment with NaB alone. Further the combination of agents caused suppression of cells in the G1 phase and an increase in the population of cells in the G2 phase. Importantly, HA enhanced the effect of NaB in both cell types, but the effect was more pronounced and significant in A2780 cancer cells. A possible anticancer effect of HDACi sodium butyrate alone or in combination with haemanthamine remained unknown in these cell types and the present study contributes to its enlightment. Our observations reported here point to the need for continued development of strategies for sensitizing cancer cells to therapies that kill cells by inducing DNA damage.

This work was supported by Charles University grant Progres Q40.

**Audience Take Away:**

- Our work represented the first study elucidating the mechanisms of antitumor action of haemanthamine and sodium butyrate alone or in combination in human ovarian cancer cells and in normal human fibroblasts.
- The findings support the synergistic potential of haemanthamine and sodium butyrate application to selectively impair cancer cell viability and proliferation.

## Biography

Martina Seifrtová is an assistant professor and researcher in Department of Medical Biochemistry in Faculty of Medicine in Hradec Králové. Her research is focused on clarifying the mechanisms that regulate cell cycle arrest, DNA reparation and induction of apoptosis after application of DNA damage-inducing agents. At present, she aims to the anticancer effect of substances of natural origin, particularly of alkaloids from Amaryllidaceae family. In collaboration with other departments, she participates in the study of the antitumor effect of newly synthesized PUMA inhibitors and in the study of cytotoxicity of magnetic cores and complex thermosensitive packs.

# The human papillomavirus E6 protein targets apoptosis-inducing factor (AIF) for degradation

**Masaru Shimada*, MD, PhD[1], Akio Yamashita, PhD[2], Motohide Ichino, PhD[3], Takao Kinjo, PhD[4], Kenji Okuda, MD, PhD**

[1]Department of Molecular Biodefense Research, Yokohama City University, Yokohama 236-0004, Japan
[2]Department of Molecular Biology, Yokohama City University, Yokohama 236-0004, Japan
[3]Department of Immunology, Yokohama City University, Yokohama 236-0004, Japan
[4]Division of Morphological Pathology, Department of Basic Laboratory Sciences, School of Health Sciences, University of the Ryukyus, Okinawa 903-0215, Japan

Apoptosis-inducing factor (AIF) is a flavoprotein that, upon translocation to the nucleus, induces DNA fragmentation, leading to apoptosis via a caspase-independent pathway. This study demonstrates that the E6 component of human papillomavirus (HPV) inhibits this activity. E6 is able to bind to all of three forms of AIF (precursor, mature, and apoptogenic) and co-localized with apoptogenic AIF. E6 derived from HPV16 (a known cancer-causing type) lead to the degradation of AIF. This degradation was blocked by the proteasome inhibitor MG132. Of interest, degradation of AIF was not induced by E6 derived from HPV6 (a type that does not cause cancer). E6 from HPV16, but not E6 from HPV6, suppressed AIF-induced chromatin degradation in vitro and STS (a protein kinase inhibitor)-induced apoptosis in vivo. Moreover, there was a significant decrease in apoptosis in HPV6 E6-expressing cells when treated with AIF siRNA, but not in HPV16 E6-expressing cells after STS treatment. These findings demonstrate that E6 from cancer-inducing HPV types block AIF-mediated apoptosis and that AIF may represent a novel therapeutic target for HPV-induced cervical cancer.

# Development of novel radioprotective agents based on small molecule inhibitors

**Radim Havelek[1]*, Jan Marek[2], Martina Seifrtova[1], Ales Tichy[2,3] Jaroslav Pejchal[4], Lenka Zarybnicka[3], Alzbeta Filipova[3], Zuzana Sinkorova[3] and Martina Rezacova[1]**

[1]Department of Medical Biochemistry, Faculty of Medicine in Hradec Kralove, Charles University, 500 03 Hradec Kralove, Czech Republic

[2]Biomedical Research Center, University Hospital, 500 05 Hradec Kralove, Czech Republic

[3]Department of Radiobiology, Faculty of Military Health Sciences, University of Defence in Brno, 500 01 Hradec Kralove, Czech Republic

[4]Department of Toxicology and Military Pharmacy, Faculty of Military Health Sciences, University of Defence in Brno, 500 01 Hradec Kralove, Czech Republic

Radiation therapy (RT) is commonly used as a component of anticancer therapy for a wide range of cancers. At present, it is estimated that half of all cancer patients will receive radiotherapy during the course of their treatment for cancer. The therapeutic activity of ionizing radiation on cancer cells is primarily based on the cell cytotoxicity derived from the inhibitory effects of radiation on vital biochemical processes in cancer cells. Unfortunately, the interaction of radiation with cells during RT can also cause side effects by damaging noncancerous, healthy tissues surrounding the cancer cells. In this regard, targeting the BH3-only Bcl-2 family pro-apoptotic protein known as p53-upregulated mediator of apoptosis (PUMA) had previously been reported to show radioprotective effects. The presented work is focused on the design, synthesis and in vitro screening of PUMA drug inhibitors as novel radioprotective agents for radiation anticancer therapy and as radioprotectors or mitigators for situations including radiation accidents or radiation terrorism.

The aim of this work was to design a set of new potential inhibitors of PUMA-like compounds. The compounds were designed based on the structural research of substances with the same or similar effects known from the literature. The data prediction was applied in order to analyze the suitability of use. The selected structures were then synthetically prepared according to the standard synthetic approaches and verified for their identity and purity by NMR and MS.

To investigate anti-proliferative and cytotoxic activities of the prepared small molecule PUMA inhibitors alone, we determined the cytotoxic effect on cell survival using a panel of 9 human cancer cell lines of different tissue origin (Jurkat, MOLT-4, A549, HT-29, PANC-1, A2780, HeLa, MCF-7 and SAOS-2) compared with non-cancerous human lung fibroblasts MRC-5. Single-dose testing of growth inhibition in the screening panel of human cell lines was performed with 10 newly prepared PUMA inhibitors at a concentration of 10 μM. Proliferation of cells was evaluated at the end of 48 h culture with evaluated inhibitors using the WST-1 tetrazolium salt proliferation assay. The measurements showed that treatment with prepared PUMA inhibitors at 10 μM resulted in no significant changes in the cell proliferation compared to 0.1% DMSO sham control exposure.

**Audience Take Away:**

- Ten novel PUMA inhibitors were prepared and analysed. All newly synthetized PUMA inhibitors were screened for anti-proliferative activity against panel of human cancer cells, which spanned cell lines from different tissue types. None of the inhibitors showed considerable reduction of cells proliferation or cytotoxicity. Our data suggest that presented PUMA inhibitors and its structure-based derivatives are promising radioprotective candidate drugs for further development.

## Biography

Radim Havelek works at the Department of Medical Biochemistry, Faculty of Medicine in Hradec Kralove, Charles University, where he focuses on study of compounds with potential for use in the treatment of cancer diseases (natural alkaloids Amaryllidaceae, Papaveraceae, Fumariaceae, Solanaceae, new semi-synthetic derivatives of alkaloids, metallocenes, magnetic nanoparticles), cellular response to genotoxic stress at cellular and molecular level, study of cellular response to genome damage in the direction of cell cycle arrest, apoptosis, or activation of stress-induced premature senescence.

# Exosomal gastrokine 1 is a theragnostic target for gastric cancer

**Jung Hwan Yoon*, Ph.D., Won Sang Park, M.D., Ph.D.**
Department of Pathology, College of Medicine, The Catholic University of Korea, 222 Banpo-daero, Seocho-gu, Seoul 06591, South Korea

GKN1 is a stomach-specific protein which is produced by gastric mucus-secreting cells and secreted onto the apical cell surface. Previouly, we reported that GKN1 plays important roles in maintaining mucosal homeostasis, and in regulating cell proliferation and differentiation. Here, we determined whether exosomal GKN1 is a theragnostic marker for gastric cancer. In protein microarray assay, GKN1 binding to 27 exosomal proteins was clearly observed. GKN1 was expressed in exosomes derived from HFE-145 gastric epithelial cells by western blot and immunofluorescent assays, but not in exosomes from AGS and MKN1 gastric cancer cells. Exosomes carrying GKN1 inhibited cell proliferation and induced apoptosis in both AGS and MKN1 cells, and exosomes carrying GKN1-treated nude mice bearing MKN1 xenograft tumors exhibited significantly reduced tumor volume and tumor weight. Silencing of clathrin markedly downregulated the internalization of exosomal GKN1. Interestingly, serum GKN1 concentrations in patients with gastric cancer were significantly lower than those in healthy individuals and patients with colorectal and hepatocellular carcinomas. These results suggest that the GKN1 is secreted and internalized in the gastric epithelium by exosome-driven transfer, which inhibits gastric tumorigenesis and supports the clinical application of serum exosomal GKN1 in gastric cancer diagnosis and treatment.

**Audience Take Away:**

- GKN1 protein is located inside the exosomes.
- Exosomal form of GKN1 protein may function as a tumor suppressor and serve as a therapeutic target of gastric cancer.
- GKN1 protein in serum may be an informative diagnostic biomarker for gastric cancer.

## Biography

Jung Hwan Yoon received a B.S. and M. S. degree in genetic engineering from Cheong-ju University and a PhD in Cancer biology from the Catholic University of Korea. Yoon was postdoctoral fellow at department of pathology, the Catholic University of Korea. Yoon is currently a research instructor at the Catholic University of Korea. This project aims to provide diagnostic and therapeutic marker for gastric cancers.

# Mullerian inhibiting substance (MIS)/anti-Mullerian hormone (AMH) induces the apoptosis in endometrial cancer cells

**Miyoung Park[1]*, Sang Il Kim[1] M.D., Sung Jong Lee[1], M.D., Ph.D., David T. MacLaughlin[2] Ph.D., Patricia K. Donahoe[2] Ph.D., Joo Hee Yoon[1] M.D., Ph.D.**

[1]Department of Obstetrics and Gynecology, St. Vincent's Hospital, College of Medicine, The Catholic University of Korea

[2]Pediatric Surgical Research Laboratories, Massachusetts General Hospital, Harvard Medical School, Boston, MA 02114, USA

**Background:** Most gynecologic tumors originate from Müllerian ducts, which develop into the Fallopian tubes, uterus, cervix, proximal vagina, and from the surface epithelium of the ovary. Müllerian inhibiting substance (MIS), also known as anti-Müllerian hormone (AMH), has long been known for causing the regression of the embryonic Müllerian duct. MIS has been shown to inhibit tumor growth in vitro and in vivo, but its downstream regulated genes have not been fully elucidated. MIS initiates its effect by binding to the MIS type I and type II receptors. Since endometrial cancer is also a tumor of Müllerian duct origin and prior studies have reported antitumor properties of MIS against endometrial carcinoma cell lines, we sought to understand the molecular drivers of growth inhibition or apoptosis in endometrial cancer.We try to find out the mechanism of MIS-induced cell death in primary culture cells derived from endometrial cancer patients.

**Methods:** 3 patients with endometrial cancer FIGO stage IA were enrolled in the Department of Obstetrics and Gynecology of Seoul St. Mary's Hospital in 2012. The specimens of patients after surgery were cultured primarily in vitro. We treated those cells with purified MIS, and then analyzed the cell death mechanism. To understand the genome-wide effects of MIS on gene regulation, we performed serial gene expression analyses from 0 to 96 h at 24 h intervals after treating endometrial cancer cells with MIS.

**Results:** When the expressed genes were mapped to known biological processes, Wnt-, cancer-, proteolysis-, cytoskeleton-, cell cycle-, apoptosis-, and MAPK-signaling pathways emerged as the functions most significantly changed by MIS in endometrial cancer cells. Furthermore, western blot analysis validated that protein expression of cell cycle inhibitory genes.

**Conclusions:** MIS could be considered as a potential treatment of choice for endometrial cancer.

**Figure 1.** Endometrial cancer primary cultured cells express the MISRII by immunohistochemistry with rabbit polyclonal anti-human MISRII antibody. Chromogen : AEC. Magnification, 200 X. The right lower figure is higher magnification of the boxed area (400 X).

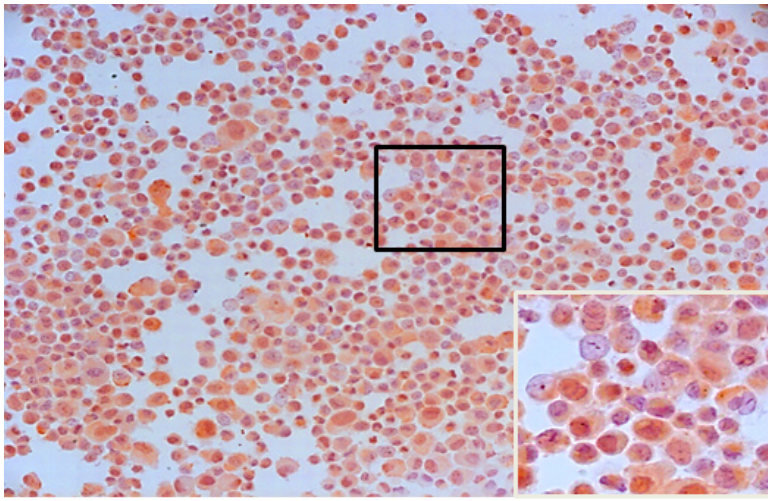


**Figure 2.** Immunohistochemistry

Endometrial cancer tissues express the MISRII by immunohistochemistry with rabbit polyclonal anti-human MISRII antiserum

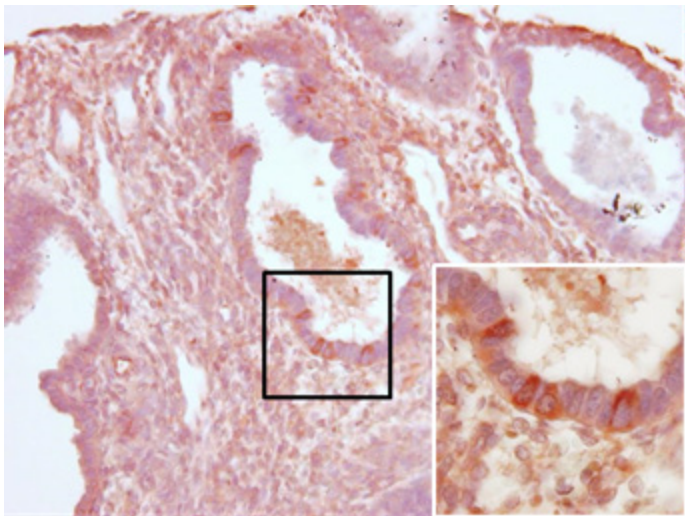
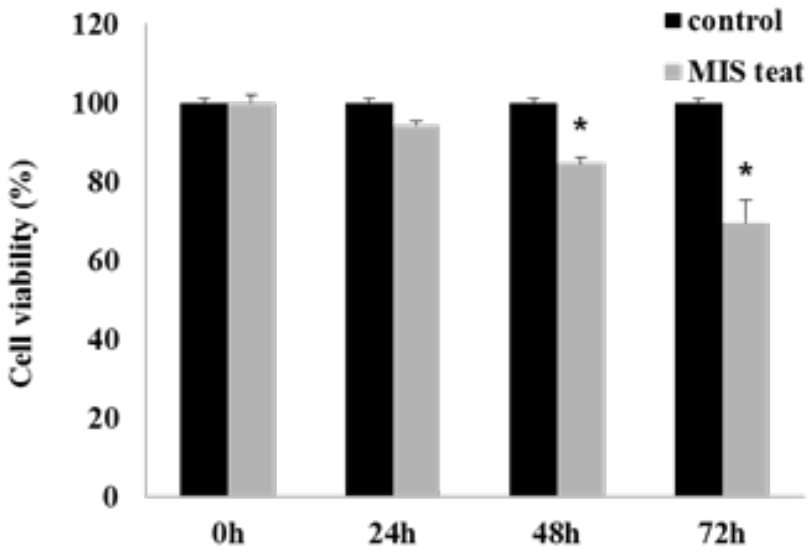


**Figure 3.** MTT assay

Endometrial cancer cells were treated with MIS, after 24, 48 and 72hours added MTT, and the absorbance was read at 550nm

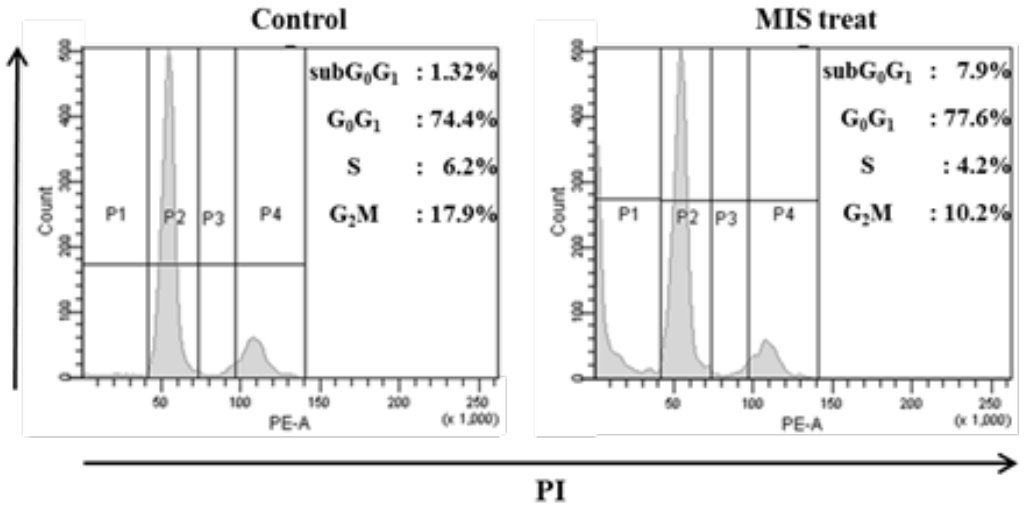



| | 0h | 24h | 48h | 72h |
|---|---|---|---|---|
| control | 100 ± 1.52 | 100 ± 2.42 | 100 ± 3.64 | 100 ± 3.25 |
| MIS teat | 100 ± 2.08 | 94.4 ± 0.93 | 84.71 ± 1.34 | 69.58 ± 5.74 |

**Figure 4.** Cell cycle assay

Endometrial cancer cells were treated with MIS, after 72hours following the treatments

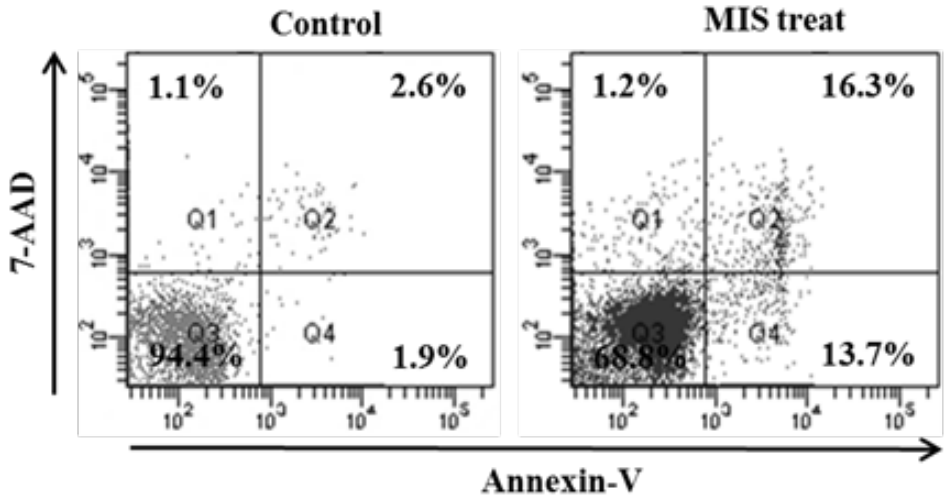
Cell cycle was measured by propidium iodide (PI) stain




| | subG0G1 | G0G1 | S | G2M |
|---|---|---|---|---|
| control | 1.7 ± 0.4 | 74.25 ± 1.3 | 6.4 ± 0.5 | 17.6 ± 0.6 |
| MIS teat | 8.1 ± 1.5 | 77.2 ± 1.1 | 2.6 ± 1.5 | 12.1 ± 1.9 |

**Figure 5.** Annexin V assay

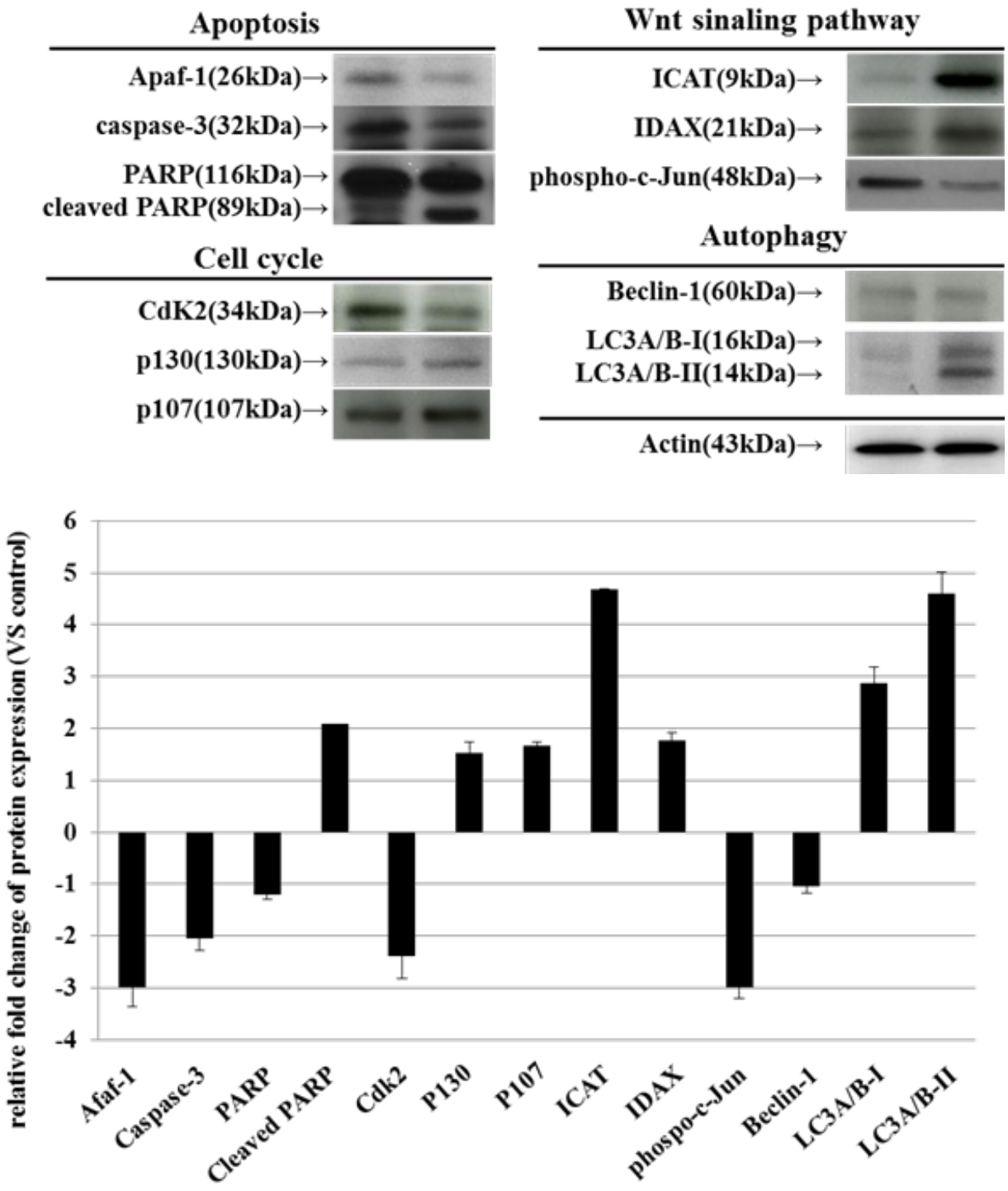
Endometrial cancer cells were treated with MIS, after 72 hours following the treatments, apoptosis was measured by Annexin-V assay




| | LL | LR | UL | UR |
|---|---|---|---|---|
| control | 93.1 ± 0.4 | 3.7 ± 1.7 | 0.8 ± 0.5 | 2.3 ± 0.8 |
| MIS treat | 67.8 ± 3.3 | 12.9 ± 1.8 | 2.1 ± 1.2 | 17.3 ± 1.2 |

**Figure 6.** Western blot analysis

Endometrial cancer cells were measured the expression of apoptosis, cell cycle, Wnt signaling pathway and autophagy-related proteins. The cells were treated with MIS for up to 72 hours.



Apoptosis

| Apaf-1 | caspase-3 | PARP | Cleaved PARP |
|---|---|---|---|
| -2.98 ± 0.37 | -2.05 ± 0.24 | -1.2 ± 0.09 | 2.08 ± 0.01 |

Cellcycle

| CdK2 | p130 | p107 |
|---|---|---|
| -2.38 ± 0.44 | 1.53 ± 0.20 | 1.66 ± 0.08 |

Wnt signal pathway

| ICAT | IDAX | Phospho-c-jun |
|---|---|---|
| 4.67 ± 0.02 | 1.76 ± 0.17 | -2.99 ± 0.21 |

Autophagy

| Beclin-1 | LC3A/B-I | LC3A/B-II |
|---|---|---|
| -1.05 ± 0.12 | 2.87 ± 0.33 | 4.6 ± 0.40 |

# Brain connectivity changes after transient stroke: Using fMRI and DTI

**Chae Ri Park, M.S.[1]*, Bumwoo Park, Ph.D.[1], Joo Young Oh, B.S.[1], W.H. Shim, Ph.D.[1,2]**
[1]Asan Institute for Life Science, University of Ulsan College of Medicine, Asan Medical Center, 88, Olympic-ro 43-gil, Songpa-gu, Seoul, 05505, Korea
[2]Department of Radiology and the Research Institute of Radiology, University of Ulsan College of Medicine, Asan Medical Center, 88, Olympic-ro 43-gil, Songpa-gu, Seoul, 05505, Korea

Stroke impairs neuro-function in the brain system and causes functional disabilities. Functional recovery mostly occurs even after a severe stroke, however, changes in the brain connectivity that underlie such recovery are poorly studied. In current study, using rat MCAO models, we monitored changes in two ways. To confirmed structural changes using Diffusion Tensor Imaging (DTI) MR image at 7days after stroke surgery. Also brain functional changes monitored using functional Magnetic Resonance Imaging (fMRI) over a period of 30 days after transient cerebral ischemic damage.

We used 7 Sprague-Dawley rats (~320g), which showed almost full recovery of both sensory and motor functions approximately 30 days at 90 min after ischemic/reperfusion in the right hemisphere. Six healthy age controlled rats were used for the control group. Functional MRI time courses during resting-state (10min, TR=1s, 9 slices) were collected. Both the voxel-wise analysis and the region of interested (ROI) based analysis were performed that voxel-wise analysis were selected in the left S1FL, and multiple ROIs were placed over the somatosensory regions. Diffusion Toolkit (http://trackvis.org/dtk/) was used to calculate voxel-wise values for relative fractional anisotropy (rFA). All rFA values in each ROI are obtained individually to generate group differences. Significance testing between groups was performed with the two-tailed unpaired t-test.

MCAO models showed the significantly increased rFA values only in penumbra (peri-infarct) region, especially in exercised group (Fig. 1). We also found that decreased brain functional connectivity in the ipsilateral (right) for both voxel-wise and ROI-based methods (Fig. 2). Interestingly, in contralateral (left), the voxel-wise analysis connectivity spatially expanded into the entire cortex area. The correlation coefficient values between ROI's somewhat increased in the contralateral hemisphere compared to the control group.

In conclusion, we showed that the renaturation of sensorimotor function is associated more with the increase and spatial expansion of functional connectivity within the contralateral than the ipsilateral hemisphere. Also, structural changes appear to occur more rapidly than functional changes in the brain recovery phase.

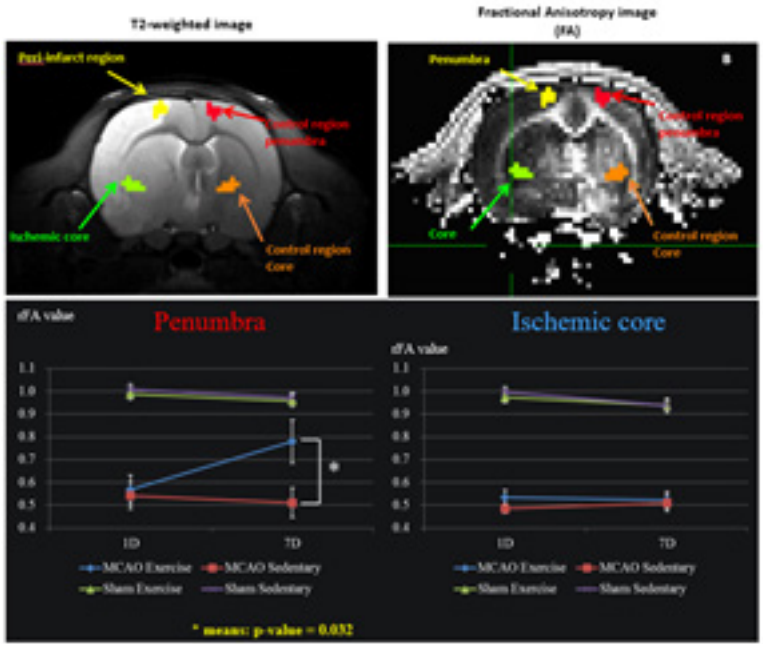



**Figure 1.** Relative FA (rFA) changes after stroke recovery. In the peri-infarct region, the rFA of MCAO model showed a statistical significant difference between the recovered group and control group at 7day after surgery.

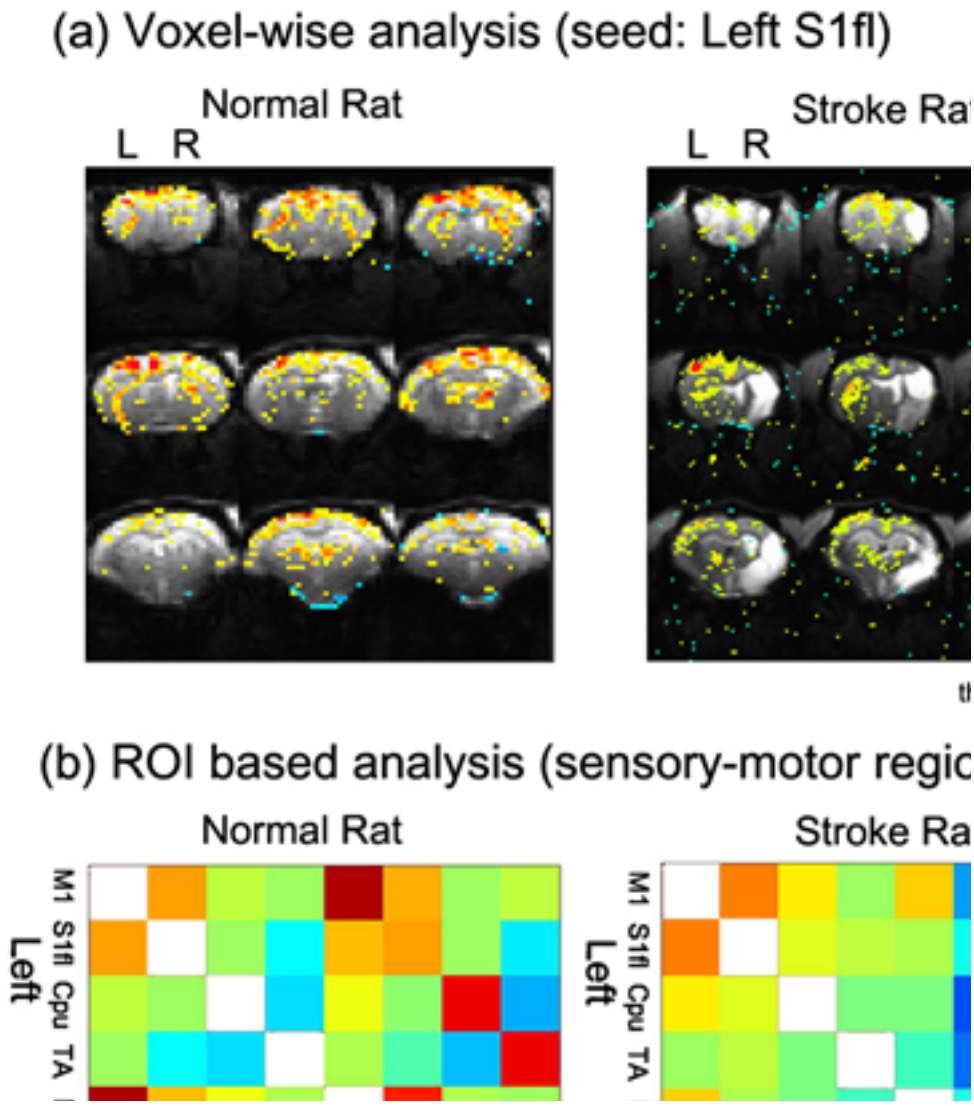



**Figure 2.** The seed-voxel analysis and the ROI-based analysis. Stroke rats showed the markedly decreased functional connectivity in the ipsilesional side (right) for both voxelwise and ROI-based methods.

**Audience Take Away:**

- Detecting Brain connectivity changes with functional MRI.
- Radiologically, we showed accessible to using various brain imagintechniques such as fMRI and DTI of interhemispheric connectivity.
- New information about advanced fMRI imaging technique.

## Biography

March 2018 - Current (Ph.D.Candidate): University of Ulsan College of Medicine, Seoul, South Korea.

Concentration: NeuroScience, Animal experiment, Stroke Image processing, Functional MRI, Brain connectivity, DTI analysis.

March 2014 - August 2017 (M.S.): University of Ulsan College of Medicine, Seoul, South Korea.

Concentration: NeuroScience, Animal experiment, Stroke

March 2006 - February 2009 (B.S.): Biology, Chungnam National University.

# Radio-sensitizing effect of low-dose acetaminophen

**Youn Kyoung Jeong*, Ph.D., Jae Eun Ju, Ph.D. candidate., Byoung Soo Kim, Ph.D., Gwang Il Kim, Ph.D., Joo Hyun Kang, Ph.D.**
Korea Institute of Radiological & Medical Sciences, Republic of Korea

Acetaminophen (APAP) is widely used to treat pain and to reduce fever, while APAP overdose causes hepatic centrilobular necrosis. Recent studies have reported that APAP alone or combined with chemotherapy inhibited cell proliferation in various cancer cells and xenografts. However, anticancer effects of APAP combined with radiotherapy are still unclear. The present study investigated whether APAP combined with radiation would enhance the anticancer effects of radiation alone in MDA-MB-231 breast cancer cell line, focusing on cell cycle regulation. APAP inhibited clonogenic cell survival and induced morphological changes in a dose-dependent manner (0~20 mM). Low dose-APAP (2 mM, survival fraction: 0.89) enhanced the radio-sensitivity of MDA-MB-231 cancer cells. In addition, combination of low-dose APAP and radiation blocked radiation-induced G2/M arrest and reduced expression of cyclinB1 protein, which is G2/M checkpoint regulator, in MDA-MB-231 cancer cells. Our results showed that low-dose APAP enhanced radio-sensitizing effect by regulating cell cycle progression. Further research is needed that APAP toxicity is assessed by production of APAP-induced toxic metabolites using LC-MS/MS analysis and then radio-sensitivity of non-toxic dose APAP is identified in MDA-MB-231 xenograft mice.

**Audience Take Away:**

- Radiosensitizer candidate.
- Drug repositioning.
- Strategy for optimal concentration setting in radiosensitive study.

## Biography

**Educations:** B.S. in biomedical laboratory science. Yonsei University. Korea, Republic of.M.S. in Pharmacy. Ewha Womans University. Korea, Republic of.

Ph.D. in Pharmacy. Ewha Womans University. Korea, Republic of.

**Professional experiences:**

2009-Present: Senior researcher, Korea Institute of Radiological & Medical Sciences. Korea, Republic of.

2004-2007: Researcher, Korea Food and Drug Administration. Korea, Republic of.

**Professional certificates:**

Diplomated Korean Board of Toxicology.

Medical Laboratory Technologist.

Teacher's license in biology.

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# DAY 2

# KEYNOTE FORUM

2nd International Conference on

# Oncology and Radiology

SEPTEMBER 17-19, 2018
ROME, ITALY

## Biography

Tamara Lah Turnsek has completed her PhD from University of Ljubljana, Postdoctoral studies from Wayne State University School of Medicine. She is the Director of National Institute of Biology. She is also the Head of National Genetic Toxicology and Cancer Biology Program and full Professor at the University of Ljubljana,teaching Tumor Biology to postgraduate level students. She has published about 150 papers in reputed journals and is a recipient of many national and international (EU, ERAnet) and inter-regional grants, including the recent Brazil CNPQ grant with the University of Sao Paolo.

# Tumour microenvironment plays a crucial role in regulating tumour progression

## Tamara Lah Turnšek

National Institute of Biology, Slovenia

Nowadays tumour heterogeneity is becoming recognized not only at phenotype, but also at molecular level, is dictating patient's specific response to therapy, and in future the treatments have to become more individualized to increase patients' survival. However, the cells of different cancer subtypes, even within a single tumour, are differentially affected not only by therapeutics, but also by various stromal cells, comprising heterogeneous tumour microenvironment. What is the final decision of the communication among various cancer cells and among the inter-tumour cells' cross talk, is hard to predict. The aim of this presentation is to illustrate the diverse response of different GBM cell subtypes to the normal bone - marrow derived mesenchymal stem cells (MSC).

To elucidate the direct interaction between bone marrow-derived MSCs and two distinct GBM cell lines, U87 and U373, we tested cells' invasion in vitro, as well as in vivo, using zebrafish embryo model (3). Since proteases are crucial for GBM cell invasion, we focused on their role in invasion of cells in MSC/GBM direct co-cultures by analysing their expression at gene and protein levels and by applying selective protease inhibitors in the 3D-invasion model in vitro.

We demonstrated that the effect of MSC/GBM cellular cross-talk on GBM cell invasion is GBM cell type specific. Namely, MSCs decreased the invasion of U87 cells, whereas they increased the invasion of U373 cells in vitro and in vivo. In contrast, both GBM cell lines increased the invasiveness of MSCs upon direct interactions. Moreover, we observed that increased U373 cell invasion in co-cultures correlated with increased expression of cathepsin B, calpain1, uPA/uPAR, MMP-9 and -14, all involved in the protease signalling cascade in GBM cells, leading to increased invasion via extracellular matrix degradation. Using selective inhibitors, we confirmed involvement of cathepsin B, MMP-9 and -14 in MSC-enhanced invasion of U373 cells. By contrast, decreased invasion of U87 upon co-culturing seemed to be independent of these proteases, implicating that the MSC regulatory potential in MSC/GBM co-cultures is dependent on GBM phenotype. Finally, we identified the genes, associated with cell response to TGF-ß that were differentially expressed in U87 vs U373 cells that could explain different response of these cell lines to MSCs.

Taken together, our findings are the first to suggest that the response of GBM cells to MSCs depends on the cancer cells' genetic subtype. This notion may be generalized to other types of stromal cells as well as to other tumours.

## Biography

Dr. Jozef Sabol is considered a highly knowledgeable and experienced expert in radiation protection applied to various medical modalities where ionizing radiation sources are used for both diagnostic and therapeutic purposes. He is the author of more than 200 scientific papers as well as more than 5 monographs on radiation protection applied to medical fields (e.g., Introduction to Radiation Protection Dosimetry, Singapore; Radiation Protection in Radiotherapy, Prague etc.). He spent 8 years working at the IAEA in Vienna where he specialized in the implementation of the Agency's safety standards in its Member States.

# Assessment of the radiation risk to workers and patients in radiation oncology

## Dr. Jozef Sabol, Ph.D., DSc., Prof. (Assoc)

Department of Crisia Management, PACR, Czech Republic

Radiation oncology is based on the use of ionizing radiation sources which deliver a prescribed dose to the identified tumour. The source may irradiate the tumour from outside by external radiation or, the tumour is exposed to the radiation emitted by a radionuclide, which is incorporated in the cancerous tissue. In both cases, the personnel engaged in the treatment may be exposed to some radiation doses which have to be kept as low as possible taking into account all possible circumstances. In addition to receiving a planned relatively high dose to the tumour, the patient may also be exposed to some doses affected healthy tissues which are located close to the tumour. This exposure, although comparatively much lower that the dose to the tumour, has also to be reduced to a very minimum possible. The requirement follows a very basic principle of radiation protection aimed at the reduction of undesirable exposure as much as possible since any dose, whatever low, can be harmful due to stochastic radiation effects which lead to the development of cancer with the probability proportional to the radiation exposure.

**Audience Take Away:**

- The paper will summarize the latest development and requirements regarding radiation protection related to the use of ionizing radiation and radionuclides in medicine with special emphasis on radiation oncology.
- The audience can learn what is the current approach in using radiation sources to meet some new regulatory requirements based on international standards and recommendation of International Commission on Radiological Protection, International Atomic Energy Agency and World Health Organization.
- The participants will acquire some useful information in order to improve the radiation protection of workers, patients and the public in line with the current philosophy of protection against harmful effects of ionizing radiation and minimize the undesirable radiation exposure.

## Biography

Dr. Wassil Nowicky - Dipl. Ing., Dr. techn., DDDr. h. c., Director of "Nowicky Pharma" and President of the Ukrainian Anti-Cancer Institute (Vienna, Austria). Has finished his study at theRadiotechnical Faculty of the Technical University of Lviv (Ukraine) with the end of 1955 with graduation to "Diplomingeniueur" in 1960 which title was nostrificated in Austria in 1975. Inventor of the anticancer preparation on basis of celandine alkaloids "NSC-631570". Author of over 300 scientific articles dedicated to cancer research. Dr. Wassil Nowicky is a real member of the New York Academy of Sciences, member of the European Union for applied immunology and of the American Association for scientific progress, honorary doctor of the Janka Kupala University in Hrodno, doctor "honoris causa" of the Open international university on complex medicine in Colombo, honorary member of the Austrian Society of a name of Albert Schweizer. He has received the award for merits of National guild of pharmacists of America. the award of Austrian Society of sanitary,hygiene and public health services and others.

# Radioprotective effect of the anti-cancer preparation NSC-631570 (UKRAIN)

## Wassil Nowicky

Ukrainian Anti-Cancer Institute, Austria

When NSC-631570 has been used in clinic, it was observed that the patients treated with this drug tolerate the concomitant radiotherapy much better. The adverse effects of this aggressive treatment modality were significantly reduced to minimal. This gave reason to study radioprotective properties of NSC-631570 in the in vitro and in vivo tests.

It was proven the radioprotective effect of NSC-631570 was far superior compared to such of its raw materials taken separately, both measured by survival of mice irradiated by different doses and by the protection coefficient. For example, at a dose of 5.25 Gy protection coefficient of NSC-631570 was 95.0 ± 4.6 vs 50.8 ± 4.6 in the control. These observations suggested that the radio protective effect of Ukrain differs significantly from such of its raw materials.

The radioprotective effect of NSC-631570 was also studied and confirmed on in vitro models on the human skin firbroblasts HSF1 and HSF2 as well as lung fibroblasts CCD32-LU. As evaluation parameters were chosen cytotoxicity, apoptosis induction, cell cycle course, and the expression of TP53 and p21. Additionally, following malignant cell lines were used: MDA-MB-231 (human breast tumor), PA-TU-8902 (pancreas cancer), CCL-221 (colorectal cancer), and U-138MG (glioblastoma).

The cytotoxicity of NSC-631570 was time- and dose dependent. The combination of NSC-631570 plus ionizing radiation (IR) enhanced toxicity in CCL-221 and U-138MG cells, but not in MDA-MB-231 and PATU-8902 cells. Most strikingly, a radioprotective effect was found in normal human skin and lung fibroblasts. Flow cytometry analyses supported differential and cell line-specific cytotoxicity of NSC-631570. CCL-221 and U-138MG cells accumulated in G2 after 24h treatment with NSC-631570, whereas no alterations were detected in the other tumor cells and normal fibroblasts tested. Differential effects of NSC-631570 in modulating radiation toxicity of human cancer cell lines and its protective effect in normal human fibroblasts suggest that this agent may be beneficial for clinical radiochemotherapy.

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# DAY 2

# SPEAKERS

2nd International Conference on

# Oncology and Radiology

SEPTEMBER 17-19, 2018
ROME, ITALY

# Gemcitabine-based neoadjuvant treatments in borderline resectable pancreatic ductal adenocarcinoma (BR-PDAC): A systematic review and meta-analysis of individual patient data

**Dr. Francesco Giovinazzo[1]* MD, PhD, FEBS(HPB), Fiammetta Soggiu[2], Hasham Ahmad[3], Chang Moo Kang[4], Yuichi Nagakawa[4], Mark Zalupski[5], Sarah Yentz[5], Scott Helton[6], J. Bart Rose[7], Chie Takishita[8], Yuichi Nagakawa[8], Mohammad Abu Hilal[1]**

[1]Department of Surgery, University Hospital of Southampton NHS Foundation Trust, Southampton, United Kingdom
[2]University of Milan, National Cancer Institute, Milan, Italy
[3]University Hospital of Leicester NHS Trust, Leicester, UK
[4]Division of HBP Surgery, Department of Surgery, Yonsei University College of Medicine, Seoul, Korea
[5]University of Michigan, Ann Arbor, MI
[6]Section of General, Thoracic and Vascular Surgery, Department of Surgery, Virginia Mason Medical Center, Seattle, WA
[7]Section of Surgical Oncology, University of Alabama, Birmingham, AL.
[8]Department of Gastrointestinal and Pediatric Surgery, Tokyo Medical University, 671 Nishishinjuku, Shinjukuku, Tokyo 1600023, Japan

**Background:** Several non-randomized studies have investigated gemcitabine-based neo-adjuvant treatments followed by surgery in BR-PDAC. We aimed to explore the effectiveness of this treatment on overall survival (OS) in resected patients.

**Methods:** A computerized search of PubMed, Embase, Ovid Medline and Cochrane Library was carried out to retrieve all articles published on neoadjuvant treatment for BR-PDAC from the time of database inception to 31 March 2017. The primary outcome was OS. Secondary outcomes were disease-free survival (DFS), chemotherapy toxicity and R0 resection. Primary and secondary outcomes were calculated using the individual participant data (IPD). Patients were staged as BR-PDAC according to the NCCN preoperative radiological criteria (version 2.2016).

**Findings:** Median OS in the seven included studies ranged between 22.9-41.2 and 9.3-15.4 months in resected and non-resected patients, respectively (Table). Four centers provided IDP of 170 (68%) patients treated with gemcitabine-based regimens; 121 (71%) patients also received pre-operative radiation. Pooled median patient level OS were 27.2 (95% CI 23-31.3) and 20.4 (95% CI 12.7-28) months in the resected and non-resected group (p=0.03) (Figure). DFS after resection was 17.9 (95% 14.3-21.5) months. The different gemcitabine based protocols did not show any significantly OS differences. Eighty-two (48.2%) patients experienced Grade III-IV adverse events. Resection and R0 resection rates were 62% (105 patients) and 88% (92 patients), respectively.

**Interpretation:** Gemcitabine-based neoadjuvant therapy followed by surgery is an effective option in BR-PDAC. Median OS in both resected and non-resected patients appears longer than with upfront surgery. RCTs should further investigate treatment sequencing and specific elements of neoadjuvant therapy regimens.

**Audience Take Away:**

- This is the first meta-analysis combining individual data from 4 studies with 170 patients with BR-PDAC in a homogenous cohort underwent to GEM-NAT followed by surgery. 170 (68%) patients who received Gem-NAT, with additional radiotherapy in 121 (71%). Pooled median patient-level OS was 27.2 (95%CI 23 - 31.3) and 20.4 (95%CI 12.7 - 28) months in resected and non-resected groups (p=0.03).
- The median overall survival in our study is similar to the one reported with FOLFIRINOX and better than previously reported with Gemcitabine alone. In the no resection group the median overall survival suggest that this approach may select the patient candidate to resection and represent a good palliative option. Gem-NAT may represent a valid option to patient not treatable with FOLFIRINOX because the performance status. Two phases II ongoing trials (NCT02125136 and NCT02717091) will further clarify the role of GEM-NAT in this subgroup of patients.

## Biography

The author is a clinician in HPB surgery with an interest in Hepatobiliary and Pancreatic Cancer research including Gastroenteropancreatic Neuroendocrine Tumors (GEP-NETs). Currently, he is working in HPB in University Hospital of Southampton (UK). He hold a PhD degree from the Pancreas Unit in the University of Verona and has worked in several prestigious university around the world including Yale University and King's College Hospital.

# A novel therapeutic target in multistage tumorigenesis

**Myron R. Szewczuk, Ph.D.**
Queen's University, Canada

Stromal cells and growth factors play important roles during tumor initiation and progression. Growth factors not only mediate normal biological processes such as development and tissue repair but also tumorigenesis by contributing to proliferation and transformation in neoplastic cells. It is essential in the clinical setting that targeted therapies are to circumvent multistage tumorigenesis, including genetic mutations at the different growth factor receptors, tumor neovascularization, chemoresistance, immune-mediated tumorigenesis and the development of tissue invasion and metastasis. Firstly, the cell-surface molecular signaling platform will be described in controlling Neu1 sialidase activity, and discuss its relevance in cancer cell signaling. Neuraminidase-1 (Neu1) has recently emerged as a central target in sialidase-mediated regulation of tumorigenesis. Recent evidence indicates that Neu1 plays a much more profound role in human cancers than previously expected. Second, the current understanding of Neu1 activity associated with cancer development will be summarized, and outline the key roles of Neu1 during various stages of tumorigenesis, including regulation of growth factor receptor signaling, control of TOLL-like receptor (TLR) signaling and immune-mediated tumorigenesis, regulation of epithelial-mesenchymal transition (EMT), metastasis and acquired chemoresistance, and regulation of tumor vascularization.

## Biography

For the past 37 years, Dr. Szewczuk is Full Professor of Immunology and Medicine, Queen's University, Kingston, Ontario Canada. Dr. Szewczuk's recent research has focused on the role of glycosylation in receptor activation with a particular focus of TOLL-like, nerve growth factor Trk, EGFR and insulin receptors. He has discovered a novel receptor-signaling platform and its targeted translation in multistage tumorigenesis.

# Neoadjuvant treatment in pancreatic cancer: How far are we from standardization?

**Giulia Zumbo* MD, Fiammetta Soggiu MD, PhD, Francesco Giovinazzo MD, PhD, FEBS(HPB)**
Southampton General Hospital, UK

Pancreatic cancer is currently the 4th cause of death by cancer in Europe as well as in the US, where there have been 55,440 new cases and an estimated 44,330 deaths in 2018. Despite the different therapeutic strategies currently available, the overall 5-year survival remains 8%. Moreover, due to complex extensions that the tumor can have, even when not metastatic, only 10–20% of the patient is eligible for upfront surgery with a 5-year survival raising to 10–30%. The current trend for non-metastatic pancreatic adenocarcinoma is to differentiate three categories based on vascular involvement assessed by preoperative imaging: resectable (15%), borderline resectable (20%) and locally advanced disease (35%).

Different strategies and combination of surgery and neoadjuvant and/or adjuvant therapies are currently investigated for those categories. Although neoadjuvant therapy had shown beneficial effects for pancreatic cancer treatment, currently, treatment sequencing and specific elements of neoadjuvant treatment are still under investigation. The benefit of a neoadjuvant approach may consist in select the patient with a less aggressive biological disease, control the micrometastatis and avoid the risk of drop-out from adjuvant treatment related to the post-operative complications and/ or decline in the functional status.

Palliative gemcitabine (gem) has demonstrated increased overall survival and improved quality of life compared to 5-FU for advanced pancreatic cancer (5.6 vs 4.4 months, p = 0.0025). Capecitabine alone was explored for preoperative borderline patients demonstrating lack of progression disease and improved resectability and survival. Other chemotherapeutic protocols included FOLFIRINOX (OS of 22.1 months - range 16.7–34 months), Gemcitabine, Taxane, Capecitabine (GTx) (19.4 months-range 15.6–25 months), gem associated with cisplatin or nab-paclitaxel or oxaliplatin or bevacizumab or docetaxel or S1 (OS of 16.1 months range 7.3–45 months).

Regarding resectable pancreatic cancer, the gold standard treatment is surgery followed by adjuvant chemotherapy. Nevertheless, neoadjuvant treatment strategies are increasingly being employed for resectable pancreatic cancer. Patients with resectable cancer who received neoadjuvant therapy revealed an overall survival of 23.3 months. A Meta-analysis including 1056 patients with resectable disease have shown an overall survival of 30.0 (24.5-46) and 10 (9-11) months in resected and not resected patients respectively undergone Neoadjuvant. Similar results have shown by two case series on patients treated with Gem+Ox (OS 27.2 months) or Gem+RT OS (22.7 OS months). In another study combining Gem with Cisplatin and RT the overall survival in 90 patients was 17.4 months. Paclitaxel and docetaxel alone followed by RT were explored in two different studies showing 12 months OS and 15.5 months OS, respectively.

The choice of neoadjuvant treatment for patients with borderline resectable pancreatic cancer is widespread. Several agents and combination were studied compared to upfront surgery. Gemcitibine single-agent use showed 2 years survival reached in 40,7% of the patients and OS of 21 months when compered to surgery (26.1% and 12 months) with an hazard ratio 1.495 (95% confidence interval 0.66-3.36) in an intention-to-treat analysis. Another study analyzed FOLFIRINOX followed by gemcitabine/ capecitabine resulting in 22 months OS (range 18–35 months).

The locally advanced disease consists in a tumor that contacts the superior mesenteric or hepatic arteries for more than 180°. That stage was formerly known as unresectable and it is considered inoperable. Less agreement is seen in literature regarding the infiltration of the superior mesenteric vein and the extent involvement and the celiac artery. In a systematic review patients with locally advanced pancreatic cancer revealed an overall survival of 20.5 months if a resection was performed after successful neoadjuvant therapy. Several therapeutically approaches are available, however, the choice is mainly led by the patient performance status. Although the systemic treatment can be given also with gemcitabine, nab-Paclitaxel, mFOLFIRINOX have become the standard of care. In a recent systematic review and meta-analysis the median overall survival after neoadjuvant was 24.2 months (95% CI 21.7–26.8).

**Audience Take Away:**

- This session will give a clear and systematic idea about the employment of neoadjuvant treatment in pancreatic cancer, underlining the most recent developments but also what is still missing in order to standardise its use.
- It also aims to advise clinicians for a good treatment choice, currently used just in selected centres, showing consistent and important results for neoadjuvant therapy use.

- The session is also a good summarisation of what is currently been studied and what need to be explored while providing solid inputs for further research. We strongly believe that a systematic use of neoadjuvant therapy will substantially benefit the future practice.

## Biography

Giulia Zumbo is currently a Trust Fellow at the Southampton General Hospital in the UK. Prior to this she worked as a Research Fellow at the National Amyloidosis Center, Royal Free Hospital in London. She has written and collaborated to 11 original researches (two of which in submission) and one review. She is currently involved in Pancreatic Cancer research with several projects regarding malnutrition assessment by CT in patients undergoing pancreatoduedonectomy and neoadjuvant therapy in resectable pancreatic cancer. She also is an invited reviewer for Journal of Cardiovascular Magnetic Resonance (JCMR).

# Characterization of tumorspheres generated from primary mesenchymal colon cancer cells for the study of colorectal cancer progression

**Marina De Rosa[2*], Mimmo Turano[1], Valeria Costabile[2], Andrea Cerasuolo[3], Francesca Duraturo[2], Raffaella Liccardo[2], Paolo Delrio[4], Ugo Pace[4], Daniela Rega[4], Concetta Anna Dodaro[5], Marco Milone[6], Paola Izzo[2]**

[1]Department of Biology, University of Naples Federico II, Naples, Italy;
[2]Department of Molecular Medicine and Medical Biotechnology, University of Naples Federico II,Naples, Italy;
[3]Molecular Biology and Viral Oncology Unit, Istituto Nazionale per lo studio e la cura dei tumori, "Fondazione Giovanni Pascale" IRCCS-Naples, Italy;
[4]Colorectal Surgical Oncology, Istituto Nazionale per lo studio e la cura dei tumori, "Fondazione Giovanni Pascale" IRCCS-Naples, Italy;
[5]Advanced Biomedical Sciences Department, University of Naples Federico II, Naples, Italy;
[6]Department of Clinical Medicine and Surgery, University of Naples Federico II, Naples, Italy

EMT and its reverting process mesenchymal-epithelial transition (MET), are physiological processes occurring during embryonic development and tissue remodelling that confer plasticity to cancer cells. It has been suggested that EMT and cell plasticity could be responsible for the acquisition of chemotherapy resistance and metastasis development in several tumours, including CRCs. We previously isolated and characterized at a molecular level two primary CRC cell coltures from tumour tissues of patients 88 and 93 of our bio-bank (the T88 and T93 coltures). As previously described, T93 cells showed a CIN phenotype, while T88 cells showed a MIN one, with high MSI. We demonstrated that T88 and T93 cells were mesenchymal colon cancer cells that had undergone EMT from epithelial adenocarcinoma cells and simultaneously expressed epithelial (Cks and E-Cadherin) and mesenchymal (Vimentin and N-Cadherin) markers. High levels of EMT-associated transcription factors (Twist and Snail) and several stemness markers were also found. These finding were in accordance with previous data indicating that EMT induces the expression of stem cell-specific genes, and might represent a source of cancer stem-like cells. We also showed that incubation with LiCl, a specific GSK-3β inhibitor, induces MET.

We also characterised our experimental system of adherent primary mesenchymal colon cancer cells and their paired tumourspheres more in depth, by analysing the localisation and expression of a larger panel of markers, including E- and N-cadherin, CD133, CD144v6, ALDH1 and LGR5. Furthermore, we explored the effects of LiCl on cell motility and cell plasticity of CRC cell coltures.

Thus, we confirmed the epithelial/mesenchymal features of these cells and demonstrated that they were characterized by nuclear localisation of several stemness markers, including Nanog, Oct4, Sox2, LGR5, ALDH1, CD133 and CD44v6. Interestingly, we observed atypical nuclear N-cadherin, CD133 and Cd44v6 localisation in mesenchymal CRC cells. We studied the effects of LiCl, a specific GSK-3β inhibitor, on our cellular model, demonstrating that LiCl blocks the migration of T88 and T93 cells. We also observed that LiCl affects stemness features, abolishing expression of all mesenchymal and stemness markers, thus altering the dynamics of tumourspheres formation and cell plasticity. As recently demonstrated for other cancer types, such as glioma, LiCl, a drug already used in clinical practices for treating bipolar disorders, could represent an alternative therapy in colon cancer care and/or able to sensitize cancer cells to chemo-radio-therapy, through down-regulation of EMT and stem cell biomarkers, thus inhibiting crucial cancer cell features, such as motility and plasticity.

**Audience Take Away:**

- EMT is an essential physiological mechanism which cancer cells mutuate during tumour progression. This presentation will be usefull for the reader because it analysed primary cultures greatly enriched of mesenchymal cancer cells, representing an innovative model to study the role of EMT in cancer progression.
- The study also shed light on the in vitro effect of LiCl incubation on motility and stemness of cancer cells, suggesting that LiCl could be a useful drug in colon cancer care that have to be better investigate.
- Finally, the talk will explain characterization of tumorspheres generated from primary mesenchymal colon cancer cells, illustrating a model to study molecular basis of cancer cell plasticity. We also hypothesize a role that the observed atypical nuclear N-cadherin, CD133 and Cd44v6 localisation in mesenchymal CRC cells, could have during cancer progression, opening new perspectives in cancer research.

## Biography

Dr Marina De Rosa achieved, with full marks, a degree in Biological Sciences at University of Naples "Federico II" in 1991. In 1998 she received the title of PhD in Biotechnology and in 2000 she received the title of specialist in Biochemistry and Clinical Chemistry. That same year, she was appointed of a four-year post-doctoral research grants. Currently she is Researcher and Assistant Professor of "Biochemistry" at the University of Naples Federico II. She is author of about 90 publications, 35 of which are articles on indexed scientific journals with a total of 496 citations (h-index:12), according to Scopus database.

# Enhancing the drug load of PSMA-specific targeted drugs

**José Carlos dos Santos[1]*, Julia Han Noll[1], Ulrike Bauder-Wüst[2], Martin Schäfer[2], Matthias Eder[2], Klaus Kopka[2], Uwe Haberkorn[1] & Walter Mier[1]**

[1]Heidelberg University Hospital, Department of Nuclear Medicine, Heidelberg, Germany

[2]Deutsches Krebsforschungszentrum, Division of Radiochemistry and Radiopharmacology, Heidelberg, Germany

Prostate cancer is the most frequently diagnosed cancer type for men and also shows a high mortality. The current treatment of prostate cancer involves active surveillance, radical prostatectomy, radiotherapy, hormone therapy and chemotherapy. However, all these approaches involve several side effects and the loss of quality of life. Targeted therapy is the new hope for prostate cancer treatment. In this new approach, a target binding structure is conjugated to an effector. Consequently, this increases the concentration at the target site which also leads to fewer side effects. The prostate- specific membrane antigen (PSMA) is an enzyme that is overexpressed in prostate cancer cells and is therefore a suitable target for Prostate cancer therapy. The urea-based binding motif Lys-NH-CO-NH-Glu has shown to bind to PSMA with high affinity, while lipophilic linkers further optimize binding properties. The goal of this work was to optimize the drug load of this PSMA binding motif. As a consequence, the drug concentration at the tumor site can be increased specifically. Different numbers of DOTA, a chelator used for endoradiotherapy, were conjugated to the PSMA binding motif via a lysine multimer. DOTA I, DOTA II and DOTA IV were synthesized with 1, 2 and 4 DOTA molecules respectively. The compounds synthesized were evaluated in internalization experiments and PET scans of an LNCaP mouse. The results were compared to the properties of MB17, a promising compound in clinical trials. The PET scans showed specific enrichment in the tumor for the compounds with up to two DOTA molecules. Furthermore, the clearance of the molecules synthesized from the tumor was slower when compared to MB17. The internalization ratio for DOTA I (15.7%) and II (13.4%) were much higher than the one for MB17 (9%), even though one hydrophobic linker was not present in the molecules synthesized. Based on these results, further optimization of the molecules synthesized presents a great potential for the drug load-optimized targeted therapy of prostate cancer.

**Audience Take Away:**

- Targeted Therapy
- Drug design
- Theranostic radiopharmaceutical
- PET Imaging
- Endoradiotherapy

## Biography

Studies in Chemisty, Graduation: diploma (licentiate) in chemistry. State University of South-West Bahia-Brazil (UESB).

Master "Medicinal Chemistry" at University of Regensburg, Germany and University of Lisbon, Portugal(Faculdade de Farmácia da Universidade de Lisboa).

Master thesis and trainee at German Center for Cancer Research Heidelberg (Deutsches Krebsforschungszentrum Heidelberg, DKFZ) in cooperation with National Center for Tumour Diseases (Nationales Centrum für Tumorerkrankungen, NCT).

Subject: Isolation, structure elucidation and properties of polyphenolic compounds from Litchi chinensis (Sapindaceae)

Doctorate(PhD) at Faculty of Biosciences at University of Heidelberg, department of Nuclear Medicine at Kopfklinik of University Hospital in Heidelberg in cooperation with German Center for Cancer Research Heidelberg (Deutsches Krebsforschungszentrum Heidelberg, DKFZ).

# Influence of family income and medical insurance coverage on health-related quality of life and optimism in cancer patients at a Hong Kong private hospital: A cross-sectional study

**Chiu Sai Yiu Richard[1]* BMRSc, Yang Zuyao[2] Ph.D.**
[1]Hong Kong Baptist Hospital, Hong Kong
[2]Chinese University of Hong Kong, Hong Kong

Health-related quality of life (HRQL) and optimism are different health domains that have been proven as important prognosis factors in cancer patients. A number of studies, in turn, have explored income and medical insurance coverage as predictors of the health domains. As previous studies were mostly conducted in the western countries, the objective of this study was to examine the association in the private health sector in Hong Kong.

The study was conducted cross-sectionally with a structured questionnaire in traditional Chinese. HRQL, consisted of physical and mental domains, was assessed with the RAND 12-item Health Survey version 2 (SF-12v2). Optimism was assessed with the Life Orientation Test revised (LOT-R). The two primary predictors were family income and medical insurance coverage. Other covariates included gender, age, education, marital status, number of children, religion, employment status, cancer stage, cancer diagnosis, previous cancer treatments, and previous consultation with oncologists.

A sample of 539 cancer patients was identified and a total of 480 questionnaires were collected. After excluding those with substantial amount of missing data, a total of 428 questionnaires were used to determine the association using logistic regression. Scores calculated from SF-12v2 and LOT-R were originally continuous but were divided into two groups using their respective medians.

After adjusting for other covariates in the regression models, no significant association was observed with family income as the predictor. Income-related health inequity, as evident in many other countries, seemed to be absent in Hong Kong. Hong Kong's unique healthcare system and its money culture might be the reasons behind this indifference. Medical insurance coverage, the other primary predictor, was a significant and positive predictor of optimism with p-value less than 0.01. This association was consistent in the subgroup analysis comparing those with previous cancer treatments and those without. Significant difference between the subgroups occurred in the association between mental domain and medical insurance coverage.

The association was nonexistent for the subgroup with previous cancer treatments whereas significant and positive correlation was observed for those without. This observation was in fact consistent with some longitudinal studies, in which income had little effect on HRQL for those with previous cancer treatments. Possible explanation may lie in their differences in choosing their treatment plans.

The significant association between medical insurance coverage and optimism might be an indication that the cost of cancer treatments was indeed a financial burden to many cancer patients in Hong Kong. Cancer support organization and healthcare practitioners in the private sector should recognize and assist both their medical and financial needs with the aim of improving overall survival rate.

**Audience Take Away:**

- Income-related health inequity is one of the major issues in public health, especially in those countries with heavily private-funded healthcare system. In the study, this inequity seemed to be absent. How can we, as healthcare practitioners and policy makers, improve access to quality healthcare for our cancer patients?
- In the study, medical insurance coverage was observed to provide relief in perceived financial stress in cancer patients. For the cancer patients without prior cancer treatments (i.e. at baseline), even those medical insurance with minimal coverage had shown to be associated with improved optimism and mental wellbeing. The benefit of medical insurance coverage should not be underestimated at baseline.
- As shown in the subgroup analysis, the benefit of medical insurance coverage seemed to diminish after receiving cancer treatment, regardless of the extent of the insurance coverage. What are some possible ways to relieve the financial burden of the cancer patients as they are undergoing cancer treatments?

## Biography

Richard is a registered radiation therapist and medical dosimetrist. Since 2008, Richard has worked in different cancer centres located in Hong Kong and Canada. Richard is currently studying part-time at the Chinese University of Hong Kong, and is a master degree candidate in Epidemiology and Biostatistics. His research interest is in exploring and improving the quality of life of cancer patients as they are battling the deadly disease. His current research is investigating the risk factors for anxiety and depression in cancer patients.

# Anatomic options of vessels and hemodynamic redistribution of the blood flow at the selective ophthalmic arterial infusion (SOAI) at children with the intraocular retinoblastoma

**I. Pogrebnyakov*, B. Dolgushin, I.Trofimov, A. Kukushkin, E. Virshke**
SRI of clinical and experimental radiology of N.N.Blokhin CRC, Moscow, RussianFederation

**Purpose:** Describing of methodology of a SOAI in organ-preserving treatment of children with an intraocular retinoblastoma and demonstrating the various ways of alkylating agent delivery to a tumor.

**Materials and methods:** 316 SOAI procedures to 110 children (129 eyes) have been performed from 2011 to 2017. 2 methods of a SOAI were applied: 1) the microcatheter technique - superselective catheterization of an eye artery or collateral branches of an ECA at blood flow hemodynamic redistribution; 2) the micro-balloon technique.

**Results:** Technical success was 95,8% (303 procedures). From 245 procedures with using of a microcatheter infusion was carried out in: a. ophthalmica – 196 (80%), a.meningea media – 27 (11%), a.infraorbitalis – 20 (8,2%), a. temp. superficialis – 1 (0,4%), a.facialis – 1 (0,4%). From 61 procedures with using of micro-balloon 58 were successful. We didn`t manage to put a balloon more distally than the place of an entry of an eye artery in 3 cases. Unsuccessful attempts – 13 cases: failure of catheterization of a femoral artery – in 3, a kinking/koyling of the ICA – in 3, a vascular collapse as a result of reaction to contrast agent and/or mechanical impact on ICA – in 3, lack of contrasting of a retina – in 3, an occlusion of an ICA – in 1.

**Conclusion:** Possession and use of various techniques for alkylating agent delivery to an eye tumor allows to achieve the maximum effect and doesn't depend on anatomy options and blood flow hemodynamic redistribution in the main vessels of an eye.

# Principles of radiotherapy in head and neck cancers

**Neeraj Jain* MBBS, DNB, Amandeep Kaur M.Sc, Kanchan Sachdeva M.Sc. Dip. R.P., Ramita Sharma M.Sc., Dip. R. p.**
Sri Guru Ram Das University of Health Science, India

Head and neck malignancy is a very common cancer among Indian males. This is attributable to common habit of chewing Tobacco, Gutkha, beetel and beetel nuts etc. Presentation is ususally at advanced stage. Quiet often surgery is ruled out due to advanced stage. Options for management left are Chemotherapy and Radiotherapy. Usually concurrent Chemo Radiotherapy is given. Head and neck region is very complex anatomically. The aim of giving Radiotherapy in such cancers is to achieve maximum local control with minimal toxicity to normal and vital structures. In the past parallel opposing conventional beams were used and there was considerable damage to vital structures. Now a days treatment is delievered with highly sophisticated linear Accelerators. Intensity Modulated and image guided treatment is given. Treatment is verified at regular intervals. if any discrepancy found replanning is done. With the newer technologies it is possible to deliever Biological effective Dose to tumour for better control while restricting the radiation dose to vital structures. Doses close to 70Gy are given in concurrent setting and 60-66 Gy in post operative setting.

**Audience Take Away:**

- Guidelines for Radiotherapy in head and neck cancers.
- Technique of delievering Radiotherapy.
- Long term and short term complications following Radiotherapy.

## Biography

Dr Neeraj Jain is Associate Prof Radiation Oncology At Sri Guru Ram Das University Of Health Sciences Amritsar. He is eminent Radiation Oncologist and participated in Numerous national and international conferences and presented papers. He is Vice Chairman of Indian College Of Radiation Oncologists (ICRO). ICRO is an academic wing of AROI i.e. Association Of Radiation Oncologists of India.

# New perspective in cancer research: The impact of small coding RNAs on cancer cells

**Çağrı Öner*, Asst. Prof. Dr., M.Sc.; Ph.D.**
Maltepe University, Medical Faculty, Department of Medical Biology and Genetics, 34857, İstanbul/Turkey

Cancer has the highest incidence according to other diseases nowadays. Various mechanisms take part in carcinogenesis, one of these mechanisms is small non-coding RNAs. Various studies and researchers determined that small non-coding RNAs are the novel and key molecules of cancer development which do not code protein. These RNAs can be classified into three main groups; small interfering RNAs (siRNAs), micro RNAs (miRNAs) and PIWI interacting RNAs (piRNAs). siRNAs are 18-24 nucleotide (nt) in length, dicer dependent and originated from long double stranded RNA. miRNAs are 18-24 nt in length, dicer dependent and originated from miRNA loci which is found in genomic DNA. miRNAs are associated with Argonaute (AGO) proteins for transcriptional repression or degradation of target mRNA. Furthermore, miRNAs might have tumor suppressive or oncogenic functions according to their target gene and its functions. In our studies about miRNAs showed that miR-126 and its complementary miR-126* can be more effective in metastasis and recurrence. Furthermore, piRNAs are 23-31 nt in length, dicer independent and originated from germ and somatic cells, especially germ cells. piRNAs are associated with one of the type of AGO proteins which is called PIWI proteins. Although piRNAs are first thought that they play an important role in embryogenesis (especially spermatogenesis) via transposon silencing, recent studies are shown that they also have effect on cancer development and biology. The expression of piRNAs and PIWI proteins can be effected by various mechanisms of cell. Hormonal regulation is one of these mechanism, one of our researches shows that exogenous estrogen or androgen uptake might cause some cancer types, breast and prostate cancer, to be more aggressive and to affect expression of piRNAs. Furthermore, the researches about miRNAs and piRNAs show that these two non-coding RNAs can be originated from same gene regions and can affect their expressions during carcinogenesis.

In the advanced stages of cancer and metastasis; our lifetime is decreasing. Once cancer has metastasized, treatments are becoming ineffective. If we can prevent the aggressiveness and invasiveness of cancer cells earlier (in benign stage) by aiming to prevent metastasis and developing new therapies like gene therapy. We must learn to live with cancer as well as other diseases such as diabetes, hypertension etc.

**Audience Take Away:**

- The audience can understand the exact mechanisms of non-coding RNAs (not only miRNAs but also piRNAs) and the differences between them.
- The audience can use the information for their future researches about cancer development.
- The audience also will inform about special miRNAs and piRNAs which take part in cancer cells.
- The presentation will have open a new insight to the audience for battling cancer.
- The presentation will give information about the usage of ncRNAs for cancer or treatment.

## Biography

Asst. Prof. Dr. Çağrı ÖNER is working in Maltepe University, Medical Faculty, Department of Medical Biology and Genetics in İstanbul/TURKEY. He is interested in Non-coding RNAs (especially siRNAs, miRNAs and piRNAs) and their relationship with cancer and its recurrence and metastasis. He especially researches the role of non-coding RNAs in cancer development, metastasis and cancer recurrence. Furthermore, Çağrı ÖNER is interested in cancer biology and genetics, cell death mechanisms, cellular signaling and ophthalmology. He especially used tissue and cell culture, gene expression (real time PCR, PCR), cell behavior (motility, viability, adhesion, invasion and proliferation) and protein expression (Western Blotting, ELISA and immunohistochemistry) methods in assays. Asst. Prof. Dr. Çağrı ÖNER is member of European Society of Cancer Research (EACR), Molecular Cancer Research Association (MOKAD), Association of Medical Biology and Genetics and Cell Death Research Association (HÖAD).

# Nanobodies and OncoFinder: A combined approach for identification of molecular changes in glioblastoma

**Ivana Jovčevska[1*], Ph.D., Alja Zottel[1], BSc., Neja Šamec[1], Ph.D., Jernej Mlakar[2], M.D., Jernej Šribar[3], Ph.D., Igor Križaj[3], Ph.D., Serge Muyldermans[4], Ph.D., Anton A. Buzdin[5], Ph.D., Radovan Komel[6], Ph.D.**

[1]Institute of Biochemistry, Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia
[2]Institute of Pathology, Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia
[3]Jožef Stefan Institute, Ljubljana, Slovenia
[4]Cellular and Molecular Immunology, Bioengineering Sciences Department, Vrije Universiteit Brussel, Brussels, Belgium
[5]Shemyakin – Ovchinnikov Institute of Bioorganic Chemistry, Russian Academy of Sciences, Moscow, Russia
[6]Institute of Biochemistry, Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia

Glioblastoma multiforme is the most frequent primary malignancy of the central nervous system. Despite the clinical management, patients succumb to the disease in 12 to 18 months after initial diagnosis, while for recurrent glioblastoma life expectancy is reduced to 6 months. Glioblastoma lethality is attributed to late diagnosis, difficult surgical removal due to intracranial location, tumor heterogeneity, aggressiveness, infiltration into surrounding brain tissue and resistance to available therapy. Targeting glioblastoma is difficult due to lack of specific biomarkers. Despite the constant efforts of researchers to identify glioblastoma biomarkers, there are no major improvements in their discovery. Our work presents an unconventional nanobody-based approach for selection of glioblastoma specific proteins (PMID: 25419715, PMID: 28498803 and PMID: 29707108). Nanobodies are llama heavy-chain only antibodies which are small in size (14 kDa), hydrophilic, resistant to non-physiological pH and elevated temperatures, and with high sequence similarity to the VH part of human immunoglobulins which makes them non-immunogenic. With nanobodies we selected a panel of proteins (ACTB/NUCL complex, VIM, NAP1L1, TUFM, DPYSL2, CRMP1, ALYREF and TRIM28) which showed differential expression when compared to reference samples. Highest change in protein expression levels was observed for ALYREF, CRMP1 and VIM. Then, OncoFinder software was used for creating an interaction network among these proteins. Results were also analyzed using TCGA dataset, which suggested NAP1L1, NUCL, CRMP1, ACTB and VIM genes to differentiate between glioblastoma and lower grade gliomas, and proposed the use of DPYSL2 as a "glioma versus normal" biomarker. In silico findings were confirmed using a small scale study that showed significant changes at mRNA expression levels for VIM, DPYSL2, ACTB and TRIM28. Afterwards, we examined cytotoxic effect of all nanobodies on different glioblastoma cell lines and astrocytes. Most promising results were observed for NB179 and NB314 targeted against NAP1L1 and DPYSL2 respectively, which reduced NCH421k cell growth down to 74% and 68%. Moreover, migration assay was performed to test possible use of our nanobodies in inhibiting glioblastoma cell migration. The strongest effect was observed for NB79 targeted against the intracellular protein vimentin, which completely inhibited U87MG cell migration. At last, vimentin was found overexpressed in FFPE glioblastoma tissue samples. We report here the development of a unique method for selection of deregulated glioblastoma proteins. Due to selectivity of NB179 and NB314 towards NCH421k glioblastoma stem cell line we suggest their possible use for development of targeting strategies. As indicated by the migration assay, we anticipate that vimentin plays an important role in the migratory and invasive nature of glioblastoma. Although widely expressed, we recommend further exploration of vimentin as a biomarker for glioblastoma malignancy.

**Audience Take Away:**

- The audience will get information about alternative methods for biomarker identification in cancer research. They will also learn about the benefits of nanobodies over classical immunoglobulins, and their potential use in experimental techniques like immunocytochemistry. Further development of the nanobodies for in vitro and later on in vivo purposes will be open for discussion.

## Biography

Ivana Jovčevska is a post-doctoral researcher working in the field of oncology. She is dealing with the problem of brain cancer, glioblastoma in particular, since the beginning of her research career. She has been collaborating on two international projects that use advanced techniques for selection of glioblastoma specific proteins. Her research focus is mostly on proteomic analysis of glioblastoma tissue samples and identification of molecular changes that contribute to gliomagenesis.

# Wwox expression inhibits growth of irradiated cancer cells in vivo

**Bahadir Batar[1]* Ph.D., Kay Huebner[2] Ph.D.**

[1]Department of Medical Biology, Namik Kemal University School of Medicine, Tekirdag, Turkey

[2]Department of Cancer Biology and Genetics, The Ohio State University Comprehensive Cancer Center, Columbus, OH, USA

Our previous results suggest that Wwox-deficient cells exhibit increased survival of ionizing radiation-induced double strand breaks. To determine if the IR resistance of Wwox-deficient cells persists in vivo, Wwox-induced (231/Wwox-pos) and Wwox-deficient (231/Wwox-neg) breast cancer cells were tested for tumor growth in immunocompromised mice. The rationale was that despite irradiating the same number of cells for the two groups, more 231/Wwox-neg cells would survive IR, forming tumors more quickly than 231/Wwox-pos cells. Both groups of cells were exposed to 5 Gy IR, immediately harvested and injected (1 × 107 cells per mouse) subcutaneously into the flanks of athymic nude mice. Control mice from each group were unexposed to IR and exhibited mean tumor latencies (days from injection to first sign of tumor) that were not different: 11 days for 231/Wwox-neg cells and 14 days for 231/Wwox-pos cells. For mice receiving irradiated cells, 7/8 mice injected with 231/Wwox-neg cells formed tumors, whereas 6/8 mice injected with 231/Wwox-pos cells formed tumors. Of the tumor-bearing mice, those injected with 231/Wwox-neg cells had significantly shorter tumor latencies (mean 17 days) vs mice receiving 231/Wwox-pos cells (mean 28 days). Next, we sought a human cancer database with expression and clinical data for cancers treated with radiation to determine if loss of Wwox enabled tumor cell resistance to radiation and decreased overall patient survival in a human model. In cancers treated with radiation, reduced Wwox expression correlated significantly with decreased overall survival vs Wwox normal cancers, suggesting that loss of Wwox facilitates resistance to radiation therapy, disease recurrence and shorter overall survival.

**Audience Take Away:**

- This research will provide novel clues for identification of new targets for prevention of therapeutic resistance and increased overall survival in a variety of cancers.
- Wwox status will be beneficial in devising future cancer treatment strategies.
- Several of future Wwox projects will provide translational research involving oncologists, pathologists, biostatisticians and bioinformaticists, in collaboration with our basic science laboratory.

## Biography

Bahadir Batar is an Asst. Prof. at the Namik Kemal University Medical School, Turkey. He received his Ph.D. from Cerrahpasa Medical School of Istanbul University in 2013, Turkey. He has worked as a postdoctoral fellow at The Ohio State University Comprehensive Cancer Center during the 2014-2016. His primary research interest is in the area of molecular biology and genetics of cancers. Dr. Batar has been working on projects to understand the role of loss of the FHIT and WWOX fragile genes in initiation and progression of several cancers and therapeutic resistance.

# Human cytomegalovirus infection in febrile patients with hematological malignancies at Uganda cancer institute

**Guido Ocung[1]* MSc, Margaret Lubwama[1, 3] Mmed, Prossy Kiconco[2] BSc, Alfred Okeng[2] BSc, Enock Wekiya[1] MSc, Jackson Orem[3] PhD., and Freddie Bwanga [1, 2] PhD.**

[1]Makerere University, Uganda
[2]MBN Clinical Laboratories, Uganda
[3]Uganda Cancer Institute, Uganda

**Introduction:** The use of chemotherapy as well as disease specific factors have been recognized as the main predisposing factors for life-threatening opportunistic infection among patients with hematological malignancy, which often presents as fever. Among the viral infectious complications, Human cytomegalovirus (HCMV) has been reported outside Uganda as a major opportunistic complication. However limited data exists on the burden and contribution of HCMV infection among febrile patients with hematological malignancy at Uganda Cancer Institute and this greatly hampers therapy strategy in managing febrile illness. To evaluate the frequency and risk factors for HCMV in febrile patients with underlying hematological malignancies.

**Methods:** We conducted a cross-sectional study between June and August 2017, blood samples were collected from 161 feverish patients receiving chemotherapy for various hematological malignancies at the Uganda Cancer Institute. Detection of HCMV IgG and IgM as markers of infection was performed with an Indirect ELISA while a qualitative PCR was used to detect HCMV DNA extracted from whole blood at MBN Clinical Laboratories.

**Results:** Of the161 participants evaluated for HCMV infection, 86(53%) were females. The median age in the study was 29 years [IQR 17- 43], 128(80%) were on intensive chemotherapy. Interestingly, HCMV seroprevalence based on IgG and/IgM positivity was found in 106/161(66%) and active infection based on a positive IgM and HCMV DNA PCR was detected in 23/161(14.3%) while 5/161(3%) tested positive for HCMV DNA in the analyzed samples.

**Conclusion:** Evidence from this study suggests that two thirds of febrile patients with hematological malignancy had been infected with HCMV. Overall, the rate of HCMV infection/reactivation ranges between 3 and 66% and that high dose steroid therapy appears as the most relevant, though putative, risk factor. Taken together, this finding highlights the need for routine screening and monitoring of febrile patients with underlying hematological malignancies for HCMV active infection.

**Audience Take Away:**

- Our study demonstrated the presence of HCMV DNA in blood of febrile patients with underlying hematological malignancy, interpreted as reactivation of latent HCMV infection.
- Hence, the need for routine screening and monitoring of febrile patients with underlying hematological malignancy for HCMV active infection.
- Here, we recommend future studies aimed at predicting HCMV reactivation as well as evaluating the efficacy of treatment strategies directed against HCMV reactivation in these patients.

## Biography

Ocung Guido BBLT, MSc.|Makerere University Kampala-Uganda. Guido holds a Bachelor of Biomedical Laboratory Technology (BBLT) from Makerere University, Kampala and graduated in Jan 2018 with a degree of Master of Science in Immunology and Clinical Microbiology at the same University. During his MSc program, working under the supervision of Freddie Bwanga PhD., Margaret Lubwama Mmed., and Jackson Orem PhD., Guido studied the burden and associated factors of Human cytomegalovirus infection among febrile patients with hematological malignancies at Uganda Cancer Institute. Guido is privileged to be awarded a 2018 Dr. LEE Jong-wook fellowship that starts in October 2018. He is interested in studying emerging and neglected infectious disease.

# Quality assurance of VMAT head and neck cancer treatment using PRESAGE® dosimeter

**Jalil ur Rehman[1,2,3]*, Muhammad Isa[5], Nisar Ahmad[1], H M Noor ul Huda KhanAsghar[1], Zaheer Abbas Gilani[1], James C.L. Chow[4], Muhammad Afzal[2], and Geoffrey S. Ibbott[3]**

[1]Department of Physics, Balochistan University of Information Technology, Engineering & Management Sciences, Quetta 87300, Pakistan.

[2]Department of Physics, TheIslamia University of Bahawalpur, Bahawalpur, Pakistan.

[3]The University of Texas MD Anderson Cancer Center, Houston, TX, USA.

[4]Princess Margaret Cancer Centre, ON, Toronto, Canada.

[5]Department of Physics, Hafiz Hayat Campus University of Gujrat, Gujrat, Pakistan.

**Background:** Accurate three dimensional dosimetry is essential in modern radiotherapy techniques such as volumetric modulated arc therapy (VMAT) and intensity modulated radiation therapy (IMRT). In this research work, the PRESAGE® dosimeter was used as quality assurance tool for VMAT planning for head and neck cancer.

**Material and Method:** Computer tomography (CT) scans of an Image Radiation Oncology Core (IROC) Head and Neck anthropomorphic phantom with both IROC standard insert and PRESAGE® insert were acquired separately. Both CT scans were imported into the Pinnacle (9.4 version) TPS for treatment planning, where the structures (PTV, OARs) and TLDs were manually contoured and used to optimize a VMAT plan. Treatment planning was done using VMAT (dual arc: 182°-178°, 178°-182°). Beam profile comparisons and gamma analysis were used to quantify agreement with film, PRESAGE® measurement and TPS calculated dose distribution.

**Results:** The average ratio of TLD measured to calculated doses at the four PTV locations in the H&N phantom were between 0.95 to 0.99for all three VMAT deliveries. Dose profiles were taken along the left-right, the anterior-posterior and superior-inferior axes and good agreement was found between the PRESAGE® and Pinnacle profile. The mean value of gamma results for three VMAT deliveries in axial and sagittal planes were found to be 94.24% and 93.16% when compared to film and Pinnacle respectively. The average values comparing the PRESAGE® results and dose values calculated on Pinnacle were observed to be 95.29% and 94.38% in the said planes respectively using a 5%/3mm gamma criteria.

**Conclusion:** The PRESAGE® dose measurements and calculated dose of pinnacle show reasonable agreement in both axial and sagittal planes for complex dual arc VMAT treatment plans. In general, the PRESAGE® dosimeter is found to be a feasible quality assurance (QA) tool of VMAT plan for HN cancer treatment.

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