29th Euro-Global Summit on

Cancer Therapy & Radiation Oncology

July 23-25, 2018 | Rome, Italy

Special Session

Day 1

Euro Cancer 2018

Guilin Tang, J Cancer Sci Ther 2018, Volume 10
DOI: 10.4172/1948-5956-C8-144

29th Euro-Global Summit on

Cancer Therapy & Radiation Oncology

July 23-25, 2018 | Rome, Italy

Guilin Tang

University of Texas, MD Anderson Cancer Center, USA

Clonal cytogenetic abnormalities of undetermined significance

Myelodysplastic syndromes are a group of hematopoietic stem cell diseases characterized by cytopenia(s), morphological dysplasia, and clonal hematopoiesis. In some patients, the cause of cytopenia(s) is uncertain, even after thorough clinical and laboratory evaluation. Evidence of clonal hematopoiesis has been used to support a diagnosis of myelodysplastic syndrome in this setting. In patients with cytopenia(s), the presence of clonal cytogenetic abnormalities, except for +8, del (20q) and –Y, can serve as presumptive evidence of myelodysplastic syndrome. Recent advances in next generation sequencing have detected myeloid neoplasm-related mutations in patients who do not meet the diagnostic criteria for myelodysplastic syndrome. Various terms have been adopted to describe these cases, including clonal hematopoiesis of indeterminate potential and clonal cytopenia of undetermined significance. Similarly, studies have shown that certain chromosomal abnormalities, including ones commonly detected in myelodysplastic syndrome, may not be associated necessarily with an underlying myelodysplastic syndrome. These clonal cytogenetic abnormalities of undetermined significance (CCAUS) are similar to clonal hematopoiesis of indeterminate potential and clonal cytopenia of undetermined significance. Here, we review the features of CCAUS, distinguishing CCAUS from clonal cytogenetic abnormalities associated with myelodysplastic syndrome, and the potential impact of CCAUS on patient management..

Recent Publications

1. Zuo W, Wang S A, DiNardo C, Yabe M, Li S, et al. (2017) Acute leukemia and myelodysplastic syndromes with chromosomal rearrangement involving 11q23 locus, but not MLL gene. J Clin Pathol 70:244–249.
2. Goswami R S, Wang S A, DiNardo C, Tang Z, Li Y, et al. (2016). Newly emerged isolated del(7q) in patients with prior cytotoxic therapies may not always be associated with therapy-related myeloid neoplasms. Mod Pathol 29:727–34.
3. Tang Z, Li Y, Wang S A, Hu S, Li S, et al. (2016). Clinical significance of acquired loss of the X chromosome in bone marrow. Leuk Res 47:109–13.

Biography

Guilin Tang is a Hematopathologist and Cytogeneticist, Section Chief of Clinical Cytogenetic Laboratory in the Department of Hematopathology, and Adjunct Medical Director of the Department of School of Health Professions. Her clinical interests include diagnosis of hematologic neoplasms (both leukemia and lymphomas) and cancer cytogenetics. Her major research interest is the characterization and risk stratification of cytogenetic abnormalities in various types of hematological malignancies, to better understand the pathogenesis, identify new clinicopathologic entities and predict patient prognosis. She is also very interested in characterization of clinically indolent cytogenetic clones (clonal cytogenetic abnormalities of undetermined significance), especially those emerged following cytotoxic therapies.

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Scientific Tracks & Abstracts
Day 1

Euro Cancer 2018

Sessions:

Cancer Therapies | Radiation Oncology | Organ Defined Cancers

Session Chair
Christopher S Lange
Downstate Medical Center, Brooklyn, NY, USA

Session Introduction

Title: **Clinical Indications for mammography in men and correlation with breast cancer**
Kyungmin Shin, University of Texas, MD Anderson Cancer Center, USA

Title: **Volumetric modulated arc (radio) therapy in pets treatment: The "La Cittadina Fondazione" experience**
Mario Dolera, The National Foundation for Veterinary Studies and Research, Italy

Title: **Combining 2D angiogenesis and 3D osteosarcoma microtissues to improve vascularization**
Hassan Chaddad, University of Strasbourg, France

Title: **The important overlapping problem between malign and benign thyroidal nodules in cancer patients with FDG-PET/CT**
Fikri Selcuk Simsek, Firat University, Turkey

Title: **EGF and TGFα motogenic activities are mediated by the EGF receptor: Identification of the signalling pathways involved in oral cancer**
Aye Myat Thwe, University of Dundee, UK

Title: **Role of free-base and metallated porphyrin derivatives promoting apoptosis as a consequence of cancer photodynamic therapy: Synthesis, characterization and photobiological activities.**
Devashish Sengupta, Assam University, India

Title: **Natural fluorescence for cancer diagnosis**
Aurelija Vaitkuviene, Vilnius Unversity, Lithuania

Kyungmin Shin, J Cancer Sci Ther 2018, Volume 10
DOI: 10.4172/1948-5956-C8-144

Clinical indications for mammography in men and correlation with breast cancer

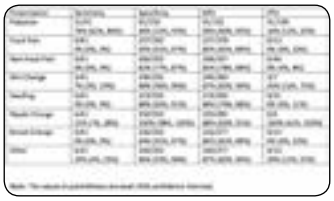
Kyungmin Shin
The University of Texas, MD Anderson Cancer Center, USA

Purpose: To examine presenting clinical symptoms and imaging findings and correlate them with biopsy-proven breast cancer in men.

Method & Materials: 429 male patients who presented for mammography at one institution between January 2004 and December 2014 were retrospectively evaluated. Of the 429 patients, 291 presented with clinical symptoms for diagnostic mammography and 138 presented for screening mammography. The presenting clinical symptoms in 291 patients were recorded and correlated with imaging (mammography and sonography) and histopathology findings.

Results: A total of 291 patients were included. Multiple symptoms were possible and there were a total of 318 clinical symptoms. 190 (60%) presented with palpable abnormalities, 44 (14%) with non-focal pain, 31 (10%) with swelling, 14 (4%) with breast enlargement, 13 (4%) with focal pain, 13 (4%) with other symptoms, 7 (2%) with skin changes and 6 (2%) with nipple discharge/changes. 290 patients underwent mammography and 176 patients underwent sonography. A total of 41 cancers were diagnosed, most invasive ductal carcinoma. Statistical analysis of the clinical symptoms demonstrated that nipple discharge/changes and skin changes (mostly with associated palpable abnormalities) had the highest sensitivity. Analysis of mammography findings revealed that 52 patients showed either a mass or a focal asymmetry on mammography, of which 38 (73%) were diagnosed with cancer. Only three patients (1%) who had neither a mass nor a focal asymmetry were diagnosed with cancer.

Conclusion: Correlating clinical symptoms and imaging findings can help to develop more accurate probabilities for timely and accurate diagnosis of breast cancer in men. Clinical symptoms of nipple discharge/changes, skin changes with associated palpable abnormalities and mammographic findings of masses and focal asymmetries were associated with male breast cancer. Pain, breast enlargement and swelling were unlikely to be associated with breast cancer.



Recent Publications

1. Shin K, Martaindale S and Whitman G J (2018) Male breast magnetic resonance imaging: When is it helpful? Our experience over the last decade. Curr Prob Diagn Radio. DOI: 10.1067/j.cpradiol.2018.01.002.
2. Shin K, Caudle A S, Kuerer H M, et al. (2016) Radiologic mapping for targeted axillary dissection: needle biopsy to excision. AJR 207(6):1372–1379.
3. Shin K, Phalak K, Hamame A and Whitman G J (2015) Interpretation of breast MRI utilizing the BI-RADS 5th edition lexicon: how are we doing and where are we headed? Curr Prob Diagn Radio. 46(1):26–34.
4. Pinell-White X A, Etra J, Newell M, Tuscano D, Shin K and Losken A (2015) Radiographic implications of fat grafting to the reconstructed breast. Breast J. 21(5): 520–525.

Biography

Kyungmin Shin MD is an Assistant Professor at the Department of Diagnostic Radiology at the University of Texas, MD Anderson Cancer Center, section of Breast Imaging. After obtaining her Diagnostic Radiology training at University of Virginia Health System and Breast Imaging Fellowship Training at Emory University, she began her academic career at Baylor College of Medicine, Houston, Texas, in 2013. In 2014, she joined University of Texas MD Anderson Cancer Center and currently practices multimodality breast imaging. She has a keen interest in clinical research, especially in tomosynthesis and breast MRI, and is actively participating in several clinical research projects.

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Mario Dolera, J Cancer Sci Ther 2018, Volume 10
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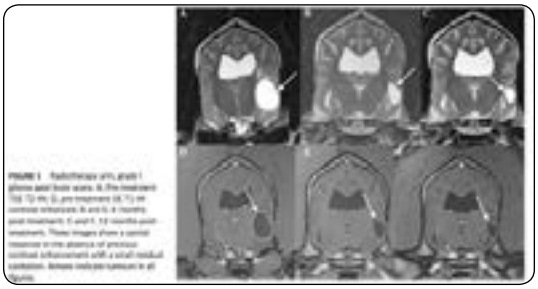
Volumetric modulated arc (radio) therapy in pets treatment: The "La Cittadina Fondazione" experience

Mario Dolera
La Cittadina Fondazione Studi e Ricerche Veterinarie, Italy

Volumetric modulated arc (radio) therapy (VMAT) is a modern technique for cancer irradiation widely used in human radiotherapy that allows high doses to be delivered to tumor volumes and low doses to the surrounding organs at risk (OAR). Veterinary clinic managing cancers in small animals (dogs, cats, rabbits) takes a natural advantage from this feature due to the small target volumes and distances between target and the OAR. In particular, sparing the OAR permits dose escalation and hypofractionation regimens reduce the number of treatment sessions with a simpler manageability in the veterinary field. Multimodal volumes definition is mandatory for the small volumes involved and a positioning device precisely reproducible with a setup confirmation is needed before each session for avoiding target missing. Also, the treatment plan elaboration must pursuit hard constraints and objectives and its feasibility has to be evaluated with a per patient quality control. The aim of this work is to report our center results with hypo-fractionated stereotactic irradiation of neural tumors in dogs interpret to brain meningiomas and gliomas, trigeminal nerve tumors, brachial plexus tumors, onco-endocrinology in dogs related to pituitary and adrenal tumors with vascular invasion and rabbit thymomas. In comparison with literature data, VMAT as a safe and viable alternative to 3D conformal radiotherapy, cone-based stereotactic radiotherapy as well in selected cases to surgery or chemotherapy alone or as an adjuvant therapy in pets.



Recent Publications

1. Dolera M, Malfassi L, Pavesi S, Finesso S, Mazza G, et al. (2017) Computed tomography, magnetic resonance imaging and a novel surgical approach of atlanto-axial instability with incongruence in dogs. J Vet Med Sci. doi: 10.1292/jvms.16-0077.
2. Dolera M, Malfassi L, Bianchi C, Carrara N, Finesso S, et al. (2017) Frameless stereotactic radiotherapy alone and combined with temozolomide for presumed canine gliomas. Vet Comp Oncol. 16(1):90–101.
3. Dolera M, Malfassi L, Bianchi C, Carrara N, Finesso Set al. (2017) Frameless stereotactic volumetric modulated arc radiotherapy of brachial plexus tumours in dogs: 10 cases. Br J Radiol. 90(1069):20160617.
4. Dolera M, Malfassi L, Pavesi S, Finesso S, Sala M, et al. (2016) Volumetric-modulated arc stereotactic radiotherapy for canine adrenocortical tumours with vascular invasion. J Small Anim Pract. 57(12):710–717.
5. Dolera M, Malfassi L, Mazza G, Urso G, Sala M, et al. (2016) Feasibility for using hypofractionated stereotactic volumetric modulated arc radiotherapy (VMAT) with adaptive planning for treatment of thymoma in rabbits: 15 cases. Vet Radiol Ultrasound. 57(3):313–20.

Biography

Mario Dolera completed his degree in Veterinary Medicine, Specialist in Pathology and Clinical of Animal of Affection (Orthopedics), PhD Veterinary Clinical Sciences (Neurology). Head of La Cittadina Fondazione Studi e Ricerche Veterinarie Romanengo (neuroscience, imaging and radiation oncology). Author of 40 scientific publications and 14 conference communications.

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Hassan Chaddad, J Cancer Sci Ther 2018, Volume 10
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Combining 2D angiogenesis and 3D osteosarcoma microtissues to improve vascularization

Hassan Chaddad
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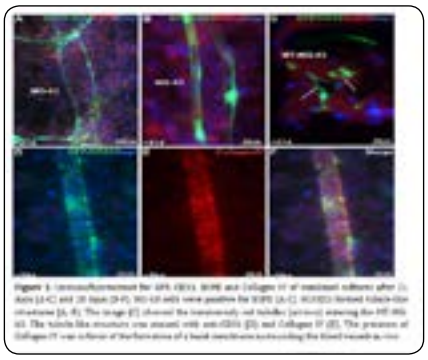
Introduction: The number of patients suffering from cancers worldwide is increasing, and one of the most challenging issues in oncology continues to be the problem of developing active drugs economically and in a timely manner. Considering the high cost and time-consuming nature of the clinical development of oncology drugs, better pre-clinical platforms for drug screening are urgently required. So, there is need for high-throughput drug screening platforms to mimic the *in vivo* microenvironment. Angiogenesis is now well known for being involved in tumor progression, aggressiveness, emergence of metastases, and also resistance to cancer therapies.

Materials & Methods: In this study, to better mimic tumor angiogenesis encountered *in vivo*, we used 3D culture of osteosarcoma cells (MG-63) that we deposited on 2D endothelial cells (HUVEC) grown in monolayer. Combination of 2D HUVEC/3D MG-63 was characterized by indirect immunofluorescence, scanning electron microscopy, optical microscopy and mRNA expression (qPCR).

Results: We reported that endothelial cells combined with tumor cells were able to form a well-organized network, and those tubule-like structures corresponding to new vessels infiltrate tumor spheroids. These vessels presented a lumen and expressed specific markers as CD31 and collagen IV. The combination of 2D endothelial cells and 3D microtissues of tumor cells also increased expression of angiogenic factors as VEGF, CXCR4 and ICAM1.

Conclusion: The cell environment is the key point to develop tumor vascularization *in vitro* and to be closer to tumor encountered *in vivo*.



Biography

Hassan Chaddad has completed his Pharmacy Degree from Lebanese International University (LIU) and his Masters in Pharmacology from USEK University in Lebanon. He is now pursuing his PhD from Strasbourg University, Faculty of Medicine (France).

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Fikri Sekcuk Simsek et al., J Cancer Sci Ther 2018, Volume 10
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The important overlapping problem between malign and benign thyroidal nodules in cancer patients with FDG-PET/CT

Fikri Sekcuk Simsek[1] and **Yavuz Narin**[2]
[1]Firat University, Turkey
[2]Elazig Medical Park Hospital, Turkey

Statement of the Problem: Thyroidal nodules are often detected in patients referred for another disease called incidentaloma. The nodule frequency in autopsies is as high as 50%. Due to advances in imaging methods, the numbers of detected nodules have been increasing and this affects cancer patients, too. Widespread use of FDG-PET/CT in these patients, which provides the opportunity of full body imaging are one of the main factors of this. In patients who already have malignancy, characterization of incidentalomas is an important problem. The low FDG uptake of normal thyroid tissue suggests that PET/CT may be useful in characterizing thyroidal incidentalomas. However, increased FDG uptake in some benign conditions makes it difficult. In this study, we aimed to reveal a clinical problem that may occur if the characterization of thyroidal incidentaloma in cancer patients performed with FDG-PET/CT.

Methodology & Theoretical Orientation: FNAB/histopathology results of 16/33 patients with incidentaloma who had elevated thyroidal FDG uptake shown by FDG-PET/CT were evaluated. Five patients had histopathological evaluation, 11 had cytological evaluation and 17/33 patients didn't have any pathological result.

Findings: 4/16 patients were diagnosed with malignancy, 3/16 non-specific atypical changes and 9/16 benign incidentaloma. SUVmax of benign nodules was between 3.22–16.94 and malignant nodules were between 3.57–12.52. When results were thoroughly analyzed, 3/9 (33%) of the benign incidentalomas had higher SUVmax than all malignant nodules (13.16, 16.83, 16.94). In addition, 7/9 (77.8%) benign nodules had higher SUVmax than malignant nodule with SUVmax 3.57.

Conclusion & Significance: There is a considerable overlap in SUVmax of thyroidal incidentalomas in cancer patients. Thus, we propose that, characterization of thyroidal nodules based on SUVmax cannot be a reliable approach.

Recent Publications

1. Chun A Reum, Jo Hye Min, Lee Seoung Ho, Chun Hong Woo, Park Jung Mi, et al. (2015) Risk of malignancy in thyroid incidentalomas identified by fluorodeoxyglucose-positron emission tomography. Endocrinol Metab 30:71–77.
2. Inga-Lena Nilsson, Fabian Arnberg, Jan Zedenius and Anders Sundin (2011) Thyroid incidentaloma detected by fluorodeoxyglucose positron emission tomography/computed tomography: Practical Management Algorithm World J Surg. 35:2691–2697.
3. Nakamoto Y, Tatsumi M, Hammoud D, Cohade C, Osman M M, et al. (2005) Normal FDG distribution patterns in the head and neck: PET/CT evaluation. Radiology 234:879–85.
4. Mortensen J D, Woolner L B, Bennett W A (1955) Gross and microscopic findings in clinically normal thyroid glands. J Clin Endocrinol Metab. 15:1270–1280.

Biography

Fikri Selcuk Simsek completed his Bachelor's, Master's and Doctorate Degrees from Eskişehir Osmangazi University, Medicine Faculty. Presently, he is working as an Assistant Professor in Nuclear Medicine Department at the Firat University. His expertise is cancer evaluation with PET/CT scanning, differentiated thyroidal carcinomas, benign thyroidal disorders, and radionuclide therapeutic approaches. He has published approximately 25 scientific articles and given oral speeches.

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Aye Myat Thwe, J Cancer Sci Ther 2018, Volume 10
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EGF and TGFα motogenic activities are mediated by the EGF receptor: Identification of the signaling pathways involved in oral cancer

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University of Dundee, UK

Epithelial to mesenchymal transition (EMT) is the process by which cells change shape from being tightly connected epithelial cells to more motile mesenchymal cells. EMT has been reported to facilitate cancer cell migration. Cell motility is an initial first step on the road to metastasis. Epidermal growth factor (EGFR) has been reported to be overexpressed in oral cancer and is often related with poor prognosis. Epidermal growth factor (EGF) and transforming growth factorα (TGFα) are ligands that bind to EGFR and can affect a number of different cellular processes, including cell proliferation, migration, angiogenesis and inhibition of apoptosis. We aimed to measure proliferation, migration, morphology change of HSG, AZA1, HaCaT, TYS, by cell counting, photo microscopic image capturing and scratch assay in relation with addition of growth factors at 1 ng/ml, 10 ng/ml, 50 ng/ml and 24 hrs, 48 hrs, 72 hrs. 50 ng/ml of growth factors induce cell morphology changes EMT like phenotype with finger like projection, cell scattering and increase cell migration while no reliable different in cell proliferation. These morphology changes are completely blocked by one hour pre-treatment with 5 μM gefitinib (EGFR tyrosine kinase inhibitor, 5 μM erlotinib (EGFR kinase inhibitor) and PD25 μM (inhibitors of MEK1 and MAKP kinase) in HSG and AZA1 cell lines. The cell migration of TYS and HSG cell lines are completely blocked by one hour pre-treatment with one hour pre-treatment with 5 μM gefitinib (EGFR tyrosine kinase inhibitor, 5 μM erlotinib (EGFR kinase inhibitor) and PD25 μM (inhibitors of MEK1 and MAKP kinase).

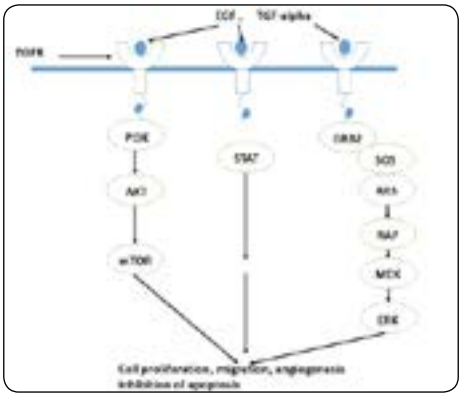

Figure 1: EGFR signaling in oral cancer.

Biography

Aye Myat Thwe graduated from Myanmar with a Bachelor of Dental Surgery in 2010. After practicing as a Dentist for two years, she came to UK to study at University of Dundee. She received an MRes in Oral Cancer, and progressed into the PhD programme. She is now in the 3rd year of her PhD programme.

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Devashish Sengupta, J Cancer Sci Ther 2018, Volume 10
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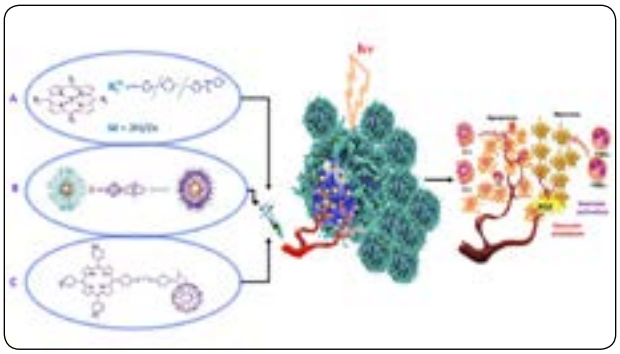
Role of free-base and metallated porphyrin derivatives promoting apoptosis as a consequence of cancer photodynamic therapy: Synthesis, characterization, and photobiological activities

Devashish Sengupta
Assam University, India

Structural modifications of free-base and metallated hydrophilic porphyrin macrocycles: (a) with combinations of different cationic/anionic/neutral aromatic functions at the meso-positions, (b) capable of forming nanocomposites with Fe3O4 nanoparticles, and (c) functionalized with fullerenes through linkers via electrovalent or covalent interactions are designed, synthesized, isolated and characterized. Redshifts of absorption wavelengths beyond 640 nm along with the production of high quantum yields of singlet oxygen were achieved through the mentioned modes of derivatization of porphyrins under photodynamic conditions. Upon treatment of various cancer cell lines with these photosensitizers (PSs), some of them demonstrated significant ability to upregulate cellular reactive oxygen species (singlet oxygen) along with the promotion of apoptosis. The structure-activity relationship (SAR) that evolved between the photochemistry, photophysics and photobiological activities of these derivatives is indicative of their roles as well-suited candidates for non-invasive targeted oncological photodynamic therapy (PDT). Efficient accumulation of some of these PSs into the oxygen-rich cell organelles like mitochondria, further establish their potentials as possible alternatives to the commercially used PSs to treat malignant tumors in cancer PDT.



Recent Publications

1. Sengupta D, Mazumdar Z H, Mukherjee A, Sharma D, Halder A K, et al. (2018) Benzamide porphyrins with directly conjugated and distal pyridyl or pyridinium groups substituted to the porphyrin macrocycles: Study of the photosensitising abilities as inducers of apoptosis in cancer cells under photodynamic conditions. Journal of Photochemistry and Photobiology B 178:228–236.
2. Mazumder Z H, Chattopadhayaya S, Sharma D, Banerjee S and Sengupta D (2017) Synthesis of unsymmetrical water-soluble cationic pyridinium mesoporphyrinic free-base porphyrins and its Zn (II) complex: photophysical and photocytotoxicity evaluation. IOSR Journal of Applied Chemistry (IOSR-JAC) 10(7):43–50.

Biography

Devashish Sengupta has completed his PhD from The University of Sydney, Australia, under the supervision of Professor Peter A Lay. He is currently working as an Assistant Professor at the Department of Chemistry, Assam University, Silchar, Assam, India. His research interests include the photobiochemistry related to cancer photodynamic therapy, and antiviral activities of synthetic amphiphilic photosensitizers like fullerenes, porphyrins, porphyrin analogues, and other bioactive synthetic derivatives.

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Aurelija Vaitkuviene et al., J Cancer Sci Ther 2018, Volume 10
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Natural fluorescence for cancer diagnosis

Aurelija Vaitkuviene and **J V Vaitkus**
Vilnius University, Lithuania

Digitalization of human body samples evaluation fits to personalized medicine requirements by person's and sample data use in diagnostic algorithm. Fluorescence spectroscopy techniques are under intense introduction into the smart applications for everyday life. Cancer was one of the target areas. Endometrial pathology was an area where chemical dynamics of changes in the tissues was well recognized. Endometrial tissue samples, also endometrial washing were tested by fluorescence spectroscopy to create diagnostic algorithms, based on pathology standards. Both endometrial objects were successfully classified for benign vs. malignant condition recognition with proper accuracy. For cervical cancer prevention, both *in vivo* and *in vitro* fluorescence diagnostics devices and programs were created by local and international resources. While imaging technologies manifested as far-off practical application, the cervical smear spectroscopy was revealed to be reasonable for, at point of care application. The special diagnostic program creation for smear discrimination resulted in automatization of diagnostics, which further could be applied for data clouding and application in remote regions by health care personnels. The so called "optical biopsy" technology is the example of space science landing on the human utility level, where pure molecular information is classified by "golden standard" of pathology means. So medical experience transfer into modern technology results in the expansion of highest standards application globally.

Biography

Aurelija Vaitkuviene PhD, MD is affiliated as a Senior Researcher at Vilnius University. She graduated from the Vilnius University, defended PhD thesis in 1984 and later trained at Wensky Laser Center in Chicago, Northwestern University (USA), at Lund University (Sweden). She is a Founding Member of the International Academy for Laser Medicine and Surgery (Florence, Italy), Past President of International Society for Laser Surgery and Medicine, and was a President of the International Phototherapy Association (IPTA), served Vilnius University as a Representative for European Cervical Cancer Association (ECCA). She has published more than 40 papers in scientific journals.

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Notes:

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Day 2

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Christopher S Lange

Downstate Medical Center, Brooklyn, NY, USA

Applying Koch's postulates to test the cancer stem cell basis of cancer

We tested the cancer stem cell (CSC) hypothesis using the patented Hybrid Spheroid (HS) Assay (HSA) and by applying Koch's postulates to test its validity. The HSA is an *in vitro* assay that enables one to take a viable sample of an individual patient's tumor, make a single cell suspension, mix it in known proportions with human fibroblasts (AG1522) and dispense a known number of cells of the mixture into each well of ultra low attachment (ULA) 96-well plates to agglomerate into 1 HS/well, each containing an average of <1 CSC. The HS provides an analog of the CSC niche, enabling the CSC to proliferate (with some daughters differentiating into amplifying transit cells (ATCs)) and undergo 10–15 symmetric divisions before exhausting the nutrients. This satisfies the McCulloch and Till (spleen colony assay) requirements for a stem cell. Applying Koch's postulates, we answer the following questions: Does the patient's tumor contain cells with CSC properties?; Can we isolate and propagate these cells?; Can these cells induce the tumor *in vivo*?; Do these cells contain and express specific gene products that give them CSC properties?; If we disrupt these genes, do the cells lose their CSC properties?; If we eliminate the CSCs do we eliminate the cancer? The HSA was applied to tumor samples taken from individual endometrial adenocarcinoma patients and correctly predicted, based on CSC radioresistance, in patients who fail their standard-of-care treatments. It was therefore concluded that the CSC hypothesis is validated in the HSA.

Biography

Christopher S Lange is the Associate Chair, Department of Radiation Oncology, SUNY Downstate Medical Center, Brooklyn (2010–Present), Professor of Molecular and Cell Biology, School of Graduate Studies, SUNY Downstate Medical Center (1992–Present), Professor, Director, Radiobiological Division, Department of Radiation Oncology, SUNY Downstate Medical Center (1980–Present), Associate Director, Residency Program, SUNY Downstate Medical Center (2009), Assistant Professor of Radiology, Radiation Biology and Biophysics, University of Rochester School of Medicine and Dentistry, New York (1969–1980), NHS Senior Research Officer, Christie Hospital and Holt Radium Institute, Manchester, England (1968–1969), NHS Research Officer, Christie Hospital and Holt Radium Institute, Manchester, England (1962–1968), MRC Research Assistant, Radiobiology Laboratory, Churchill Hospital, Headington, England (1961–1962).

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Scientific Tracks & Abstracts
Day 2

Euro Cancer 2018

Sessions:

Clinical Oncology | Chemotherapy | Cancer Screening

Session Chair
Jaime Tisnado
Virginia Commonwealth University, USA

Session Chair
Kang-Yell Choi
Yonsei University, South Korea

Session Introduction

Title: ***In vivo* quantitation of circulating tumor cells with high-speed confocal microscopy in mouse tumor model**
Howon Seo, Korea Advanced Institute of Science and Technology, South Korea

Title: **A new disulfide-stabilized diabody against bFGF and the inhibition of cancer**
Ning Deng, Jinan University, China

Title: **Through which pathway does Trastuzumab and miR-122-5p combinatorial administration lead breast cancer cells to apoptosis: Intrinsic or extrinsic pathway?**
Sercan Ergun, Ordu University, Turkey

Title: **Investigation of piR-36707 and piR-36741 expression levels in renal cell (Transparent Cell Type) carcinomas**
Diler Us Atlay, Ordu University, Turkey

Title: **Leptin receptor antagonist as a potent histone deacetylases (HDACs) inhibitor in ovarian cancer cells**
Ewa L Gregoraszczuk, University in Kraków, Poland

Title: **Comparing BRAF mutation status in corresponding primary and metastatic cutaneous melanomas: Implications on optimized targeted therapy**
Ibrahim Khalifeh, American University of Beirut Medical Center, Lebanon

Howon Seo, J Cancer Sci Ther 2018, Volume 10
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In vivo quantitation of circulating tumor cells with high-speed confocal microscopy in mouse tumor model

Howon Seo
Korea Advanced Institute of Science and Technology, South Korea

The circulating tumor cells (CTCs) have been considered as a seed for cancer metastasis and the level of CTCs in metastatic cancer patients has been considered as a valuable indicator for predicting the grade of cancer metastasis, efficacy evaluation of anti-cancer therapy, and potential early diagnosis of cancer recurrence. Currently, ex vivo isolation of CTCs based from a peripheral blood sample has been a major strategy for the quantitation of CTCs. However, accurate quantitation of rare CTCs, as few as 1~2 cells per ml of blood sample in patients with metastatic cancer, is technically challenging and suffers extremely low sensitivity. These limitations can be overcome by using intravital flow cytometry which provides direct detection and quantitation of circulating cells in blood flow. For direct observation of fast-flowing cancer cells in the bloodstream, a custom-built high-speed video-rate laser-scanning confocal microscope system was implemented. After the intravenous injection of cancer cells and long circulating reference cells such as red blood cells (RBCs), a dynamically changing number of circulating cancer cells and RBCs was continuously monitored by real-time imaging. By extracting the calibration factor from hemocytometric imaging analyses with intravenously injected RBCs, we could estimate the level of intravenous injected CTCs in the whole blood of a mouse. To evaluate the degrees of cancer metastases with *in vivo* CTC-quantitation approach, an orthotopic tumor mouse model was used. The dynamic change of metastatic CTC-level was observed during a few hours and the longtitudinal change of metastatic CTC was monitored in a single mouse, *in vivo*.

Biography

Howon Seo is pursuing an Integrated Master's and Doctoral Degree program at Korea Advanced Institute of Science and Technology in South Korea. He completed his Bachelor's Degree in Biochemistry and has worked in intravital imaging of circulating tumor cells with high-speed confocal microscopy. He is interested in the study of cancer metastasis and metastatic cancer therapy.

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Notes:

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29th Euro-Global Summit on

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July 23-25, 2018 | Rome, Italy

A new disulfide-stabilized diabody against bFGF and the inhibition of cancer

Ning Deng
Jinan University, China

Angiogenesis plays a critical role in tumor growth. Fibroblast growth factor-2 (FGF-2) is one of the most important angiogenic factors. The over-expression of bFGF plays a crucial role to promote tumor growth, progression and metastasis. Neutralizing antibodies against FGF-2 may suppress the growth of tumor cells by blocking the FGF-2 signaling pathway. In our lab, we scanned human anti-bFGF antibody from the phage antibody library. The results showed that the human anti-bFGF antibody could significantly inhibit the tumor angiogenesis and inhibit the tumor growth and migration. Based on this antibody, a newly small molecular antibody of disulfide-stabilized diabody (ds-Diabody) against bFGF was constructed by site-directed mutation and overlap extension PCR (SOE-PCR) at the position of VH44 and VL100 in the scFv. The ds-Diabody was expressed in *Pichia pastoris* system. We found that the ds-Diabody against bFGF could maintain good antigen binding activity and stability *in vitro* and *in vivo*. The ds-Diabody against bFGF could efficiently suppress the proliferation, migration and invasion of human lung cancer (A549 cells) and breast cancer (MCF-7 cells), inhibit bFGF-induced activation of downstream signaling regulators, phospho-Akt and phospho- MAPK. In the nude mouse xenograft model, the ds-Diabody against bFGF could significantly inhibit tumor growth, tumor angiogenesis and lymphangiogenesis. The ds-Diabody against bFGF showed stability *in vivo* and could more effectively suppress the tumor growth through blockade of bFGF signaling pathway and inhibition of tumor angiogenesis, which may make it a potential therapeutic candidate antibody drug for human lung cancer therapy.

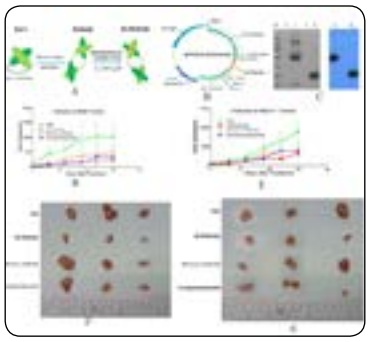

Figure 1: Construction and function of ds-Diabody against bFGF. A construction of ds-Diabody; B expression vector; C expression of ds-Diabody; D growth curve of lung cancer; F growth curve of breast cancer; F tumors of lung cancer; G tumors of breast cancer

Recent Publications:

1. Yaxiong Cai, Shuange Yao, Ning Deng, et al. (2017) Inhibition activity of a disulfide-stabilized diabody against basic fibroblast growth factor in lung cancer. Oncotarget 8(12): 20187–20197.

2. Yinghua Li, Zhengfang Lin, Ning Deng and Bing Zhu (2017) Delivery of VP1 siRNA to inhibit the EV71 virus using functionalized silver nanoparticles through ROS mediated signaling pathways. RSC Adv. 7:1453–1463.

3. Yaxiong Cai, Jinxia Zhang, Ning Deng (2016) Construction of a disulfide-stabilized diabody against fibroblast growth factor-2 and the inhibition activity in targeting breast cancer. Cancer Science 107(8):1141–1150.

4. Shoumei Bai, Patrick Ingram, Yu-Chih Chen, Ning Deng and Ronald J Buckanovich (2016) EGFL6 regulates the asymmetric division, maintenance, and metastasis of ALDH+ovarian cancer cells. Cancer Res. 76(21):6396–6409.

5. Chuping Zheng, Jinsheng Wang, Ning Deng and Jie Liu (2014) Functional selenium nanoparticles enhanced stem cell osteoblastic differentiation through BMP signaling pathways. AdvancedFunctional Materials 24(43):6872–6883.

Biography

Ning Deng has his expertise in antibody drug and tumor polypeptide vaccine around tumor angiogenesis inhibition. He has established antibody design and construction system, included the phage antibody library, affinity maturation and improvement based on antibody structural simulation, evaluation system for tumor peptide vaccine. He also researched on the mechanism of tumor angiogenesis in ovarian cancer and stem cell evaluation.

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Notes:

Sercan Ergun, J Cancer Sci Ther 2018, Volume 10
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Through which pathway does trastuzumab and miR-122-5p combinatorial administration lead breast cancer cells to apoptosis: Intrinsic or extrinsic pathway?

Sercan Ergun
Ordu University, Turkey

Statement of the Problem: In most of breast cancer cells, HER2 receptors are known to be cleaved by an ectodomain sheddase, ADAM10, to liberate HER2 extracellular domain (ECD). This provides ligand-independent growth to breast cancer cells and trastuzumab, anti-HER2 agent, cannot inactivate HER2 by binding ECD portion of it. In our previous studies, we found that miR-122-5p, miRNA targeting ADAM10, and trastuzumab combinatorial administration to HER2-positive breast cancer cell line, SKBR3, increases the efficiency of trastuzumab by leading SKBR3 cells to apoptosis more through blocking the sheddase activity of ADAM10 on HER2. The aim of this study is to display that miR-122-5p, together with trastuzumab, leads SKBR3 cells apoptosis by which pathway: intrinsic or extrinsic.

Methodology & Theoretical Orientation: SKBR3 cells were first transfected with the miR-122-5p mimic for 48 hours. Then, 0.5 μM trastuzumab was applied to miR-122-5p-transfected SKBR3 cells and non-transfected SKBR3 cells for 24 hours. Next, the expression levels of CASP3, *CASP8* and *CASP9* genes, which are key molecules in apoptotic pathway, were examined by real-time PCR.

Findings: Expression levels of *CASP3* and *CASP8*, but not *CASP9*, increased significantly in miR-122-5p-transfected Trastuzumab-administered SKBR3 cells when compared to non-miR-122-5p transfected Trastuzumab-administered SKBR3 cells. A significant increase in the expression level of *CASP8* with *CASP3* showed apoptosis to be activated via extrinsic pathway (instead of the mitochondrial intrinsic pathway regulated by *CASP9*) with the effect of miR-122-5p in trastuzumab-administered SKBR3 cells.

Conclusion & Significance: Consequently, the apoptosis enhancing effect of trastuzumab and miR-122-5p combinatorial administration through extrinsic pathway may be presented as a new treatment option for HER2+ breast cancer.

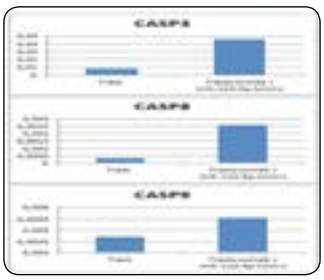

Figure 1: Comparison of expression levels of *CASP3, 8, 9* genes between SKBR3 cells administered with trastuzumab and trastuzumab + miR-122-5p-mimic.

Recent Publications:

1. Ergun S, et al. (2014) Expression patterns of miR-221 and its target caspase-3 in different cancer cell lines. Mol Biol Rep. 41:5877–5881.
2. Wang B, et al. (2012) MiR-122 inhibits cell proliferation and tumorigenesis of breast cancer by targeting IGF1R. PLoS One 7(10):e47053.
3. Pollack M and Leeuwenburgh C (2001) Apoptosis and aging: role of the mitochondria. J Gerontol A Biol Sci Med Sci. 56(11):B475–B482.

Biography

Sercan Ergun is working as Teaching Assistant in Ordu University and is about to finish his PhD in Department of Medical Biology and Genetics of Ondokuz Mayıs University. He was included as Researcher in a team studying briefly epigenetic changes in disease mechanisms of different types of cancers, including oncogenic/tumor suppressor gene and miRNA expression level changes, cell death mechanism analysis, development of some cancer therapy agents' efficiencies via miRNAs. Now, he is part of a team studying *in silico* miRNA and ceRNA analysis, miRNA heterogenetiy, piRNA expression changes in different cancer types, especially urological cancers. He has many published many articles related to these studies. He and his team have conducted many studies on different diseases other than cancer, like Glanzmann's thrombasthenia, hemophagocytic lymphohistiocytosis, immune thrombocytopenic purpura, familial mediterranean fever, βeta (β)-thalassemia, secondary hyperparathyroidism and he has many other articles on them.

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Notes:

Diler Us Altay et al., J Cancer Sci Ther 2018, Volume 10
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Investigation of piR-36707 and piR-36741 expression levels in renal cell (transparent cell type) carcinomas

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[1]Ordu University, Turkey
[2]Ondokuz Mayıs University, Turkey

Background: Piwi interacting RNA (piRNA) is the main class of small non-coding RNA molecules expressed in animal cells. Some of the piRNAs expression increases and shows oncogenic properties; while on the other hand, some of their expression decreases and shows tumorigenic properties in specific cancer types.

Objective: The present research is in comparison within normal and tumor renal biopsy specimens taken from patients with clear cell renal cell carcinoma (RCC), and in kidney tissue samples of non-transfected RCC patients who were operated for different reasons, two possible piRNAs (piR -36707 and piR-36741) expression levels, which are not related before but probably related to RCC.

Methodology & Theoretical Orientation: Between January 2016 and January 2017, formalin-fixed paraffin embedded (FFPE) specimens were obtained from 19 patients who had undergone partial or radical nephrectomy for diagnostic purposes and who had a clear cell RCC diagnosis in urology and pathology in the Ondokuz Mayıs University, Faculty of Medicine (OMÜTF). Tumor tissue sample and a healthy tissue sample from the same patient were included in the study. FFPE was made from tissue using a total RNA isolation kit. The piRNA-specific cDNA synthesis kit was used to convert the resulting piRNA into cDNA. piR-36707 and piR-36741 expression levels were measured using commercially available primers and real-time PCR kit specific to these piRNAs. Statistical significance analysis of the levels of piRNA expression was performed between the two groups.

Findings: Expression levels of piR-36707 and piR-36741, calculated by the comparative 2-ΔΔCt curve between tumor and normal kidney tissues, are given in comparison in Figure 1. The higher expression levels of piR-36707 and piR-36741 in tumor tissues than normal tissues give them a potential oncogenic function. However, when this relationship was examined by statistical methods, it was seen that p value was above 0.05 for both piRNAs and these changes were not significant.

Conclusion & Significance: According to the literature, this is the first study that relates to clear cell RCC pathogenesis and piR-36707 and piR-36741 genes. Prospectively, all genes in the target of piR-36707 and piR-36741 are studied as panels to achieve universal and comprehensive data for the pathogenesis of clear cell RCC.

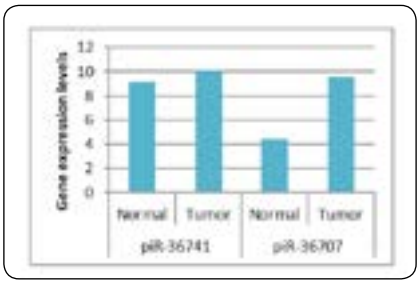

Figure 1: Comparison of expression levels of piR-36741 and piR-36707 between tumor and normal kidney tissues.

Recent Publications:

1. Ciccarese C, et al. (2016) The prospect of precision therapy for renal cell carcinoma. Cancer Treatment Reviews 49:37–44.
2. Parekh H and Rini B I (2016) Emerging therapeutic approaches in renal cell carcinoma. Expert Review of Anticancer Therapy 15(11):1305–14.

3. Yang X, et al. (2015) Detection of stably expressed piRNAs in human blood. International Journal of Clinical and Experimental Medicine 8(8):13353–13358.
4. Siddiqi S and Matushansky I (2012) Piwis and piwi-interacting RNAs in the epigenetics of cancer. Journal of Cellular Biochemistry 113(2):373–80.

Biography

Diler U S Altay is working as Assistant Professor in Ordu University. She completed her primary, secondary and high school education in Ordu. She graduated from the Department of Biochemistry at Ege University, Turkey. After working in the private sector for a short time, she completed her PhD in the Department of Biochemistry at Karadeniz Technical University in 2015 and was appointed as Assistant Professor at Ordu University in January 2016. She is still continuing her studies at Ordu University. She has published articles in three national and 19 international journals. Her work areas include cancer modeling, cachexia, weight loss hormone, oxidant-antioxidant system in animals.

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Notes:

Ewa L Gregoraszczuk et al., J Cancer Sci Ther 2018, Volume 10
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Leptin receptor antagonist as a potent histone deacetylases (HDACs) inhibitor in ovarian cancer cells

Ewa L Gregoraszczuk, K Zajda and **E Fiedor**
Jagiellonian University, Poland

Post-translational histone modifications can play an important role in the cancer development. Leptin, produced by adipose tissue has been identified as a growth factor in certain hormone related cancers including ovarian cancer. Currently, several groups of scientists are working on synthesizing leptin receptor blockers, and number of leptin receptor antagonist were tested in breast, colon and prostate cancer, suggesting their future use in anticancer therapy. The question arises whether the leptin receptor blockers may also act as inhibitors of HDAC in ovarian cancer. As a model we used the epithelial ovarian cancer (chemoresistant-OVCAR-3 and primary-CaOV-3) and folliculoma (adult –KGN and juvenile- COV434) cell lines. Two antagonists: superactive human leptin antagonist-SHLA and quadruple leptin mutein -LAN 2 (L39A/D40A/F41A/I42A have been applied. Particular cell lines were treated with leptin in a dose of 40 ng/ml (noted in obese women) and antagonist in a dose 1000 ng/mL Effect of blockers on *HDACs (1,2,3,4,5,6 7,8,9)* gene (real time PCR) and protein expression (western blot) were tested, HDACs expression was higher in OVCAR-3>CaOV-3, and higher in COV434>KGN. Leptin increased *HDAC 1, 7* and *9* gene expression only in OVCAR-3, while in granulosa tumour cells increased *HDAC 2, 6, 7* in KGN and 9 in COV434. SHLA was the most potent HDACs inhibitor in OVCAR-3 cells and reversed stimulatory effect of leptin on *HDAC1, 9* gene, and *HDAC4, 5* protein expressions. In granulosa tumor cells, Lan-2 seemed to be most potent inhibitor. Reversed stimulatory effect of leptin on HDAC9 gene expression and *HDAC 1, 5* protein expression in COV434 cells in KGN cell line both antagonist reversed stimulatury effect of leptin on *HDAC 5, 6, 7*. It was concluded that leptin receptor antagonist as HDACs inhibitors should be emerged as an exciting new class of potential anticancer agents. However, histopatological type of cancer should be taken into consideration in the choice of leptin receptor inhibitors.

Recent Publications:

1. Fiedor E and Gregoraszczuk E L (2017) Superactive human leptin antagonist (SHLA), triple Lan1 and quadruple Lan2 leptin mutein as a promising treatment for human folliculoma Cancer Chemother Pharmacol 80:815–827.
2. Fiedor E and Gregoraszczuk E L (2016) The molecular mechanism of action of superactive human leptin antagonist (SHLA) and quadruple leptin mutein Lan-2 on human ovarian epithelial cell lines. Cancer Chemother Pharmacol. 78:611–622.

Biography

Ewa L Gregoraszczuk specializes in Reproductive Endocrinology as well as Hormone Dependent Cancer. She graduated from the Jagiellonian University in Krakow, Poland. From 1998, she has been the Professor of Endocrinology, Head of Department of Physiology and Toxicology of Reproduction. She has authored 173 peer-reviewed articles in leading journals such as Biology of Reproduction, Reproduction, Reproductive Toxicology, Toxicology, Cancer Chemotherapy and Pharmacology. She is a Member of the Polish Endocrinology Society, International Society of Endocrinology (ISE), The New York Academy of Sciences, and The European Tissue Culture Society. She has been a Promoter for 60 MD, 16 PhD and 3 Habilitations. Her research topics are focused on the effects of metabolic hormones produced by adipose tissue in light of the increasing incidence of obesity and related problems in reproduction and hormone dependent cancer; reprotox and canceriogenic action of endocrine disruptors, testing antiepileptic drugs as a potent anticancer in combination with chemotherapy; testing leptin receptor blockers as a novel treatment for ovarian cancer.

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Ibrahim Khalifeh, J Cancer Sci Ther 2018, Volume 10
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Comparing BRAF mutation status in corresponding primary and metastatic cutaneous melanomas: Implications on optimized targeted therapy

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Background: Selective oral BRAF inhibitors show promising results in the treatment of metastatic melanomas. Consequently, this mandates checking the concordance of BRAF status in primary (PM) and metastatic (MM) melanomas to optimize individual targeted therapy.

Design: Extended BRAF testing for 9 mutations on 95 lesions from 40 patients (men/women: 27/13; age= 59 13 years) including 40 PM with their corresponding MM (n=42), recurrences (n=9) and second primaries (n=4) was performed. Multiple metastatic sites were present in 9 patients [2 sites (n=6), 3 sites (n=2) and 4 sites (n=1)].

Results: BRAF mutation status was obtained for 85/95 (89.5%) lesions. V600E was the only identified mutation type documented in 35.4% of PM vs. 18.9% of MM. The overall PM-MM BRAF status discordance rate was 32.3% (11/34), and this was significantly more frequent in PM with mutant BRAF (8/12; 67%) versus PM with wild-type BRAF (3/22; 14%, p=0.005) Patients with metastasis to lymph nodes (3/20; 15%) were less likely to be discordant compared to those with metastasis to other sites (8/14; 57.1%, p=0.023). Females (7/13; 53.8%) were more likely to have discordant PM-MM BRAF status than males (4/21; 19%, p=0.06). Patient age was similar in patients with concordant and discordant BRAF status (58 13 vs. 62 14 years; p=0.41). PM anatomic location (p=0.23) and time-to-metastasis (p=0.55) were also unrelated to PM-MM BRAF mutation discordance. Discordant BRAF mutation status was predicted by multivariate binary logistic regression: 1) the presence of a mutant BRAF in PM [OR (95% C.I.) = 23.4 (2.4-229.7)] and 2) male gender [OR = 0.094 (0.01-0.93)]. MM-MM BRAF concordance was available for 6 possible comparisons and displayed a 100% concordance rate.

Conclusion: A high discordant rate implies the need for re-testing of the MM before initiation of BRAF targeted therapy. High MM-MM concordance advocates that testing the most accessible metastatic site is sufficient to obtain accurate BRAF mutation status.

Recent Publications:

1. Zgheib E, Habib R, Moukarbel R and Khalifeh I (2016) Old world leishmaniasis: an ancient disease with nonstandardized microscopic and clinical classifications. J Cutan Pathol. 43(10):815–20.
2. Alam E, Abbas O, Moukarbel R and Khalifeh I (2016) Cutaneous leishmaniasis: an overlooked etiology of midfacial destructive lesions. PLoS Negl Trop Dis. 10(2):e0004426.
3. Saroufim M, Charafeddine K, Issa G, Khalifeh H, Habib R, et al. (2014) Ongoing epidemic of cutaneous leishmaniasis among Syrian refugees, Lebanon. Emerging Infectious Diseases 20(10).
4. Antar A, El Hajj H, Jabbour M, Khalifeh I, El-Merhi F, et al. (2014) Primary effusion lymphoma in an elderly patient effectively treated by lenalidomide: case report and review of literature. Blood Cancer Journal 4(3).
5. El Khoury J, Khalifeh I, Kibbi A G and Abbas O (2013) Cutaneous metastasis: clinicopathological study of patients from a tertiary care center in Lebanon. Int J Dermatol. doi: 10.1111/j.1365-4632.2012.05650.x.

Biography

Ibrahim Khalifeh After earning his MD from Damascus Medical School in 1999, completed a surgery internship (2000-2001) and pathology residency (2001-2002) at American University of Beirut Medical Center. In 2002, he left for the USA where he did four years of training in Pathology and Laboratory Medicine at Wayne State University in Detroit (2002-2006), Oncologic Pathology and Cytopathology fellowships at MD Anderson Cancer Center (2006-2008) then he joined the University of Alabama where he completed one year of fellowship in Dermatopathology (2008-2009). Dr. Khalifeh is a diplomat of the American Board of Anatomic and Clinical Pathology, Cytopathology and Dermatopathology. He joined the Department of Pathology and Laboratory medicine at AUBMC in 2009 as assistant professor. He has been involved in multiple projects related to cutaneous leishmania, melanoma, dysplastic nevi and BRAF.

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July 23-25, 2018 | Rome, Italy

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Day 3

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Christopher S Lange, J Cancer Sci Ther 2018, Volume 10
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29th Euro-Global Summit on

Cancer Therapy & Radiation Oncology

July 23-25, 2018 | Rome, Italy

Christopher S Lange

Downstate Medical Center, Brooklyn, NY, USA

Cancer Stem Cells: How do we determine which cells they are?

Biography

Christopher S Lange is the Associate Chair, Department of Radiation Oncology, SUNY Downstate Medical Center, Brooklyn (2010–Present), Professor of Molecular and Cell Biology, School of Graduate Studies, SUNY Downstate Medical Center (1992–Present), Professor, Director, Radiobiological Division, Department of Radiation Oncology, SUNY Downstate Medical Center (1980–Present), Associate Director, Residency Program, SUNY Downstate Medical Center (2009), Assistant Professor of Radiology, Radiation Biology and Biophysics, University of Rochester School of Medicine and Dentistry, New York (1969–1980), NHS Senior Research Officer, Christie Hospital and Holt Radium Institute, Manchester, England (1968–1969), NHS Research Officer, Christie Hospital and Holt Radium Institute, Manchester, England (1962–1968), MRC Research Assistant, Radiobiology Laboratory, Churchill Hospital, Headington, England (1961–1962).

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29th Euro-Global Summit on

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Special Session

Day 3

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Ibrahim Khalifeh

American University of Beirut Medical Center, Lebanon

Monitoring immune response in tumors

There is growing awareness and importance of the input and insights of different specialties to understand and monitor tumor microenvironment and consequently understand the mechanisms of response and resistance to various cancer treatments. Although current immune monitoring strategies pose clinical challenges, advances in approaches and techniques are improving our ability to better understand immune responses in the tumor microenvironment. In addition to this, improvements in genomic profiling have allowed for a deeper understanding of the influence of mutational burden and other genomic factors on anti-tumor immunity. Continued progress in immune monitoring strategies will help us better understand who will benefit from therapy and will help guide rational choice of treatment as well as proper timing, sequence, and combinations of therapeutic regimens. With the increasing use of immunomodulatory agents in clinical practice, there is a growing interest in assessing anti-tumor immune responses via tissue-based and blood- based assays. However, complexities exist in this analysis, particularly when considering use of archival versus fresh tissue cryopreservation has been shown to alter certain immune cell subsets and cytokine profiles as well as gene expression profiles formalin fixed paraffin embedded (FFPE): mutational burden and neoantigen prediction, genomic variants are lost by using FFPE dynamic properties of the immune system and that archival tissue is often collected in advance of treatment of interest may make data obtained from archival tissue less relevant. This is particularly pertinent with the use of immune checkpoint inhibitors in clinical trials and in standard of care treatment, where assessment of programmed death receptor-1 ligand to determine treatment This may in part explain why clinical studies have produced varying results regarding utility of PD-L1 as a predictive biomarker for selection of patients in which archival tissue was often used for PD-L1 determination. Another rapidly emerging area of investigation that must be considered in the context of anti-tumor immune responses is the microbiome. The microbiome refers to the entire community of bacteria (and their genomes) within an organism, and the number of bacteria within a human outnumbers the number of human cells by at least 10:1. There is a growing role of the microbiome in health and disease, and evidence that the gut microbiome may shape anti-tumor immune responses as well as responses to immune checkpoint blockade and other immunotherapies. Tumor-microenvironment interactions require longitudinal assessment throughout the course of therapy. Optimize concordance between tissue-based and blood-based techniques to assess immune responses will offer better assessment and monitoring.

Biography

Ibrahim Khalifeh, after earning his MD from Damascus University's Medical School in 1999, completed a Surgery Internship (2000–2001) and Pathology Residency (2001–2002) at the American University of Beirut Medical Center. In 2002, he left for the USA where he did four years of training in Pathology and Laboratory Medicine at Wayne State University in Detroit (2002–2006), Oncologic Pathology and Cytopathology Fellowships at MD Anderson Cancer Center (2006–2008), and then he joined the University of Alabama where he completed one year of Fellowship in Dermatopathology (2008–2009). He is a diplomat of the American Board of Anatomic and Clinical Pathology, Cytopathology and Dermatopathology. He joined the Department of Pathology and Laboratory Medicine at AUBMC in 2009 as an Assistant Professor. He has been involved in multiple projects related to cutaneous Leishmania, melanoma, dysplastic nevi and BRAF.

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Scientific Tracks & Abstracts
Day 3

Euro Cancer 2018

Sessions:

Cancer Treatment | Cancer Diagnosis

Session Chair
Carina Mari Aparici
University of California, USA

Session Introduction

Title: **Cancer stem cell marker EpCAM is involved in resistance to chemotherapy and poor prognosis in ovarian cancer patients**
Takeshi Motohara, Kumamoto University, Japan

Title: **Selective Internal Radiation therapy (SIRT) in the Angiography Suite**
Grace Moscatelli, Western Sydney University, Australia

Title: **Targeting the AKT/mTOR/STAT3 pathways through a ROS- dependent Ubiquitin proteasome degradation in breast cancer by the natural polyphenol compound, carnosol**
Rabah Iratni, United Arab Emirates University, UAE

Takeshi Motohara, J Cancer Sci Ther 2018, Volume 10
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Cancer stem cell marker EpCAM is involved in resistance to chemotherapy and poor prognosis in ovarian cancer patients

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[2]University of Oxford, UK

The cancer stem cell hypothesis considers cancer stem cells as the main culprits of driving tumor initiation, metastasis, and resistance to conventional chemotherapy. Several previous studies have supported the premise that EpCAM proves to be a useful marker for the isolation of subsets enriched for cancer stem cells in many solid cancers, including ovarian cancer. We investigated the role of EpCAM in the resistance to platinum-based chemotherapy and the potential relevance of EpCAM to the clinical outcomes of patients with epithelial ovarian cancer. Here, we have showed that ovarian cancers containing high levels of EpCAM have a significantly much lower probability of achieving overall responsive rates after first-line platinum-based chemotherapy. Furthermore, multivariate analysis demonstrated that EpCAM expression in primary tumors is an independent risk factor for tumor resistance to chemotherapy, indicating that EpCAM expression is a predictive biomarker of chemotherapeutic response. Consistent with these clinical observations, in *in vitro* assays, we also found that treatment with chemotherapeutic agents enhances the cell surface expression of EpCAM in ovarian cancer cells. In association with anti-apoptotic mechanisms, the subpopulation of EpCAM-positive cancer cells showed a significantly higher viability than EpCAM-negative cells in response to chemotherapy. In an *in vivo* mouse model, platinum agents preferentially eliminated EpCAM-negative cells in comparison with EpCAM-positive cells, indicating that the remaining subpopulation of EpCAM-positive cells contributes to tumor recurrence after chemotherapy. Finally, we revealed that an increased expression of EpCAM in primary tumors was involved in a shortened overall- and progression-free survival in ovarian cancer patients. Our findings highlight the clinical significance of EpCAM in the resistance to chemotherapy and provide a rationale for EpCAM-targeted therapy to improve chemoresistance in ovarian cancer patients. Targeting EpCAM should be a promising approach to effectively eradicate the cancer stem cells as the putative root of ovarian cancer.

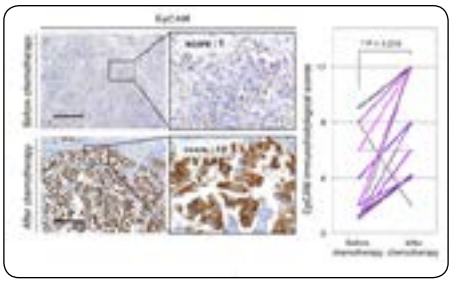

Figure 1: Immunohistochemical analysis with anti-EpCAM antibody of ovarian cancer tissues from patients treated without preoperative chemotherapy. Statistical analysis of the immunohistochemical scores of EpCAM in paired samples. The scores of EpCAM expression are significantly higher in ovarian cancer tissues from patients treated with chemotherapy than in those from matched patients treated without chemotherapy.

Recent Publications:

1. Tayama S, Motohara T, Fujimoto K, Narantuya D, Li C, et al. (2017) The impact of EpCAM expression on response to chemotherapy and clinical outcomes in patients with epithelial ovarian cancer. Oncotarget 8:44312–44325.
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3. Tjhay F, Motohara T, Tayama S, Narantuya D, Fujimoto K, et al. (2015) CD44 variant 6 is correlated with peritoneal dissemination and poor prognosis in patients with advanced epithelial ovarian cancer. Cancer Sci. 106:1421–1428.
4. Motohara T, Masuko S, Ishimoto T, Yae T, Onishi N, et al. (2011) Transient depletion of p53 followed by transduction of c-Myc and K-Ras converts ovarian stem-like cells into tumor-initiating cells. Carcinogenesis. 32:1597–1606.

Biography

Takeshi Motohara is Assistant Professor in Department of Obstetrics and Gynecology, Kumamoto University, Japan. He is now engaged in research on molecular biology of ovarian cancer in Ovarian Cancer Cell Laboratory, Weatherall Institute of Molecular Medicine, Nuffield Department of Obstetrics and Gynaecology, University of Oxford as a Visiting Postdoctoral Research Scientist. He is distinguished gynecologic oncologist in Japan. His research is focused on understanding the molecular mechanisms of evolution of ovarian cancer, especially cancer stem cell, and on the development of novel therapeutic strategies for ovarian cancer.

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Notes:

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Selective Internal Radiation therapy (SIRT) in the Angiography Suite

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Patients with isolated colorectal cancer (CRC) liver metastases require surgical resection as the treatment of choice when feasible. Unfortunately most patients are not surgical candidates for this treatment option due to tumour size, location, multifocality or insufficient hepatic reserve. One of the several nonsurgical treatment options available to patients who are unable to receive resection who have liver-isolated CRC metastases is a procedure known as Selective Internal Radiation Therapy (SIRT) also known as transarterial radioembolisation or radioembolisation. SIRT is a minimally invasive procedure performed in the angiography suite (similar to theatres) by an Interventional Radiologist (proceduralist). There are two parts: "work up" phase where the patient is assessed as an outpatient for suitability for the procedure then patient specific dose is ordered followed by the SIR-Spheres Y-90 resin microspheres implantation phase both performed in the angiography suite. The multidisciplinary team ensure that the patient is as comfortable and safe for the procedure ensuring an optimised journey during this vulnerable period for the patient.The radiologist initially gains arterial access through the groin which may be ultrasound guided and is followed by the introduction of guide wires and a thin catheter. Once the doctor identifies the hepatic artery which is the primary blood supply feeding the liver tumours, millions of radioactive microspheres or SIR-Spheres are implanted via the catheter directly to the liver tumours. The microspheres are about one third the diameter of a strand of hair in size. Beta radiation is a common type of radiation used in nuclear medicine therapy and diagnostic procedures. This procedure takes advantage of the fact that the portal vein is the primary blood supply for normal liver parenchyma and by selectively irradiating tumours, the surrounding healthy tissue will be relatively unaffected. The patient would normally have a baseline CT/ PET scan prior to the procedure followed by a progress scan between four weeks and three months post treatment. Although this treatment is not a permanent cure, there is a greater possibility for patients who have primary or secondary liver cancer to increase survival benefit in combination with quality of life and potentially undergo liver tumour resection or liver transplant as the tumour size reduces especially when combined with standard chemotherapy. Although this is normally a single treatment, some patients may be retreated with SIR-Spheres and procedural complications including pain and nausea may be treated with analgesia and antiemetics. Reduced appetite, fever or tiredness may also be experienced by the patient for several days post procedure though it is encouraged to maintain a healthy balanced diet.

Biography

Grace Moscatelli has completed her Bachelor of Nursing at University of Western Sydney and is currently studying Bachelor of Nursing with Professional Honours Specialising in Anaesthetic and Recovery Nursing at University Of Tasmania. She is a Registered Nurse working in the Radiology, Nuclear Medicine and PET department at a local Sydney hospital in Australia. She has presented at Medical Imaging Nurses Association National Conference in Melbourne in 2017.

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Notes:

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Targeting the AKT/mTOR/STAT3 pathways through a ROS-dependent ubiquitin proteasome degradation in breast cancer by the natural polyphenol compound, carnosol

Rabah Iratni, Hussain El Hasasna and **Halima Al Samri**
United Arab Emirates University, UAE

We have previously showed that carnosol significantly inhibited the viability and colony growth of triple negative breast cancer cells and induced ROS-dependent beclin-1-independent autophagy and subsequent apoptotic cell death. Here were analyzed the molecular mechanism through which carnosol exerts its anti-cancer activity. Mechanistically, we found that carnosol inactivated the AKT/mTOR pathway by promoting the proteasome-dependent degradation of both proteins. Strikingly, we also found that carnosol targets Stat3 to degradation. Proteasome inhibition restored these proteins to a level comparable to control cells. The proteasomal degradation of mTOR, which occurred as early as 30 minutes post- carnosol treatment was concomitant with an overall increase in the level of ubiquitinated proteins and translated stimulation of proteolysis by the proteasome. Interestingly, we found that the treatment of the breast cancer cells with N-acetylcysteine, an ROS inhibitor, not only restored AKT/mTOR/Stat3 proteins to a level comparable to control cells, but also dramatically reduced carnosol-induced cell death and blocked the activation of autophagy and apoptosis. Our findings demonstrate that carnosol exerts its anti-breast cancer activity through stimulation ubiquitin proteasome system which consequently triggers both autophagy and apoptosis, making it a potential and valuable source of novel therapeutic cancer drug.

Biography

Rabah Iratni completed his PhD in Cellular and Molecular Biology from the University Joseph Fourier Grenoble 1 (France) and Post-doctorate from the University of Medicine and Dentistry of New Jersey (USA). He is currently a Professor at the United Arab Emirates University. His lab focuses on the discovery of new biologically active natural products, to evaluate their potential as therapeutic agents against breast cancer and determine their mechanism(s) of action. He also has a strong interest in the understanding of the epigenetic basis of cancer with focus on breast cancer. He has authored several papers in prestigious journals including Cell, Science, Molecular Cell, Genes & Development, PNAS, etc.

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Notes:

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Day 3

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The key to the riddle of the mechanism of most CVD and cancer is in arteriovenous anastomoses

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Problem: The lack of a systematic approach in modern medicine led her to stagnation. The problem of the mechanism of CVD and cancer is not solved. All this, apparently, was due to the division of medicine into separate directions. Each direction operates according to its own rules, there is no system.

Goal: The purpose of this work is to find and substantiate the true mechanism of many diseases from the point of view of the system.

Methods: Participation in scientific conferences, discussions with leading Russian cardiologists, retrieval of information search in the literature.

Results: It was shown [1] that large changes in human health occur due to the suboptimal work of large arteriovenous anastomoses (AVA). AVA may exist between the mesenteric artery and portal vein [2]. The very existence of AVA is necessary to reduce blood pressure (BP). When opening AVA there is a sharp decrease in BP, when closing - increase [3]. Physical activity is the key to the correct operation of the AVA. But under stress, hypodynamia, with excessive nutrition, there are violations of the mechanism of opening\closing the AVA. Hollow veins overflow, the venous bed expands its volume, damaged valves, the pressure difference between the arterioles and veins becomes insufficient to supply cells with food and oxygen. Fluctuations in venous blood lead to mechano-induced arrhythmias [1]. Oxidative stress occurs in the tissues. Through the walls of blood vessels there is a leakage of blood, so increases the tissue pressure and volume. Begin swelling, stagnation, obesity, varicose veins, thrombosis, primarily in the lower half of the body, then in the entire volume. Individual cells, deprived of oxygen supply, are modified, subject to necrosis, mutate, turn into cancerous [4, 5]. There are many CVD, including heart failure (HF) [6]. Edema is known to be associated with HF. According to the data of real measurements [7] in people with HF the perivascular zone is the widest (about 150 microns), and in healthy people it is much narrower (90 microns). Result: increased body size and weight. And no matter the quality of food. The volume of food and liquids absorbed is important. It is natural to assume that there is, as a rule, a bouquet of diseases - this is the work of open AVA.

Conclusions: The New theory of the CVD and cancer finds more and more positive arguments and facts. It is necessary to confirm the universality of the New theory in special experiments.

Recent Publications:

1. Evgeny A Shirshin, et al. (2018) In vivo optical imaging of the viable epidermis around the nailfold capillaries for the assessment of heart failure severity in humans. Journal of Biophotonics 29.
2. Ermoshkin V (2017) The cause of some cancers because of the open arteriovenous anastomoses. J Gastrointest. Cancer Stromal Tumor 2:111.
3. Ermoshkin V I (2016) New theory of arrhythmia. Conceptual substantiation of arrhythmia mechanisms. Cardiometry 8:6–17.
4. Ermoshkin V (2016) Pathological role of the "invisible" anastomoses. J Bioengineer & Biomedical Sci 6:209.

Biography

Vladimir Ivanovich Ermoshkin completed his Graduation in Physics department at Moscow State University in 1978. He has worked at Russian New University (RosNOU) as Physicist. He took part in 5 International Conferences on Cardiology. He has published about 20 articles on Cardiology in Prominent magazines.

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