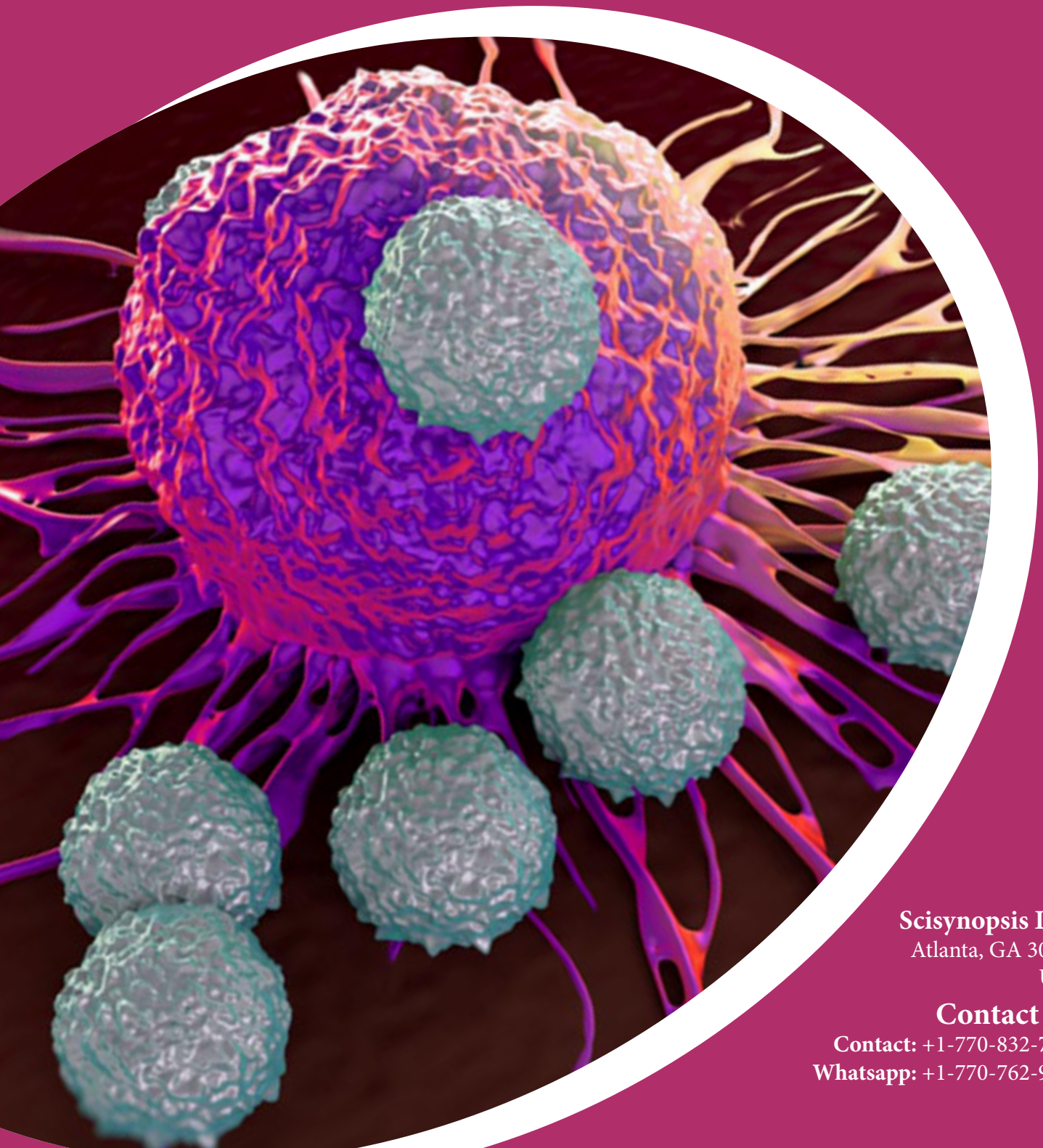
SCI SYNOPSIS

International Conference on

Cancer and Oncology Research

June 19-20, 2023
Rome, Italy



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Conference Programme

Conference Programme

June 19-20, 2023, Belstay Roma Aurelia, Rome, Italy

Day 1: 19 June, 2023

Meeting Hall: Parioli 1

8.30 - 8.45	**Registrations**
8.45 - 9.00	**Introduction**

Keynote Presentations

9.00 - 9.45 — **Gradimir Dimitrijevic,** Institute for Blood Transfusion, Serbia

Title: Biochaga and Biodihydroquercetin Excellent Supplements in Oncology

Oral Presentations

Session Chair: **Gradimir Dimitrijevic,** Institute for Blood Transfusion, Serbia

Sessions: Oncology | Cancer Biology | Cancer Pharmacology | Types of Cancer | | Organ Specific Cancer | Skin Cancer | Cancer Biomarkers | Radiation Oncology | Cancer Treatment and Therapies | Medical Oncology | Gynecologic Cancer | Cancer Metastatis | Imaging

9.45 - 10.15 — **Ivan P. Gorlov and Olga Y. Gorlova,** Baylor College of Medicine, USA

Title: Identification of Lung Cancer Drivers by Comparison of The Observed and The Expected Numbers of Missense and Nonsense Mutations in Individual Human Transcripts

Group Photo: 10.15 - 10.30

Networking & Refreshments @ Bar: 10.30 - 11.00

11.00 - 11.30 — **Jarrod Longcor,** Cellectar Biosciences, Inc., USA

Title: Iopofosine I 131 Treatment in Late Line Patients with Relapsed/Refractory Multiple Myeloma Post Anti-BCMA Immunotherapy

11.30 - 12.00 — **Lucia Mundo,** University of Limerick, Ireland

Title: The Proprierities of EBV-Encoded BILF1, A Poorly Known G-Protein Coupled Receptor Gene and its Therapeutic Potential

12.00 - 12.30 — **Maria Teresa Gentile,** University of Campania "L.Vanvitelli", Italy

Title: NRSF/REST Mediates Vasculogenic Mimicry in Melanoma Cell Lines

12.30 - 13.00 **Emmanuel A. Babington,** University Hospitals of Leicester NHS Trust, United Kingdom

Title: B-Flow Imaging in A Case of Bladder Tumour

Lunch @ Seguimi: 13.00 - 14.00

14.00 - 14.30 **Revital Azulay,** Meuhedet Health Fund, Israel

Title: Early Detection of Colon Cancer - From Research to Practice

14.30 - 15.00 **Daniela Vargová,** Comenius University, Slovakia

Title: Immunobiochemical Aspects of Clear Cell Renal Cell Carcinoma (CCRCC): A Preliminary Study

15.00 - 15.30 **Maria Pelullo,** Sapienza University, Italy

Title: The Activation of Jagged1 Signaling by Chemotherapeutic Agents Counteracts the Oxaliplatin/5-fluorouracil - Mediated Anti-Cancer Effects: A Novel Mechanism of Drug Resistance in Colon Cancer

15.30 -16.00 **Irina Groisman,** Institut Gustave Roussy, France

Title: CPEB1 Orchestrates a Fine-Tuning of miR-145-5p Tumor Suppressive Activity on TWIST1 Translation in Prostate Cancer Cells

Networking & Refreshments @ Bar: 16.00 - 16.30

16.30 - 17.00 **Silvia Belluti,** University of Modena and Reggio Emilia, Italy

Title: The NF-YA Splicing Signature Controls Aggressiveness of Colon Cancer by Regulating Cell Metabolism and Different Types of Cell Migration

17.00 - 17.30 **Ehsan Pourkarimi,** Hamad Bin Khalifa University, Qatar

Title: Tryptophanyl tRNA Synthetase (WARS1) Depletion Leads to Genomic Instability

17.30 - 18.00 **Saule Balmagambetova,** West Kazakhstan Marat Ospanov Medical University, Kazakhstan

Title: Comparative Analysis of Breast Cancer Chemotherapy Outcomes in Kazakhstan Before and During the Cardio-Oncology Program Implementation

18.00 - 18.30 **Ugo Rovigatti,** University of Florence, Italy

Title: Anti-GD2 Immunotherapy in Neuroblastoma: Successes, Challenges and Consequent Need for New Cancer Modeling

Day 1 Concludes followed by Awards Ceremony

Day 2: 20, June, 2023

Meeting Hall: Parioli 1

Keynote Presentation

10.00 - 10.45 — **Suresh Alahari,** LSU Health New Orleans, USA

Title: Nischarin, A Novel Tumor Suppressor Regulates Breast Cancer Progression through Interaction with Multiple Proteins

Oral Presentations

Session Chair: **Suresh Alahari,** LSU Health New Orleans, USA

Session Chair: **Jedrzej Antosiewicz,** Medical University of Gdańsk, Poland

Sessions: Breast Cancer | Robotic Oncology | Pediatric Oncology | Neuro Oncology | Cancer Pharmacology | Role of AI in Cancer | Cancer Drug Market | Oncology Nursing | Covid and Its Impact on Cancer | Head And Neck Cancer

10.45 - 11.15 — **Nauf Bou Antoun,** Kingston University London, United Kingdom

Title: Investigating Mechanisms of Drug Resistance in Cervical Cancer

Networking & Refreshments @ Bar: 11.15 - 11.45

11.45 - 12.15 — **Heer Shah,** University of Oxford, United Kingdom

Title: Evaluating the Systemic Management Options in Advanced Pulmonary Carcinoid Tumours: A Systematic Review (Medical Treatment – All Types of Systemic Anti-Cancer Therapies (SACT))

12.15 - 12.45 — **Aléxia Thamara Gasparin,** Hilab, Brazil

Title: Oncological Hospital Performance of The Hilab System, A New Point-of-Care Hematology Analyzer

12.45 - 13.15 — **Donatella Romaniello,** Alma Mater Studiorum University of Bologna, Italy

Title: IL-1 Induced Senescence: Mechanism of Resistance to Anti-EGFR Antibody Therapy

Lunch @ Seguimi: 13.15 - 14.00

14.00 - 14.30 — **Gabriel Pasquarelli do Nascimento,** University of Brasilia, Brazil

Title: Omega-3 and Ovarian Cancer: The Pyroptosis-Inducing Effects of Docosahexaenoic Acid (DHA)

14.30 - 15.00 **Markus Bredel,** University of Alabama, USA

Title: Novel EGFR Ectodomain Mutations and Resistance to Anti-EGFR and Radiation Therapy in H&N Cancer

15.00 - 15.30 **Angela Pallangyo,** Kilimanjaro Christian Medical University College, Tanzania

Title: The Burden of Human Immunodeficiency Virus Infection Among Women with Breast Cancer in Northern Tanzania, Pathological Features, Treatment Utilization and Clinical Outcome

15.30 - 16.00 **Chilaca Rosas María Fátima,** National Medical Cancer Center siglo XXI, Mexico/ National Autonomous University of Mexico

Title: Evaluation of Radiomic Profiles on MR in Patients Diagnosed with H3F3A K27M mutation in CNS Tumors

Networking & Refreshments @ Bar: 16.00 - 16.30

Poster Presentations (16.30 - 18.00)

PP - 001 **Jedrzej Antosiewicz and Ulana Juhas,** Medical University of Gdańsk, Poland

Title: Anti-Cancer Activity of Newly Synthetized 2,2'-Diselenobis(N-Propylbenzamide) is Mediated by Changes in Iron Metabolism

PP - 002 **Klaudia Zuczek,** University of Gdańsk, Poland

Title: Effects of Novel Usnic Acid Derivative on Wnt Signaling Pathway in Breast Cancer Cells

PP - 003 **Anna Herman-Antosiewicz,** University of Gdańsk, Poland

Title: The Isoxazole Derivative of Usnic Acid Disturbs Breast Cancer Cell Metabolism

PP - 004 **Zhenisgul Tlegenova,** West Kazakhstan Marat Ospanov Medical University, Kazakhstan

Title: Consecutive Steps of the First Kazakhstani Program on Early Diagnosis of Chemotherapy-Associated Cardiotoxicity in Breast Cancer Patients: Where We Are?

PP - 005 **Rabah Iratni,** United Arab Emirates University, UAE

Title: The SARS-CoV-2 Spike Protein Hijacks the Epidermal Growth Factor Receptor-Mediated Signaling in Cancer Cells

PP - 006 **Yun-Ju Chen,** I-Shou University, Taiwan

Title: Nucleophosmin-1 Interaction is Involved in Nuclear HER2-Mediated Tumor Progression and Drug Resistance

PP - 007 **Yueh-Ming Lin,** Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Taiwan

Title: Phosphatases are Involved in Celecoxib-Mediated Cancer Stemness Inhibition of Colorectal Cancer Cells

PP - 008 **Agnieszka Pyrczak-Felczykowska,** Medical University of Gdańsk, Poland

Title: The Isoxazole Usnic Acid Derivative Induces Reticular Stress in Breast Cancer Cells which Leads To ER-Phagy and Cell Death

PP - 009 **Mariola Gimla,** University of Gdańsk, Poland

Title: Pyrazole Usnic Acid Derivative as an Anti-proliferative Agent towards Pancreatic Cancer Cells

PP010 **Tarek Mohamed Kamal Mohamed Metawie,** Cairo University, Egypt

Title: Significance of Serum Survivin and -31G/C Gene Polymorphism in The Early Diagnosis of Egyptian Breast Cancer Patients

Video Presentation

VP - 001 **Aslı Elif Tanugur Samancı,** Istanbul Medipol University, Istanbul, Turkey

Title: Does Oral Care with Propolis AECT the Development of Oral Mucositis in Pediatric Oncology Patients: A Randomized Controlled Clinical Study

E-poster Presentation

EPP - 001 **Jingfen Shi,** University of Electronic Science and Technology of China, China

Title: A Rare Case Report of Pancreatic Cancer Initially Manifested as Portal Vein Thrombosis

Day 2 Concludes followed by Panel Discussion - Awards & Closing Ceremony

Virtual Programme

Virtual Programme

June 19-20, 2023 | Virtual Program

Day 1 June 19 2023, 10.00 BST

Keynote Presentation

10.00 - 10.30 — **WenQing Yang,** Founder and Chief Scientific Officer, Clin-Bridge Biotech Ltd., China

Title: Combining Antiangiogenic and Immunotherapeutic Approaches to Achieve Synergistic Efficacy in Cancer Treatment

Oral Presentations

10.30 - 10.55 — **Camilla Palumbo,** University of Rome 'Tor Vergata', Italy

Title: Antitumor Efficacy of The Proteasome Inhibitor Bortezomib on Malignant Mesothelioma: Evidence From *In Vitro* Studies And From A Syngeneic Mouse Model

10.55 - 11.20 — **Ahmed Elzawahry,** Gateshead Health NHS Foundation Trust, United Kingdom

Title: Incisional Metastatic Breast Carcinoma Deposit in A Total Knee Replacement Presenting as Peri-Prosthetic Joint Infection-A Case Report

11.20 - 11.45 — **Maria Magdalena Barreca,** University Of Palermo, Italy

Title: The Long Non-Coding RNA Regulates RBFOX2-Mediated Alternative Splicing in Colorectal Cancer

11.45 - 12.10 — **Evdokimova Sevindzh P,** Hertsen Moscow Oncology Research Institute, Russia

Title: Postoperative Chemotherapy After Surgical Resection of Metachronous Metastases of Colorectal Cancer

12.10 - 12.35 — **Patrycja Czerwinska,** Greater Poland Cancer Centre, Poland

Title: The Universality of TRIM28 Association with Cancer Stemness in Solid Tumors

12.35 - 13.00 — **Marzia Pucci,** University of Palermo, Italy

Title: The Role of Extracellular Vesicles Secreted by Colon Cancer Cells in Mediating the Nuclear Translocation of Pd-L1 in a Model of Human Healthy Hepatocytes: New Insights on Immune Checkpoint Pathways

Refreshment (13.00 - 13.30)

13.30 - 13.55 **Jassim Zaheen Shah,** Qatar University, Qatar

Title: Overview Of Cardio-Oncology and Cardiovascular Toxicity Risk Stratification Before Anticancer Therapy

13.55 - 14.20 **Marwah Suliman Maashi,** King Abdulaziz University, Saudi Arabia

Title: Characterization of the Role of Stra6 in Tumor Suppression Mechanisms

14.20 - 14.45 **Seema Devi,** IGIMS, India

Title: Dosimetric Comparison of Intensity Modulated Versus 3DCRT In Treatment of Locally Adrenal Carcinoma Cervix

14.45 - 15.10 **Brou Richmond Konan,** University Felix Houphouet-Boigny Abidjan, Cote d'Ivoire

Title: Toxicological Risk Assessment of Polycyclic Aromatic Hydrocarbons in Groundwater Resources of Abidjan, Southern Ivory Coast

15.10 - 15.35 **Syrine Ben Dhia,** Antoine Lacassagne Center, France

Title: Contact X-Ray Brachytherapy (CXB): A Relevant Niche for Rectal, Skin, Breast Cancer

15.35 - 16.00 **Loai Abdallah,** The Max Stern Yezreel Valley College, Israel

Title: Comparative Analysis of Machine Learning Algorithms for Cancer Prediction and Feature Selection

16.00 - 16.25 **Howard Bruckner,** MZB Foundation for Cancer Research, USA

Title: Chemotherapy Prolongs Survival of Patients With Resistant Cancers and Unfavourable Predictive Blood Tests

16.25 - 16.50 **Hannah Riva,** Texas Tech University Health Sciences Center, USA

Title: Treatment Modalities for Metastatic Uveal Melanoma: Where are We Now?

Poster Presentations

16.50 - 17.05 **Małgorzata Drzewiecka,** Uniwersytet Łódzki, Poland

Title: DMBC11 Melanoma Cell Line Response to DNA Double Strand Break Repair

17.05 - 17.20 **Alireza Khosravani,** Royan Institute, Iran

Title: PD-1 Blocker Boosts IL-15-Mediated NK Cells Activity Induction in Relapsed Acute Myeloid Leukemia (AML) Patients

17.20 - 17.35 **Jane Kinuthia**, Academic model providing access to health care-AMPATH, Kenya

Title: Addressing Survivorship and Supportive Care for Women and Men with Breast Cancer in Western Kenya

Day 1 Concludes

June 20 2023, 10.00 BST

Oral Presentation

10.00 - 10.25 **Krisztina Takacs-Vellai**, Eötvös Lorand University, Hungary

Title: Ev-Mediated NME1 and NME2 Modify Lipid Metabolism in Fibroblasts

10.25 - 10.50 **Trivikram Madhusoodan Deshpande and Hanmantrao D. Kanase,** Kisan Veer Mahavidyalaya, India

Title: Breast Cancer Frequency : A Review

10.50 - 11.15 **Hamed Hosseinalizadeh**, Guilan University of Medical Sciences, Iran

Title: The Use of Keratin-7 Antisense, in Conjunction with KRT7-AS Overexpression, Represents A Novel and Highly Effective Strategy to Suppress Tumorigenesis Apoptosis in Cases of Breast Cancer

11.15 - 11.40 **Mxolisi Justice Ndlovu,** University of Limpopo, South Africa

Title: Acetone Crude Extracts of *Toona cilliata, Seriphium plumosum and Schkuhria pinnata* Exhibit Antioxidant and Calcium-Dependent Apoptotic Activities Against Cervical Cancer Cells *in vitro*

11.40 - 12.05 **Ashu Chaudhary,** Kurukshetra University, India

Title: Landscaping Of Melallomacrocycles as Potential Antitumor and Anticancer Agents – A Journey of One Decade

12.05 - 12.30 **Fatemeh Ghaemi,** Royan Institute, Iran

Title: Investigating the Expression of UBE2C, LGR5, CXCL12, CCL5, CAV1 And STAT3 Genes at Protein And mRNA Levels in Metastatic and Nonmetastatic Tissues of Gastric Adenocarcinoma Patients

12.30 - 12.55 **Subhash,** Kurukshetra University, India

Title: In Vitro Cytotoxicity and Antimicrobial Evaluation of Novel Tetraaza Macrocyclic Based Ligands and It's Complexes of Cobalt (Ii): Synthesis, Characterization, DFT and Molecular Docking Studies

Refreshment (12.55 - 13.30)

13.30 - 13.55 **Soroor Eslahi,** Royan Institute, Iran

Title: Natural Killer Cell-Derived Extracellular Vesicles (NK-EVs) Exhibit Cytotoxicity on Pancreatic Cancer Spheroids

13.55 - 14.20 **Faizan Fazal,** Rawalpindi Medical University, Pakistan

Title: Pathologic Complete Response Observed in Early Stage HER2 Positive Breast Cancer Patients Treated with Neoadjuvant Therapy of Trastuzumab and Chemotherapy (C+T) Vs Trastuzumab, Chemotherapy, and Pertuzumab (C+T+P); A Comparative Meta-Analysis

14.20 - 14.45 **Parisa Shams,** Royan Institute, Iran

Title: In Vitro Generation of NK Cells From Umbilical Cord-Blood Mononuclear Cells: A Novel and Simplified Method

14.45 - 15.10 **Mohite Utkarsha Laxman,** MET's League of Colleges, Bhujbal Knowledge City, India

Title: Cancer Chemotherapy Dosage Estimation Using Optimization Assisted Kalman Filter

15.10 - 15.35 **Delbar Daneshjou,** Kian Immune Cell Co., Iran

Title: Cancer: A Type of Asexual Reproduction

15.35 - 16.00 **Yuwei Cheng,** Cleveland Clinic, USA

Title: An Effective Work-Flow to Properly Interpret Intronic Variants in Cancers

Day 2 Concludes followed by Vote of Thanks

Day 1

Oncology Congress 2023

Keynote Presentation

BIOCHAGA AND BIODIHYDROQUERCETIN EXCELLENT SUPPLEMENTS IN ONCOLOGY

Gradimir Dimitrijevic
Institute for Blood Transfusion, Serbia

Abstract:

Aim: A lot of people in Serbia, has cancer diseases, more of them after 1999. Bombing was with depleted uranium bombs and the results are now evident. Besides official therapy, with results good or not good, I am using and suggesting two Siberian supplements that are excellent in prevention, treatment and rehabilitation in cancer diseases.

Method: The methodology of using those two extremely natural supplements (powder consistency) is easy and there are no side effects of using them, when we recommend it.

Methodology and Results: Biochaga has Beta glucans that are very, very good and very potent in the suppression of tumors and immune deficiencies. It is known as "smart mushroom" because it stimulates the immune system when necessary (in USA classified as dietary supplement, in Europe and Russia, as a medical mushroom used for medical purposes). It also contains Melanin, a gene protector and DNA restorer. It improves the condition of patients suffering from food poisoning, alcohol intoxication, and tumor intoxication. Used in malignant neoplasms and in inoperable cases of tumors, if radiotherapy is not possible such as gastric, intestine, pancreatic, liver esophagus, lung cancers. It prevents malignant neoplasms and after radiation normalizes leucocyte formula .It also slow down the aging process.

Biodihydroquercetin is in antioxidant action, antioxidant and DE toxicant action, efficient in rehabilitation after chemotherapy and radiotherapy, as well as, after gamma radiation and x-ray .Antioxidant protect cells from free radicals, strengthens the walls of blood vessels and capillary, making them elastic, enhance microcirculation and promote redistribution of blood flow to small vessels. If you increase the breathing capacity the flow of oxygen to the brain and other organs, if you open the way to tens of thousands of closed capillaries, then you will not encounter any disease that cannot be cured.

What is important is that together they are very useful and effective. Nobel prize winner Linus Pauling said:" Regular use of Dihydroquercetin can extend human life by 25 years"

Biography

Gradimir Dimitrijevic has 30 years' experience in transfusion medicine, most of the time as expert in clinical transfusion but with very good experience in therapeutic apheresis and donor apheresis, as well as, blood component therapy .From few years ago introduced irradiation of blood components in Serbia in Novi Sad, and most of the blood components that are irradiated are for oncology, hematology, in adults and children. He is more than 15 years dealing with Siberian natural products, some Chinese, one African and one South American. All are extremely effective and helpful. This is his experience in all this together.

Day 1

Oncology Congress 2023

Oral Presentations

IDENTIFICATION OF LUNG CANCER DRIVERS BY COMPARISON OF THE OBSERVED AND THE EXPECTED NUMBERS OF MISSENSE AND NONSENSE MUTATIONS IN INDIVIDUAL HUMAN TRANSCRIPTS

Ivan P Gorlov[1], Olga Y Gorlova[1], Marek Kimmel[2], Spiridon Tsavachidis[1] and Christopher I Amos[1]

[1]Baylor College of Medicine, USA
[2]Rice University, USA

Abstract:

Cancer development is largely, driven by acquisition and subsequent positive selection of somatic mutations that increase proliferation and survival of tumor cells. As a result driver mutations are overrepresented and the genes related to cancer development tend to have an excess of somatic mutations in them. An excess of missense and/or nonsense mutations in a gene is an indicator of its cancer relevance. However to identify genes with an excess of potentially functional missense or nonsense mutations one needs to compare the observed and expected numbers of mutations in the gene. The expected number of somatic mutation in a gene can be estimated intrinsic propensity of the gene to mutate in a given cancer is known. Propensity of the gene to mutate can be estimated through analysis of silent mutations. The majority of silent mutations are expected to be neutral. They are the second (after missense) most common type of somatic mutations detected in tumor samples which in combination with their selective neutrality makes them ideal for an unbiased – free of effects of selection assessment of mutation rate. We used silent mutations to estimate nucleotide context-dependent mutability for all possible single nucleotide substitutions. We used LC somatic mutations from the Catalog of Somatic Mutations in Cancer (COSMIC). We focused on Lung Cancer (LC) because it is the top cancer killer worldwide and because LC has one of the highest frequencies of somatic mutations. Three major LC histological types: adenocarcinoma, squamous cell carcinoma and small cell LC were analyzed separately. We used COSMIC mutations detected by whole genome whole exome sequencing only to ensure equal targeting all transcripts.

The expected numbers of potentially functional missense and nonsense mutations in individual transcripts were estimated using (i) the number of potential sites for missense and nonsense mutations and (ii) histology-specific nucleotide context-dependent mutation rates assessed through analysis of silent mutations. We estimated how many missense and nonsense mutations are expected in COSMIC for each transcript and compared them with the observed numbers. The conducted analysis identified 26 genes with an excess of missense and/or nonsense mutations for lung adenocarcinoma, 18 genes for small cell lung cancer, and 26 genes for squamous cell carcinoma of the lung. These genes include known genes and novel lung cancer gene candidates.

Biography

Ivan P Gorlov is an Associate Professor in Baylor College of Medicine in the department of Medicine - Epidemiology & Population Science. He completed his PhD from Institute of Cytology and Genetics in Novosibirsk, Russia. His professional Interests are Bioinformatics, 'Omics" data analysis and integration and Cancer mechanisms.

IOPOFOSINE I 131 TREATMENT IN LATE LINE PATIENTS WITH RELAPSED/REFRACTORY MULTIPLE MYELOMA POST ANTI-BCMA IMMUNOTHERAPY

Jarrod Longcor[1], Natalie Callander[2], Kate Oliver[1], Asher Chanan-Khan[3] and Sikander Ailawadhi[3]

[1]Cellectar Biosciences, Inc.,USA
[2]University of Wisconsin Carbone Cancer Center, USA
[3]Mayo Clinic, USA

Abstract:

Over the past decade, significant improvements in survival outcomes have been experienced by multiple myeloma (MM) patients. However, MM remains an incurable disease and patients with triple-class refractory MM have limited treatment options and a dismal prognosis. Chimeric antigen receptor (CAR) T-cell therapy targeting B-cell maturation antigen (BCMA) has transformed the treatment algorithm of relapsed/refractory MM (RRMM), with high overall response rates. Nevertheless, a significant proportion of patients ultimately relapse despite achieving deep remission and show poor outcomes with subsequent treatment post anti-BCMA immunotherapies.1 Iopofosine I-131 (iopofosine) is a first-in-class phospholipid ether radio-conjugate that targets lipid raft microdomains on tumor cells and is internalized. Here we present seven cases of triple class refractory MM patients that relapsed or were refractory to anti-BCMA immunotherapy and treated with iopofosine plus low dose dexamethasone (LoDEX). Patient received a single fractionated cycle of 30 mCi/m^2 of iopofosine (15 mg/m^2 dosed day 1 and day 15) and received LoDEX (40 mg/week for 12 weeks) with an optional second cycle of iopofosine approximately 60 days later. Six of the seven patients achieved the minimum required total administered dose of 60 millicuries (mCi) to be in the evaluable population and 50% achieved a partial response (PR) or better.

Biography

Longcor brings to Cellectar Biosciences, Inc. more than 20 years of pharmaceutical and biotech experience and was previously the Chief Business Officer for Avillion LLP. In this role, he was responsible for executing the company's unique co-development partnership strategy. Prior to Avillion, Jarrod was the Vice President of Corporate Development for Rib-X Pharmaceuticals, Inc. (now Melinta Therapeutics) where he was responsible for identifying and concluding several critical collaborations for the company, including a major discovery collaboration with Sanofi Aventis valued over $700M. Prior to Rib-X, Mr. Longcor has held key positions in several small to midsized biotech companies where he was responsible for business development, strategic planning and operations. Jarrod holds a Bachelor of Science degree from Dickinson College, a Master of Science from Boston University School of Medicine and a Master of Business Administration from Saint Joseph's University's Haub School of Business.

THE PROPRIERITIES OF OF EBV-ENCODED BILF1, A POORLY KNOWN G-PROTEIN COUPLED RECEPTOR GENE AND ITS THERAPEUTIC POTENTIAL.

Lucia Mundo, Ciara Leahy, Pradeep Ramagiri, Matthew Pugh, Eanna Fennell, Max Robinson, Wenbin Wei, Katerina Boucholova, Andrew Bell, Lorenzo Leoncini, Stefano Lazzi, Paul G Murray and Katerina Vrzalikova

University of Limerick, Ireland

Abstract:

Burkitt lymphoma (BL), which arise from germinal centre B cells (GCB), is an aggressive non-Hodgkin B-cell lymphoma. The hallmark of nearly all BL tumours is the chromosomal translocation between the MYC gene and one of the immunoglobulins (Ig) heavy or light chain loci. In accord to the World Health Organization (WHO), BL can be classified into three forms which differ in geographic distribution, clinical presentation, and Epstein–Barr virus (EBV) association: endemic (eBL), sporadic (sBL) and HIV-associated BL. The association with EBV is highly variable, with more than 90% of the endemic cases and near 30% of HIV-associated tumours linked to EBV. The sporadic form is rarely associated to EBV, with only 10-15% cases diagnosed as EBV-positive. The majority of BL tumours express a latency type I, characterized by the expression of only EBNA1, EBV-encoded BART miRNAs and the non-coding RNA-pol III non-translated RNAs termed EBV-encoded small RNAs (EBER)-1 and EBER-2EBER RNAs. However, other latent and lytic transcripts such BILF1 have been reported in a subset of BL cases. While it is well known that EBV has a significant impact on the BL pathogenesis, the function of these virus transcripts remains largely undefined. Here we have identified a novel role for the EBV-encoded BILF1, a constitutively active viral G-protein coupled receptor that is transforming in NIH3T3 cells and which can induce tumours in nude mice. High throughput Q-PCR assay and RNA in situ hybridisation revealed that BILF1 is expressed by most tumour cells of a subset of eBL. Furthermore, BILF1-expressing cells did not express the immediate-early EBV gene, BZLF1, indicating they are latently infected. Moreover, when expressed in primary human GC B cells, the progenitors of eBL, we found that BILF1 induced a transcriptional programme that recapitulated the aberrant transcriptional programme characteristic of primary eBL, including the up-regulation of known MYC and P13-K target genes. Our data indicate that BILF1 induces an oncogenic transcriptional programme that could be important for the pathogenesis of a subset of eBL.

Biography

Mundo is a Marie Curie Fellow at the University of Limerick and Professor Adjunct in Molecular Pathology at the University of Nairobi. His research is focused on novel insights into the pathogenesis of virus-associated malignancies for the development of new therapies. Mundo has contributed several important discoveries in the field: the first description of a non-canonical EBV-latency program in non-Hodgkin lymphoma (Abate et al. PLoS Pathogens, 2015); the first documented evidence of EBV in-situ in primary tumors classified as virus-negative (Mundo et al., Frontiers in Microbiology, 2017; Mundo et al, Modern Pathology, 2020).

NRSF/REST MEDIATES VASCULOGENIC MIMICRY IN MELANOMA CELL LINES

Maria Teresa Gentile, Iolanda Camerino, Michele Grieco and Luca Colucci D'Amato
University of Campania "L.Vanvitelli", Italy

Abstract:

Melanoma, the most aggressive type of skin cancer, is responsible for the majority of deadly skin tumor. Several targeted therapies have been developed in the last few years nevertheless side effects, lack of clinical effects and resistance to treatments limit the long-term efficacy of such pharmacologic approaches. Vasculogenic mimicry (VM) is a process of alternative vascularization activated by aggressive melanoma cells that nourishes tumors with adequate blood supply to foster invasion as well as metastasis, resulting in poor prognosis for patients. Recent evidence suggests that the transcription factor NRSF/REST could be involved in the VM process. Here, we evaluated the ability of two different human melanoma cell lines to form tube-like structures and its relation with NRSF/REST gene expression, using an *in vitro* tube formation assay on a gelled basement matrix. Our results revealed that high of NRSF/REST gene is associated with the capability to form tube-like structures by melanoma cell lines. Furthermore, we demonstrated that the inhibition of NRSF/REST expression by different approaches, significantly decreased the ability of NRSF/REST expressing melanoma cells to perform VM and to migrate in a wound healing assay. Taken together, these results suggest that NRSF/REST could be involved in melanoma VM and that its inhibition could represent a good therapeutic strategy to prevent progression of melanoma disease.

Biography

Maria Teresa Gentile obtained her Master degree in Molecular Biology at the University of Naples "Federico II" and obtained the PhD in Pharmacology at the Department of Experimental Medicine of the University of Campania "Luigi Vanvitelli. Currently, she is researcher of General Pathology at the University of Campania "Luigi Vanvitelli" from June 2018. She carries out research in the field of cellular and molecular pathology. In particular, her interests are focused on the study of the molecular mechanisms underlying tumor cell proliferation, differentiation, and interaction with the extracellular matrix. She is co-author of extensively indexed publications on the field of cellular and molecular neuropathology and dozens of communications at national and international conferences.

B-FLOW IMAGING IN A CASE OF BLADDER TUMOUR

Emmanuel A. Babington
University Hospitals of Leicester NHS Trust, United Kingdom

Abstract:

This report aims to present a case that shows how B-flow imaging improved the diagnosis of a common type of bladder cancer.

A 59-year-old male presented with a three-week history of painless frank haematuria (with blood clots) and pain in the left inguinal area. Urgent ultrasound examination using a GE Logiq E10s, the 3 MHz curvilinear multi-frequency transducer revealed a 6.2 cm x 3.6 cm x 4.9 cm (L x AP x T) hypoechoic mass, with irregular wall outline, within the lumen of the urinary bladder occupying mostly the left lateral bladder compartment and obstructing the left ureteric orifice. Initially, the mass was examined using the Colour Doppler function but revealed no evidence of vascularity; then, the sonographer switched to B-flow imaging, which displayed obvious evidence of an active arterial blood flow within the mass, and raised suspicion of a malignant lesion on ultrasound. In addition, there was evidence of left hydroureteronephrosis secondary to the compression of the left ureteric orifice by the mass within the bladder. Subsequently, the patient had contrast CT to check for metastasis in the chest, abdomen, and pelvis; this revealed a 5.4 cm x 3.8 cm x 4.9 cm (L x AP x T) irregular heterogeneously enhancing lesion involving the left posterolateral bladder wall and the left vesicoureteric junction with dilatation of the left ureter and pelvicalyceal system. Multiple enlarged lymph nodes were seen in the left external iliac and para-aortic regions with AP measurements of up to 1.2 cm and 2.2 cm, respectively. The patient had transurethral resection of the 6 cm bladder tumour; further histopathology of the surgically resected specimen revealed 48 g of tissue fragments of necrotic, muscle-invasive urothelial carcinoma, grade 3, with no evident lymphovascular invasion.

Although urothelial carcinoma is a commonly encountered type of bladder cancer, this case highlights the importance of using different imaging functions on ultrasound to improve diagnosis and expedite patient management.

Biography

Emmanuel Abiola Babington is a well-experienced sonographer in the University Hospitals of Leicester NHS Trust with a significant interest in training and research. He acquired his MSc. in Medical Ultrasound from Sheffield Hallam University, UK. He has authored different scientific papers and presented on some platforms, including the British Medical Ultrasound Society (BMUS) conference.

EARLY DETECTION OF COLON CANCER - FROM RESEARCH TO PRACTICE

Revital Azulay
Meuhedet Health Fund, Israel

Abstract:

Background: Colorectal cancer leads to significant morbidity and mortality. Early detection and treatment are essential. Screening using faecal occult blood tests (FOBT) has increased significantly, but adherence to colonoscopy follow-up is suboptimal, increasing CRC mortality risk.

The aim of this study was to identify barriers to colonoscopy following a positive FOBT at the level of the patient, physician, organization and policymakers.

Methods: This mixed methods study was conducted in Israel. The study included retrospective analyses of members with positive faecal immunochemical tests, and a patient's survey with a positive test, with and without follow-up. The qualitative part of the study included focus groups with primary physicians and gastroenterologists and in-depth interviews with opinion leaders in healthcare. The intervention part included sending SMS reminders to the patients with positive FOBT.

Results: Patient lack of comprehension regarding the test was the strongest predictor of non- adherence to follow-up. We found no correlation with waiting time for appointments or distance from gastroenterology clinics. Primary care physicians underestimate non-adherence rates. They feel responsible for patient follow-up, but express lack of time and skills that will allow them to ensure adherence among their patients. Gastroenterologists do not consider faecal occult blood an effective tool for CRC detection. A SMS reminder is an effective, simple and inexpensive method for improving adherence among patients with positive colorectal screening results

Conclusion: We identified important barriers that need to be addressed to improve the effectiveness of the screening program. Targeted interventions for populations at risk for non-adherence, specifically for those with low literacy levels, and better explanation of the need for follow-up as a routine need to be set in place. SMS reminder is an effective, simple and inexpensive method for improving adherence among patients with positive colorectal screening results. Physician's attitude towards FOBT must be addressed to improve follow-up colonoscopies among their patients

Biography

Revital Azulay is working as a Quality Assurance Manager at Meuhedet Health Fund in Israel. She completed her Ph.D. Research at the Public Health Management Program, Bar Ilan University, under the supervision of Prof. Racheli Magnezi.

IMMUNOBIOCHEMICAL ASPECTS OF CLEAR CELL RENAL CELL CARCINOMA (CCRCC): A PRELIMINARY STUDY

Daniela Vargová, Ján Dargaj, Lukáš Briš, Matúš Dohál, Martina Šutovská, Jan Ľupták, Soňa Fraňova, Ján Švihra and Pavol Slávik

Comenius University, Slovakia

Abstract:

Renal cell carcinoma (RCC) is an aggressive disease with an unfavorable prognosis. The tumor microenvironment (TME) of RCC has a well-known immunogenic character. It is highly infiltrated by immune cells that produce various signaling molecules, especially cytokines. Cytokines have pleiotropic effects and play an important role in tumor-associated inflammation processes. Their actions are mediated mainly by the Jak/STAT pathway. This study examined the levels of STAT3 and 27 pathologically relevant cytokines in human clear cell RCC (ccRCC), the most common variant of RCC. Multiplex assay and ELISA were used to measure target molecules concentrations in tissue samples from 16 Slovak patients with histologically verified ccRCC indicated for nephrectomy. The differences between the levels of the molecules analyzed in the tumor versus those in the healthy kidney tissue were assessed. The correlation between cytokine and STAT3 levels was examined. The levels of the investigated molecules were evaluated with regard to disease progression. Tumor tissue showed significantly higher levels of G-CSF, IL-6, CXCL10, CCL3, and CCL4 [two-tail P/Cohen' D: 0.006/-0.829; 0.04/-0.587; <0.001/-1.405; <0.001/-1.461; < 0.0001/-1.55 respectively] than their counterparts. The STAT3 concentration was significantly higher in the healthy kidney than in the ccRCC tissue [two-tail P/Cohen' D: < 0.0001/2.403]. The levels of IL-1β and PDGF-BB increased significantly with the progression of the histopathological stage of the disease (NG) [P 0.001 and 0.025 respectively]. Intratumoral amounts of IL-12p70 and IL-15 were markedly correlated with intratumoral STAT3 levels [P/Adj.R2: 0/0.82 and 0/0.84 respectively]. The progression of the pathological stage of the disease (TNM) was associated with a substantial increase in STAT3 concentrations in the tumor [Padj 0.023]. The presented results support the significance of cytokines and STAT3 in the pathogenesis of ccRCC and indicate their clinical relevance as potential biomarkers and/or novel therapeutic targets.

Biography

Daniela Vargová is a doctor of medicine. Currently, she is enrolled in the third year of a postgraduate programme in clinical pharmacology at Jessenius faculty of Medicine in Martin Slovakia. She focuses on renal cell carcinoma at a molecular level. Her aim is to contribute to the understanding of the intricate pathogenesis of this cancer by attempting to identify potential biomarkers and/or novel therapeutic targets. She specializes particularly in immune-related molecules. The results of her previous study have already been published in one of the book series Advances in Experimental Medicine and Biology.

THE ACTIVATION OF JAGGED1 SIGNALING BY CHEMOTHERAPEUTIC AGENTS COUNTERACTS THE OXALIPLATIN/5FLUOROURACIL-MEDIATED ANTI-CANCER EFFECTS: A NOVEL MECHANISM OF DRUG RESISTANCE IN COLON CANCER

Maria Pelullo
Sapienza University, Italy

Abstract:

Objectives: Colorectal cancer (CRC) is a leading cause of mortality worldwide, characterized by metastasis and resistance to therapy. Recently, we demonstrated that $Kras^{mut}$ drives the activation of Jag1-ICD oncogene, via-ERK1/2. Herein, we explore the new intrinsic drug-resistance mechanisms, Jag1-ICD-mediated.

Methods: Human CRC cell lines were treated with different chemotherapeutic compounds (e.g. OXP, 5FU and GSIs), alone or in combination, and subjected to *in-vitro* assays, to evaluate proliferation, metastasis and chemoresistance. CRC resistant cells were obtained by chronical treatment with low doses of OXP/5FU. The resistant cells were analysed by colony-formation assays and by qRT-PCR to assess growth and gene-reprogramming ability.

Results: Herein, we evaluate the effects of OXP, 5FU and GSIs alone or in combination, on Jagged1 processing in CRC cell lines. We demonstrate that the anticancer drugs, OXP and 5FU, lead directly to a massive Jag1-ICD activation that results in the selection of a drug-resistant subpopulation. The chemoresistance mechanism is induced by a forced Jag1-ICD accumulation that protects cells from apoptosis, under the activation of Jag1-ICD-dependent pro-survival targets. In addition, GSIs induce the proliferation of Jag1-ICD positive CRC cells, functioning as tumorpromoting agents. Finally, the Jagged1 abrogation in OXP- or 5FU-resistant subpopulations is enough to restore the sensitivity to chemotherapy, confirming that drug resistance is Jag1-ICD-dependent.

Conclusion: Overall, our data show that Jagged1 processing is directly activated by the most potent chemotherapeutic agents (OXP/5FU) or by GSIs compounds. Moreover, we unveil a new role for Jag1-ICD oncogene which controls both apoptosis and proliferation, in CRC cells upon chemotherapeutic treatments. Therefore, we demonstrate the existence of a new mechanism of intrinsic drug-resistance, where Jag1-ICD functions as pivotal nuclear effector. Finally, we suggest Jagged1 as molecular predictive biomarker for the chemotherapy-outcome in CRC patients bearing $Kras^{mut}$ and over-expressing Jagged1.

Biography

Maria Pelullo, raised in South of Italy, a Biologist specialist in Clinical Pathology and Clinical Biochemistry, holds the PhD at the Sapienza University of Rome. Her career has always been characterized by the study of molecular mechanisms underlying tumors raise, focusing on dissection of Notch pathway. In detail, during her PhD she was involved in the characterization of Jagged1 protein, known ligand of Notch receptor, in the onset and proliferation of acute T-cell lymphoblastic leukemia (T-ALL). During her post-doc period, she focused her expertise on studying the the Jagged1-mediated signaling and its role in the onset, progression, and chemoresistence of colorectal cancer. During her long-time career She was involved in a several collaborations always aimed to discover the molecular mechanisms driving the physiopathology of several diseases (e.g. Medulloblastoma, Chronic Lymphocytic Leukemia, ischemic heart failure).

CPEB1 ORCHESTRATES A FINE-TUNING OF miR-145-5P TUMORSUPPRESSIVE ACTIVITY ON TWIST1 TRANSLATION IN PROSTATE CANCER CELLS

Irina Groisman
Institute Gustave Roussy, France

Abstract:

TWIST1 is a basic helix-loop-helix transcription factor, and one of the master Epithelial-to- Mesenchymal Transition (EMT) regulators. We show that tumor suppressor miR-145-5p controls TWIST1 expression in an immortalized prostate epithelial cell line and in a tumorigenic prostate cancer-derived cell line. Indeed, shRNA-mediated miR-145-5p silencing enhanced TWIST1 expression and induced EMT-associated malignant properties in these cells. However, we discovered that the translational inhibitory effect of miR-145-5p on TWIST1 is lost in 22Rv1, another prostate cancer cell line that intrinsically expresses high levels of the CPEB1 cytoplasmic polyadenylation element binding protein. This translational regulator typically reduces TWIST1 translation efficiency by shortening the TWIST1 mRNA polyA tail. However, our results indicate that the presence of CPEB1 also interferes with the binding of miR-145-5p to the TWIST1 mRNA 3′UTR. Mechanistically, CPEB1 binding to its first cognate site either directly hampers the access to the miR-145- 5p response element or redirects the cleavage/polyadenylation machinery to an intermediate polyadenylation site, resulting in the elimination of the miR-145-5p binding site. Taken together, our data support the notion that the tumor suppressive activity of miR-145-5p on TWIST1 translation, consequently on EMT, selfrenewal, and migration, depends on the CPEB1 expression status of the cancer cell. A preliminary prospective study using clinical samples suggests that reconsidering the relative status of miR-145-5p/TWIST1 and CPEB1 in the tumors of prostate cancer patients may bear prognostic value.

Biography

Irina Groisman graduated from Biology Department of Kiev State University, Kiev Ukraine with Ph.D. in Molecular Biology. After two post-doctoral trainings at Hadassah Medical School, Jerusalem University (Israel) and UMASS Medical school (USA), she worked as instructor at UMASS Medical School and then team leader at CCIB MGH, Harvard University, Boston, MA USA. Since 2009 she is holding Senior Scientist position (CR1) at INSERM, France.

Her work is related to translational regulation of gene expression, involved in cell-cycle and cancer development. It was published in high profile journals as Cell, Genes and Development, Oncogene, NAR etc., and presented at a number of conferences like Cold Spring Harbor.

THE NF-YA SPLICING SIGNATURE CONTROLS AGGRESSIVENESS OF COLON CANCER BY REGULATING CELL METABOLISM AND DIFFERENT TYPES OF CELL MIGRATION

Silvia Belluti[1], Valentina Mularoni[1], Giovanna Rigillo[1], Mirko Ronzio[2], Giacomo Miserocchi[3], Diletta Dolfini[2], Laura Mercatali[3], Andrea Alessandrini[1] and Carol Imbriano[1]

[1]University of Modena and Reggio Emilia, Italy
[2]University of Milan, Italy
[3]IRCCS Istituto Romagnolo per lo Studio dei Tumori (IRST) "Dino Amadori", Italy

Abstract:

NF-Y is a transcription factor composed of NF-YA and NF-YB/NF-YC subunits. The two NF-Isoforms, NF-YAs and NF-YAl, differentially control cell proliferation and differentiation. The analysis of patient's transcriptome profiles from The Cancer Genome Atlas database highlight increased NF-YA expression, specifically NF-YAs, in colorectal cancer (CRC), the second most deadly cancer worldwide. Despite this, patients with high NF-YAl mRNA have a lower overall survival probability. We investigated the role of NF-YA in the metabolism of CRC cells, and the measurement of mitochondrial fuel usage in live cells shows that NF-YAl overexpression enhances the capacity for glutamine pathway, one of the key metabolic pathways involved in EMT and cell dissemination. Specifically, we identified NF-YAl as direct transcriptional regulator of GLS1 glutaminase and GLULglutamine synthetase. Moreover, we demonstrate that NF-YAl overexpression can generate a hybrid epithelial-mesenchymal transition (EMT) state in CRC cells by direct transriptionalregulation of key EMT, extracellular matrix and adhesion genes. Consistently, NF-YAl enhances cell migration, both in 2D and 3D culture conditions, as highlighted by live imaging investigations.While collective migration characterizes NF-YAs-cells, fast single-cell and amoeboid-like migrationmarks NF-YAl cells. In agreement with these results, NF-YAl overexpression promotes cell dissemination in zebrafish xenografts.

Our observations imply that the two NF-YA variants can be potentially novel markers for CRCpatient stratification. Higher NF-YAl expression can be a hallmark of cancer cell dissemination by affecting cell metabolism and cell migratory abilities.

Biography

Since March 2014, Belluti has been working as a post-doctoral researcher in the Molecular Genetics lab of the Department of Life Sciences, University of Modena and Reggio Emilia, where she received her PhD in Molecular and Regenerative Medicine. Belluti has investigated the molecular mechanisms underlying the differentiation processes of muscle stem cells and, in particular, the transcriptional regulatory mechanisms associated with the development and progression of colon and prostate cancer, as well as the development of novel anticancer molecules. Belluti also studied chromatin organization and DNA replication as a visiting researcher at the University of Edinburgh and University of Dundee.
Belluti is Assistant Professor in Genetics (RTDb) at the Department of Life Sciences, University of Modena and Reggio Emilia, Italy.

TRYPTOPHANYL tRNA SYNTHETASE (WARS1) DEPLETION LEADS TO GENOMIC INSTABILITY

Ehsan Pourkarimi, Mahmoud Izadi, Tayyiba Akbar Ali and Farah Shurrab
Hamad Bin Khalifa University, Qatar

Abstract:

Improper translation or the lack of translational fidelity is associated with multiple human diseases, including cancer and neurodegeneration. In contrast to the replication error rate of nearly one mistake per 1 million base pair, mRNA translation occurs at a much lower imprecision, one amino acid per 1000. Yet, due to the multiplexing nature of translation, such low imprecision is enough for cellular hemostasis throughout organismal life. In general, the fidelity of protein translation is ensured by a family of proteins named aminoacyl tRNA synthetases (Aars), making them crucial for development and survival. Gain-of-function mutations or gene duplication of Aars genes has been reported in cancer cells, presumably supporting their unusually high translational demand. Among the Aars protein family members, the tryptophanyl tRNA synthetase (WARS1) has been reported to be linked to various human diseases spanning from intellectual disabilities to cancer and metastasis. To expand our understanding of the non-canonical function of WARS1, we investigated the effect of wars-1 depletion during mitotic and the meiotic cell cycle in the developing germline of *C. elegans*. Previously, we showed the correlation between wars-1 knockdown (KD) and improper cell division in the mitotic zone, leading to defects in germline development in *C. elegans*. Here, we further characterized the effects of WARS-1 depletion on cell cycle progression. Knocking down wars-1 in *C. elegans* resulted in cell cycle arrest at the G2/M phase transition, associated with CDK1 phospho-inactivation. More importantly, we have shown that knocking down wars-1 induces DNA damage response by activating checkpoint kinase I, CHK1. Our study shows that knocking down wars-1 results in intensive genomic instability associated with an aberrant chromosomal structure, such as forming a chromatin bridge. We, therefore, suggest that the depletion of WARS-1 results in genomic instability, linking faithful translation to genome integrity which is highly relevant to cancer progression.

Biography

Ehsan Pourkarimi did his undergraduate study at ELTE University in Budapest, Hungary. After receiving a Cancer Research UK fellowship, he moved to the United Kingdom. He joined the Lab of Prof. Anton Gartner in the Wellcome Trust Center for Gene Regulation and Expression at the University of Dundee. During his Ph.D., Dr. Pourkarimi characterized the key components of the core apoptosis machinery in C. elegans and challenged the well-accepted model of apoptosis induction. Focused on chromatin biology, his post-doctoral research delved into the effect of chromatin modifiers in cellular response during acute stress conditions. Using the SILAC-based proteomics approach, Dr. Pourkarimi demonstrated the significance of Histone H3.3 variants in aging and during acute starvation. As a Research Associate in the Lab of Dr. Iestyn Whitehouse at Memorial Sloan Kettering Cancer Center in New York City, Dr. Pourkarimi studied DNA replication.

Using C. elegans embryos, he mapped DNA replication origins, creating the first comprehensive map of DNA replication from a multicellular organism. In 2020 he moved to Qatar as principal investigator and assistant professor in Genomics and Precision Medicine (GPM) and established his research lab in Qatar. His Lab uses cutting-edge technology such as epigenome editing to tackle the fundamental question in chromatin biology, from DNA damage response to understanding the mechanism of epigenetic memory.

He also uses a model system to understand the molecular pathology of cancer-causing mutations. His lab has recently identified the role of aminoacyl-tRNA synthetase (WARS1) in genome integrity and cancer.

COMPARATIVE ANALYSIS OF BREAST CANCER CHEMOTHERAPY OUTCOMES IN KAZAKHSTAN BEFORE AND DURING THE CARDIO-ONCOLOGY PROGRAM IMPLEMENTATION

Saule Balmagambetova
West Kazakhstan Marat Ospanov Medical University, Kazakhstan

Abstract:

For early detection and treatment of cardiovascular complications in cancer patients in Kazakhstan, a cardio-oncological service is currently being created based on the postulates of the European Society of Cardio-oncology Guidelines. We compared chemotherapy outcomes in breast cancer patients before and after introducing this program at the Aktobe Cancer Center (Kazakhstan).

Methods: Between September 2021 and August 2022, we recruited 128 newly diagnosed breast cancer patients started on doxorubicin and/or trastuzumab. Echocardiography with global longitudinal strain (GLS) assessment, six-minute walk test, ECG with Holter monitoring, cardiac biomarkers (cTnI, BNP), and other tests were performed at baseline and every three months. At baseline, patients were stratified into risk groups according to the ESC recommendations. High-risk patients received cardioprotective treatment from the outset. For chemotherapy outcomes comparison, the data for 2018-2019 were taken, in total, 305 patients who were observed in the Cancer center.

Results: Compared to 2018-19, when EchoCG was performed in 60 out of 305 (19.7%) patients, in 2021-2022 all participants were provided with EchoCG. In 2018-2019, 25 (6.2%) patients had cardiovascular complications: arterial hypertension in 1.3%; rhythm and conduction disturbances in 3.6%; ischemia in 1.3%; heart failure - 0.7%; pericarditis - 0.3%. Chemotherapy was interrupted in 10.5% of patients due to cardiotoxic complications and had to be adjusted in 11.8%. There were four cardiac deaths (1.3%). By the end of January 2023, 67 patients out of 128 had been followed up for 12 months or more. There were no cases of chemotherapy cessation due to cardiotoxic complications. Mild symptomatic cardiotoxicity was revealed in 2 (1.6%) participants and a mild asymptomatic variant - in 26 (20.3%). All these cases were timely recorded, and cardioprotective treatment was adjusted.

Limitations: Interim findings reported.

Conclusion: The cardio-oncology program, which includes comprehensive cardiovascular monitoring and early intervention in case of myocardial dysfunction, has improved chemotherapy outcomes in breast cancer patients.

Biography

Saule Balmagambetova is an Associate Professor at the Oncology Department. In 2013 graduated from the Harvard Medical School's course "Principles and Practice of Clinical Research," certified in Clinical Research. Designer and Principal Investigator of scientific projects of republican importance on oncologic diseases of women's reproductive system. Professional areas: general oncology, gynecologic oncology. Research focus: multimodal treatment of breast cancer; cardiotoxicity of chemotherapy; cervical cancer; so-called "weak" HPV types and their role in cervical pathology; cancer screening issues. Currently she is a Principal Investigator of the project on breast cancer chemotherapy-linked cardiotoxicity.

ANTI-GD2 IMMUNOTHERAPY IN NEUROBLASTOMA: SUCCESSES, CHALLENGES AND CONSEQUENT NEED FOR NEW CANCER MODELING

Ugo Rovigatti
University of Florence, Italy

Abstract:

Although considered a rarer form of cancer, Neuroblastoma (NBL) is still the most common tumor in preschool age. Historically, its study was associated with important breakthroughs in cancer research and the birth of so-called precision medicine, in view of the rather frequent (approx. 1/5 of cases) amplification of MYCN (MNA). This conference-presentation was inspired by findings in NBL-MNA in both basic and clinical research, which appear paradoxical to our present knowledge and our current cancer modelling. Two of them (basic science) relate to v. extensive MYCN amplification (MNA) and were obtained by my group, but others had comparable results.

Furthermore, paradoxical clinical results were obtained at Memorial Sloan Kettering: they show that aggressive NBL (HR-NBL) cases with MNA have exceptional responses with anti-GD2 immuno-therapies (IMTs).

Starting from such paradoxical results and questions, five different areas will be overviewed:

1. New findings on the molecular mechanisms of oncogene amplification.
2. New clinical data in anti-GD2 IMTs based on vaccination (active IMT).
3. The emerging picture of immune system alterations, overly present in HR-NBL, especially with MNA.
4. New genomic NBL landscapes from recent studies, which however do not provide explanations for the successes of anti-GD2 IMTs.
5. A more likely explanation is provided by considering the ganglioside GD2 as viral receptor for MFV, a virus isolated from HR-NBL that my group has studied for several years. A review of Reoviridae also discloses that several gangliosides function as immediate receptors for this family of viruses. The presentation final considerations suggest a critical reappraisal of today's cancer modelling, which has been essentially immutable through this millennium and 3 different editions. Instead, the discussed paradoxical data suggest that a two layer model with upstream/downstream actors/drivers could reconcile the incongruence of MNA in HR-NBL and possibly of other cancer types.

Biography

Ugo Rovigatti obtained his Ph.D. degree in Molecular Biology with Summa cum Laude in 1973 and in 1999 the Tenured Professorship. From 1979 to 1999 he worked with renown Scientists such as C. Basilico, R. Weiss, H. Varmus, S. Astrin, T. Papas, D. Watson, P. Duesberg, JJ Yunis, J. Bader, J. Trentin, B. Hirt at: ICRF in London, UK; the Rockefeller University in New York; the Fox Chase Institute in Philadelphia; St. Jude Children's Hospital in Memphis, TN; the NCI in Frederick, MD; the Ochsner Foundation-Clinic in New Orleans, LA; the Baylor College of Medicine in Houston, TX. Between 1997 and 1999 he was a sabbatical professor in Switzerland (KISPI in Zurich and ISREC in Lausanne). His PI research work has been funded by grants from UICC, ICRETT, SCL, MIUR, MURST etc.

Day 2

Oncology Congress 2023

Keynote Presentations

NISCHARIN, A NOVEL TUMOR SUPPRESSOR REGULATES BREAST CANCER PROGRESSION THROUGH INTERACTION WITH MULTIPLE PROTEINS

Suresh K. Alahari
LSU Health New Orleans, USA

Abstract:

About 25 years ago, we identified a novel protein, termed Nischarin that binds preferentially to the cytoplasmic domain of the integrin alpha5 subunit, inhibits cell motility, and alters actin filament organization. Nischarin is primarily a cytosolic protein, but clearly associates with alpha5 beta1 integrin. In addition, we demonstrated that the membrane proximal region (from residues 1017 to 1030) of the alpha5 cytoplasmic tail is essential for the interaction. Mutational and biochemical analysis revealed that residues Tyr (1018) and Lys (1022) are crucial for alpha5-Nischarin interactions. These results provided evidence that Nischarin is capable of directly and selectively binding to a portion of the alpha5 cytoplasmic domain. Further studies demonstrated that the minimal alpha5 binding region of Nischarin does not affect cell migration. To characterize Nischarin's role in breast tumorigenesis and mammary gland development more completely, we deleted a critical region of the Nischarin gene (exons 7-10) from the mouse genome and observed the effects. Mammary glands in deleted animals showed delayed terminal end bud formation but did not develop breast tumors spontaneously. Therefore, we interbred the animals with transgenic mice expressing the mouse mammary tumor virus-polyoma middle T-antigen (MMTV-PyMT) oncogene. The MMTV-PyMT mammary glands lacking Nischarin showed increased hyperplasia compared to wild-type animal tissues. Furthermore, we observed significantly increased tumor growth and metastasis in Nischarin deleted animals. Surprisingly, Nischarin deletion decreased activity of AMPK and subsequently its downstream effectors. Given this finding, we treated these animals with metformin, which enhances AMPK activity. Here, we showed for the first time, metformin activates AMPK signaling and inhibits tumor growth of Nischarin lacking PyMT tumors suggesting a potential use for metformin as a cancer therapeutic, particularly in the case of Nischarin-deficient breast cancers. We uncovered the reason for this phenotype by showing that Nischarin binds to and inhibits the activity of AMP-activated protein kinase (AMPK), which regulates energy homeostasis by suppressing anabolic and activating catabolic biochemical processes. Taken together, our results indicate that Nischarin is an important AMPK inhibitor and a critical regulator of energy homeostasis, including lipid and glucose metabolism. In summary, Nischarin is a key protein functioning as a molecular scaffold and thereby hosting interactions with several protein partners to regulate breast cancer progression.

Biography

Alahari obtained his Bachelor of Science in Biology and Master of Science in Human Genetics from India in 1983 and 1986 respectively. His Ph.D. in Molecular Biology was awarded by Drexel University, Philadelphia in the year 1994. From 1994 to 1998, Dr. Alahari did a post-doctoral fellowship at the University of North Carolina at Chapel Hill. Since 1998, he has been a faculty member at the University of North Carolina and in 2004 joined the LSUHSC as Associate Professor of the Department of Biochemistry. During his tenure at the University of North Carolina, he discovered a novel protein that he termed, Nischarin.

Day 2

Oncology Congress 2023

Oral Presentations

INVESTIGATING MECHANISMS OF DRUG RESISTANCE IN CERVICAL CANCER

Nauf Bou Antoun
Kingston University London, United Kingdom

Abstract:

Objective: In order to investigate possible mechanisms of drug resistance in cervical cancer, we have generated three drug resistant (DR) human cervical cancer cell lines (CCCL; Caski, HeLa and SiHa) to an FGFR inhibitor, PD173074. The main aims of this project are to (1) characterise the PD173074-resistant cancer cervical cell lines and (2) investigate possible mechanism(s) of drug resistance by comparing their transcriptome to their equivalent wild type cell lines.

Methods: Cell proliferation, apoptosis and lateral cell migration were studied using Incucyte zoom system to examine the functional differences between the wild type and DR CCCL. Western blot analysis were performed to investigate the activation of MAPK, AKT and S6 downstream signaling pathways upon stimulation with recombinant FGF2, FGF4 or FGF7 ligands in the presence and absence of the FGFR inhibitor, PD173074. Transcriptomic analysis were performed to detect differentially expressed genes (DEG) and their protein-protein interactions between DR and wild type CCCLs.

Results: PD173074-resistant CCCL had higher IC50, were more proliferative and migratory and less apoptotic than the wild type cells with and without PD173074. Interestingly, biochemical studies revealed that in the presence of the FGFR inhibitor and after FGF2, FGF4 and FGF7 stimulation, ERK phosphorylation was abolished in both the wild type and drug resistant cells. However, there was no difference in Phospho AKT expression level at either Ser (473) or Thr (308) sites in the presence or absence of the drug in both wild type and drug resistant cell lines. Transcriptome analysis and subsequent validation revealed five upregulated and nine downregulated DEGs in drug resistant CCCL as well as several protein-protein interactions between them.

Conclusion: Our data suggest that DR cell lines have a more metastatic signature compared to wild type CCCL. Transcriptome analysis highlighted PHLDA1 and PLCB4 genes as potential mechanism of drug resistance in CCCL.

Biography

Nauf Bou Antoun, a part time PhD researcher in the department of Biomolecular Sciences at Kingston University London working under the supervision of Athina-Myrto Chioni. Her research focuses on investigating the factors that underlie the mechanism of drug resistance in cervical cancer to help designing therapeutic strategies to overcome resistance and improve treatment in this disease.

In 2017 she held a position of visiting researcher for 6 months in the Institute of Reproductive and Developmental Biology (IRDB) building at Imperial College London. During this period, she worked on a glioblastoma project from which she gained valuable skills on a wide range of laboratory techniques

In January 2019, she got awarded from Advance HE and Kingston University an Associate Fellowship in the Higher Education Academy.

EVALUATING THE SYSTEMIC MANAGEMENT OPTIONS IN ADVANCED PULMONARY CARCINOID TUMOURS: A SYSTEMATIC REVIEW (MEDICAL TREATMENT – ALL TYPES OF SYSTEMIC ANTI-CANCER THERAPIES (SACT))

Heer Shah
University of Oxford, United Kingdom

Abstract:

Introduction: Pulmonary carcinoids have been classically described as indolent, with treatment options largely focusing on surgical resection. However, with increasing prevalence and growing awareness, cases of advanced pulmonary carcinoids, have been reported. Due to the paucity of clinical trials, there is a lack of evidence-based systemic treatments, contributing to significant variation between guidelines and global recommendations. Ultimately, this leads to suboptimal management of patients with advanced disease.

Aims: To conduct a systematic review of available literature on systemic therapies in advanced pulmonary carcinoids with the aim of critically evaluating current guidelines and offering evidence-based recommendations that would improve patient outcomes.

Materials and Methods: This systematic review was conducted by reviewing relevant literature on systemic treatments for advanced pulmonary carcinoids across four databases. A total of 14,254 records met the search criteria and were thus further analysed.

Results: 28 studies were included. Three were RCTs and 18 studies contained pure pulmonary carcinoid populations. Six discrete systemic therapies were evaluated, of which chemotherapy was the most common. Four patients showed complete responses. Both immunotherapy agents and VEGF-Tyrosine Kinase Inhibitors showed higher toxics than other treatments.

Conclusion: This review suggests that pulmonary carcinoid tumours are not indolent and appropriate treatments for patients with advanced disease represents an unmet clinical need. Unfortunately, most data is retrospective, allowing observational inferences which may guide future trials. Fortunately, various systemic treatments have shown efficacy against these tumours, attenuating disease spread and prolonging survival.

Biography

Heer Shah is an internal medical trainee at the Royal Marsden Hospital in London. His research interests in collaboration with the University of Oxford focus largely on developing targeted treatments for carcinoid tumours.

ONCOLOGICAL HOSPITAL PERFORMANCE OF THE HILAB SYSTEM, A NEW POINT-OF-CARE HEMATOLOGY ANALYZER.

Aléxia Thamara Gasparin, Claudiane Isabel Franco Araujo, Patricia Schmitt, Mônica Ribas Cardoso,Juliana Beker Godoy, Ivan Lucas Reis Silva, Flavia Zhu Teng, Milena Andreuzo Cardoso, Erika Bergamo Santiago, Diego Rinaldi Pavesi Nicollete, Fernanda D'Amico Silva, João Samuel de Holanda Farias, Bernardo Montesanti Machado de Almeida, Sergio Renato Rogal Júnior and Marcus Vinícius Mazega Figueredo

Hilab, Brazil

Abstract:

Most available handheld CBC devices show high prices and do not feature calibration or control procedures, resulting in poor quality compared to standard haematology instruments. The Hilab system is a point of care (POC) haematological platform that uses microscopy and chromatography techniques for blood cells and hematimetric parameters analysis through artificial intelligence, machine learning, and internet of things techniques. Simple operation single-use test kits accompany the small-handheld device, which requires only two drops of venous or finger stick blood samples (90 uL; containing or not anticoagulant) for operation. The patient receives the report by email or SMS approximately 30 minutes after the blood collection. The first validation study obtained satisfactory results, comparing the Hilab device data with a conventional hematologyanalyzer (XE-2100, Sysmex Corporation, Japan). However, the study encompassed a few samples with haematological alterations, limiting the understanding of the device performance in patients with this profile. Thus, in the present study, we assessed the accuracy, flagging capabilities, and the sample source influence of this new POC test, compared to the CBC results provided by XE-2100(Sysmex Corporation, Japan) in Erasto Gaertner Hospital, a reference institution for the diagnosis and treatment of oncological patients. Pearson correlation, Student t-test, bias, and the Bland–Altman plot of each blood count analyte were calculated and shown. The significance level was $p \leq 0.05$. The Hilab System and XE-2100 showed a strong correlation ($r \geq 0.9$) for most evaluated parameters. The flagging capabilities of the Hilab system, compared to the manual microscopy technique, presented high sensitivity, specificity, and accuracy, including immature cell observation. Venous and capillary samples ($p > 0.05$) did not differ statistically. Therefore, based on the clinical features of oncological patients, the Hilab system mare present a fast, accurate, and low-cost alternative for reliable clinical use.

Biography

Alexie Thamara Gasparin received a bachelor's degree in Biological Sciences (2018) and a master's degree in Pharmacology (2020) from the Federal University of Parana. With over five years of experience in pharmacological natural product potential studies, her research resulted in several papers published in high-impact journals in the field of Biology, Pharmacokinetics, and Pharmacodynamics. Microscopy Research and Development Manager at Hilab (Brazil) since 2020, she focused her research and knowledge on point-of-care test development. All innovative tests have in common the connection of optical microscopy with technological concepts like the internet of things, artificial intelligence, and machine learning. During the complete blood count test (CBC) development, Alexia actively contributed to two patent filings and published a paper in the Nature scientific journal. Intending to democratize health access, she keeps working on the development of new point-of-care tests.

International Conference on
Cancer and Oncology Research

June 19-20, 2023 | Rome, Italy

IL-1 INDUCED SENESCENCE: MECHANISM OF RESISTANCE TO ANTI-EGFR ANTIBODY THERAPY

Donatella Romaniello[1,2], Valerio Gelfo[1,2], Federica Pagano[1], Enea Ferlizza[1], Michela Sgarzi[1], Martina Mazzeschi[1], Alessandra Morselli[1], Cinzia Girone[1], Francesco Borelli[1], Carmen Miano[3], Moshit Lindzen[4], Gabriele D'Uva[3] Francesco Fazi[5], Luca Tamagnone[6], Karim Rihawi[7], Andrea Ardizzoni[1,7], Yosef Yarden[4] and Mattia Lauriola[1,2]

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[2]Bologna University Hospital Authority St. Orsola-Malpighi Polyclinic, Italy
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[6]Istituto di Istologia ed Embriologia, Università Cattolica del Sacro Cuore, Italy
[7]Azienda-Ospedaliero Universitaria di Bologna, Italy

Abstract:

Historically, senescence has been considered as a safe program in response to multiple stresses in which cells undergo to irreversible growth arrest. This process is characterized by morphological and metabolic changes, heterochromatin formation and secretion of inflammatory components: the senescence-associated secretory phenotype, SASP. However, in tumor cells, it has been recently demonstrated that senescence, triggered by anti-cancer therapy may represent a temporary bypass pathway, promoting drug adaptation. Previously, in our laboratory, we reported a striking correlation between reduced sensitivity to cetuximab (CTX) and increased expression of IL-1. By using a recombinant decoy able to sequester the cytokine from the medium (TRAP IL-1), in two CRC cell lines, sensitive and resistant to CTX treatment, we proved that IL-1 harness an escaping mechanism, known as "pseudo-senescence", that drive cells into cell cycle arrest in order to reprogram. Chronic IL-1 exposure pushed cells to gradually reenter the cell cycle with a more aggressive phenotype, both highly proliferative, with stemness properties and resistant to CTX. Herein, we demonstrated in vivo, that TRAP IL-1 is able to block post-senescence phase acting as senolytic agent and improving response to the conventional therapy in a CRC xenograft model. CD1 nu/nu mice carrying palpable CTX-sensitive tumors were treated for several days until resistance was acquired. Subsequently, relapsed tumor were randomized in three groups of treatments: control, receiving only CTX, 2) TRAP IL-1, and 3) CTX+TRAP IL-1.

Interestingly, the last one demonstrated, in 14 days, to statistically decrease tumor growth, empowered CTX response, compared to the no responding control. These data were confirmed in a syngeneic model, created through engraftment, in C57BL/6N (immunocompetent mice) of EGFR engineered MC38 cells. The one expressing both high murine EGFR and murine TRAP IL-1 displayed an impressive low growth tumor rate when compared with control transfected with murine EGFR. In conclusion, IL-1 may represent a viable target to to restore CTX efficacy in CRC patients.

Biography

Donatella completed Certified as a pharmacist, postdoctoral fellow. She completed her PhD studies in December 2015 on "STAT3-mediated Signaling Pathways in Physio-Phatological Processes", at Rome's Sapienza University, where she concentrated on the biochemistry of cancer. An important part of her training has been a year-long fellowship program that enabled her to study the crosstalk between JAK and HER2 signaling in HER2+ breast cancer at Memorial Sloan Kettering Cancer Center (Manhattan), in the laboratory of Prof. Bromberg. Right after her PhD, Donatella won the Sergio Lombroso Fellowship for cancer research that allows her to continue training as postdoc at the Weizmann Institute (ISRAEL), one of world's leading multidisciplinary research center. Given her interest and understanding of ERBB signaling and resistance to targeted therapies, she joined the laboratory of Yosef Yarden for about 4 years. In <2 years she had a first author publication in Clinical Cancer Research, demonstrating the effectiveness of combination antibodies and TKI for NSCLC. Based on Donatella's findings and in collaboration with the Phase I Clinical trial Unit of the University of California (Los Angeles), an initial safety and efficacy clinical tests in patients with lung cancer have been launched. Meanwhile, she left the Weizmann Institute for Bologna University publishing in 2020 another first author publications on targeting HER3 with the Yarden group. She is currently junior assistant professor at Bologna University studying the crosstalk between IL-1 and EGFR and its implication in CRC resistant to anti-EGFR antibody treatment.

Graduated in Chemistry and Pharmaceutical Technologies, Romaniello immediately started PhD program in Biochemistry at Sapienza University (Rome). During this time, she spent one year at Memorial Sloan Kettering Cancer Center studying EGFR-STAT3 axes in mediating anti-HER2 therapy resistance. Her prevalent research activity on ERBB family of receptor continued later, thanks to the Lombroso fellowship won for two consecutive years, at the Weizmann Institute of Science, one of world's leading multidisciplinary research center. She spent almost 4 years in the lab of Y. Yarden investigating the role of EGFR and all family members, HER2, HER3 and HER4, in NSCLC progression. Today, as Junior Assistant Professor at Bologna University, she has extended her research in different EGFR dependent tumors focusing on the molecular mechanisms underlying drug resistance and testing new therapeutic strategies able to enhance or restore sensitivity to TKI (tyrosin kinase inhibitor) or mAb (monoclonat antibody) treatment.

OMEGA-3 AND OVARIAN CANCER: THE PYROPTOSIS-INDUCING EFFECTS OF DOCOSAHEXAENOIC ACID (DHA)

Gabriel Pasquarelli do Nascimento, Érika Pereira Sampaio, Jonatas Cunha Barbosa Lima, João Alexandre Ribeiro Gonçalves Barbosa, Luiz Antônio Soares Romeiro and Kelly Grace Magalhães

University of Brasilia, Brazil

Abstract:

Fatty acids (FAs), which are organic compounds that present a polar carboxyl group and a hydrocarbon chain, can be categorized in saturated and unsaturated. Among these unsaturated lipids, the polyunsaturated fatty acids (PUFAs) are of particular interest due to its greater physiological importance. The PUFA Docosahexaenoic acid (DHA), the integrant of the omega-3 family believed to display more benefits within the organism, needs to be obtained from diet, mainly from fish oil. The DHA exerts its beneficial effects by regulating membrane structure and function, interacting with the FA receptor/sensor GPR120, and influencing the synthesis of bioactive lipid mediators. Through these diverse mechanisms, DHA impacts positively the wellbeing of the individual by affecting Central Nervous System health, cardiometabolic homeostasis, immune system function, hemostasis, and neoplasm development control. Although DHA is known to display tumor suppressor activity in many types of cancers, little in known about the action of DHA on ovarian cancer. The objective of this study was to investigate whether the omega-3 docosahexaenoic acid induces pyroptotic cell death in human ovarian cancer cells A2780 in vitro. In order to investigate the influence of docosahexaenoic acid on ovarian cancer A2780 cells, the cells were stimulated with increasing concentrations of this fatty acid and analysed using flow cytometry, spectrophotometry and Western Blotting. Our results showed that docosahexaenoic acid decreased the viability of human ovarian cancer cells A2780 in a dose- and time-dependent manner, as a consequence of the induction of lytic death in these cells. We also presented that this cell death is characterized by membrane pore formation, caspase-1 activation and Gasdermin-D (GSDMD) cleavage. In addition, we described that this process depends on the activity of caspase-1. Taken together, our data indicate that docosahexaenoic acid induces the immunogenic pyroptotic cell death in human ovarian cancer cells in vitro dependent on caspase-1 activity.

Biography

Gabriel Pasquarelli do Nascimento has as expertise evaluating the impact of polyunsaturated fatty acids (PUFAs) on cancer cells *in vitro*. In addition, Gabriel investigates the role of the adipose tissue influenced by different diets on breast cancer initiation and progression in vivo. Gabriel has been conducting research in the Laboratory of Immunology and Inflammation (University of Brasilia) since 2015.

NOVEL EGFR ECTODOMAIN MUTATIONS AND RESISTANCE TO ANTI-EGFR AND RADIATION THERAPY IN H&N CANCER

Markus Bredel, Sindhu Nair, Hoa Q Trummell, Rajani Rajbhandari, Christopher D Willey, Lewis Z Shi, Zhuo Zhang, William J Placzek and James A Bonner
University of Alabama, USA

Abstract:

Purpose: EGFR-targeted monoclonal antibodies (mAbs) provide clinical benefit in some patients with H&N squamous cell carcinoma (HNSCC), but others progress with minimal response. Missense mutations in the EGFR ectodomain (ECD) can be acquired under mAb therapy by mimicking the effect of large deletions on receptor untethering and activation. Little is known about the contribution of EGFR ECD mutations to EGFR activation and anti-EGFR response in HNSCC.

Methods: We selected patient-derived HNSCC cells (UM-SCC-1) for resistance to mAb Cetuximab (CTX) by repeated, stepwise exposure to mimic what may occur clinically and identified two concurrent EGFR ECD mutations (UM-SCC-1R). We examined the competence of the mutants to bind EGF ligand or CTX. We assessed the potential impact of the mutations through visual analysis of space-filling models of the native sidechains in the original structures vs. their respective side-chain mutations. We performed CRISPR in combination with site-directed mutagenesis to test for the effect of the mutants on ligandindependent EGFR activation and sorting. We determined the effects on receptor internalization, endocytosis, downstream signaling, and radiation sensitivity.

Results: UM-SCC-1R cells carried two non-synonymous missense mutations (G33S and N56K) mapping to domain I in or near the EGF binding pocket of the EGFR ECD. Structural modeling predicted that these mutants restrict the adoption of a tethered, inactive EGFR conformation while not permitting association of EGFR with the EGF ligand or CTX. Binding studies confirmed that the mutant, untethered receptor displayed a reduced affinity for both EGF and CTX but demonstrated sustained activation and presence at the cell surface with diminished internalization and sorting for endosomal degradation. Single and double-mutant models demonstrated that the G33S mutant is dominant over the N56K mutant in its effect on EGFR activation and EGF binding. CTX-resistant UM-SCC-1R cells demonstrated cross-resistance to mAb Panitumuab but, paradoxically, remained sensitive to the reversible receptor tyrosine kinase inhibitor Erlotinib.

Conclusion: HNSCC cells can select for EGFR ECD mutations under EGFR mAb exposure that converge to trap the receptor in an open, constitutively activated state. These mutants impede the receptor's competence to bind mAbs and EGF ligand and alter its endosomal trafficking, possibly explaining certain cases of clinical mAb and radiation resistance.

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THE BURDEN OF HUMAN IMMUNODEFICIENCY VIRUS INFECTION AMONG WOMEN WITH BREAST CANCER IN NORTHERN TANZANIA, PATHOLOGICAL FEATURES, TREATMENT UTILIZATION AND CLINICAL OUTCOME

Angela Pallangyo
Kilimanjaro Christian Medical University College, Tanzania

Abstract:

Background: Breast cancer (BC) is the most common Non-AIDS Defining cancer (NADC) among Women Living with Human Immunodeficiency Virus (WLWHIV) and leading cause of cancer related deaths. The high incidence of BC among WLWHIV is partly due to the HIV and Ant Retroviral Therapy (ART) which have shown to accelerate oncogenes is process. In sub–Saharan Africa, BC in WLWHIV presents at younger age with poor prognostic factors. However, in Tanzania there is scarcity of data on BC in relation to HIV infection. The management of BC in WLWHIV is complex and costly because it has to take into account the comorbidities associated with the immunosuppression. The clinical outcome of BC among WLWHIV is poor in developing countries since BC in this group presents with poor prognostic features.

Objective of The Study: To determine the prevalence of HIV among women with BC as well as the pathological features, treatment utilization pattern and clinical outcome of these women attending Kilimanjaro Christian Medical Center (KCMC) between the year 2017 and 2021.

Materials and Methods: This was a cross sectional comparison study, conducted at Kilimanjaro Christian Medical Center, in Northern Tanzania. Records of all patients with cancer who attended the Oncology department from January 2017 to December 2021 were reviewed to collect those with BC. These cases which met the inclusion criteria were linked to KCMC Cancer registry records and KCMC medical records file in order to obtain the clients information as per the listed objectives. An electronic data collection form was employed to collect socio-demographic information, histopathological features of BC, treatment utilization as well as the clinical outcome of the study population. Data was de-identified, cleaned and analysed using statistical software Stata 15. Multiple logistic regression approach was used to determine what pathological features, treatment utilization patterns and clinical outcomes were predictors of HIV infection among BC patients. The level of statistical significance was considered at 0.05.

Results: Breast cancer was the second most common malignancy among women who attended KCMC oncology department for the five years study period. The HIV prevalence among women with BC was 6.9% (22/320) and majority of these women were above 45 years old with mean age of 55.2 years and residing in Kilimanjaro region. However, the clinic pathological features of breast cancer among the two groups of women was not different. In regard to the treatment utilization pattern, 71% and 77% of BC cases among WLWHIV neither received neoadjuvant therapy nor were they ongoing with treatment when compared to BC cases among women not infected with HIV. Moreover about 50% of cases of WLWHIV having BC were lost to follow-up when

compared to only 10% women with BC who are not infected by HIV.

Conclusion: The cancer registry was not well documented and furthermore, the treatment utilization pattern and follow-up of cases of WLWHIV with BC was poor when compared to the women with BC who are not living with HIV.

Recommendation: Health education about breast cancer should be scaled up especially to the rural areas. The cancer registries should be reviewed and updated to include the HIV status and this Cancer registry templates should be incorporated to the files of patients with BC so that all the necessary information can be filled. Moreover, HIV infection testing and counselling should be part of the investigation plan to all women with BC and the treatment of these women with both BC and HIV should be multidisciplinary with close follow-up.

Biography

Angela Pallangyo is the Medical Specialist and Pathology Lecturer for the Kilimanjaro Christian Medical Centre (KCMC) and the Kilimanjaro Christian Medical University College (KCMUCo); Moshi, Kilimanjaro, Tanzania with over three years' experience in Anatomic Pathology, teaching and clinical research. She is a Young Research Peer Fellow under THET (Transforming Health Professions Education in Tanzania) project funded by NIH with a funded project titled 'The Burden of Human Immunodeficiency Virus infection among women with breast cancer in North Tanzania, pathological features, treatment utilization and Clinical outcome' serving as PI.

She has centered on screening, early diagnosis and improved lifespan of cancer patients.Her current focus and interest include global health, Breast cancer, HPV associated malignancies and Pediatric Malignancies.

She involved in graduate research laboratory training and research supervision in the Pathology sciences. She teaches both graduate and undergraduate General and Systemic Pathology including Forensic Pathology. She has attended a number of National Pathology and oncology scientific meetings.

Recently she has been working with International Cancer Institute (ICI) of Kenya on Breast cancer study project which is a community-based study aiming at scaling up breast cancer awareness and screening services in rural areas of Kilimanjaro region.

As a practicing anatomic pathologist at a zonal tertiary and academic center in Northern Tanzania; most of my works is focused on cancer diagnosis and contribution in cancer patient management through multidisplinary tumor board discussions.

EVALUATION OF RADIOMIC PROFILES ON MR IN PATIENTS DIAGNOSED WITH H3F3AK27M MUTATION IN CNS TUMORS

Chilaca Rosas María Fátima, Contreras-Aguilar MT, Salazar-Calderon DR, Garcia-Lezama M, Piña-Sanchez P and Roldan-Valadez E

National Medical Cancer Center siglo XXI, Mexico/ National Autonomous University of Mexico

Abstract:

Introduction: Gliomas are the most frequent central nervous system tumours, with high-grade tumours being the most prevalent. The identification of H3F3AK27M mutation in diffuse midline gliomas (DMG) has been associated with a poor prognosis with a median overall survival (OS) of 11 months. Radiomic extraction is an emerging field in precision medicine, which studies features extracted from medical images that reflect the tumour microenvironment and can be associated with clinical and molecular data.

Objective: Analysis of radiomic profiles in DMG with H3F3AK27M mutation, presenting cut-off values and diagnostic performance of the significant radiomics.

Materials and Methods: Retrospective study. Initially, 91 patients with DMG were identified, but only 12 patients had the H3F3AK27M mutation and available DICOM brain MRI files. Region of interest (ROI) segmentation was performed and radiomic features were obtained in T1 postgadolinium and T2 MRI sequences using LIFEx software. Statistical analysis was performed with Mann-Whitney U test and ROC analysis.

Results: From 5,670 radiomic features, 13 demonstrated AUROC with statistical significance for progression-free survival (PFS) and 4 for OS. Diagnostic performance tests showed 9 out of 13 radiomic features with specificity for PFS greater than 90% and 1 with a sensitivity of 97.2%, for OS 3 out of 4 radiomic features demonstrated a sensitivity between 80-90%. Respecting the texture analysis, GLCM texture profile, GLZLM_GLNU, and NGLDM_Contrast were found to be relevant; there was also a trend for the role of first- and second-order radiomic features in influencing PFS and OS.

Conclusion: The role of radiomics in imaging analysis has been growing and providing increasing data about tumour profiles. These results could enrich the information about the application of radiomics and provide information to establish external validity and reproducibility, and eventually be applicated in the decision trees in diagnosis and treatment planning performed by the neurooncology team.

Biography

Chilaca Rosas María Fátima has experience in Pediatric and Young Adult Clinical Radiotherapy Oncology, Advanced Radiotherapy, Radiosurgery and Master's in science of Neuro-oncology. She has worked in translational medicine research in Mexico with the objective of new advances in diagnostic imaging and multidisciplinary planning of cancer management (surgery, oncology, genetic and radiation oncology). She has collaborated and worked with multiple private cancer centers in Mexico City and states in his country.

In the academic field, the specialist has been a member of the jury of the examining board in the specialty of Radio-Oncology and is Professor of U.N.A.M. (Universidad Nacional Autónoma deMéxico) of the Specialty of Radio-Oncology, Pediatric Medical Oncology and Pediatric Neurosurgery at the Oncology Hospital of Medical Cancer Center siglo XXI.

Day 2

Oncology Congress 2023

Poster Presentations

ANTI-CANCER ACTIVITY OF NEWLY SYNTHETIZED 2, 2'-DISELENOBIS (N-PROPYLBENZAMIDE) IS MEDIATED BY CHANGES IN IRON METABOLISM

Jedrzej Antosiewicz[1], Juhas U[1], Reczkowicz J[1], Borkowska A[1], Olszewski S[1], Ścianowski J[2], Obieziurska-Fabisiak M[2] and Pacuła-Miszewska A[2]

[1]*Medical University of Gdansk, Poland*
[2]*Nicolaus Copernicus University, Poland*

Abstract:

Objectives: Iron is an essential and irreplaceable element used by living cells during a variety of metabolic processes. Our preliminary results indicate that chronic exposure of cancer cells to stressors leads to excessive iron accumulation. The main objective of our ongoing study was to evaluate the anticancer activity of the newly synthesized Ebselen derivatives, including 2,2'-Diselenobis (N-propylbenzamide) (DPB). We assumed that the cytotoxic action of DPB was related to the impairment of the iron metabolism of cancer cells.

Methods: Our hypothesis was examined on the two phenotypically distinctive prostate cancer cell lines: DU145 and PC-3 as well as on the normal PNT1A cells.

Results: DPB restrained the cancer cell proliferation, while PNT1A were less sensitive to its action. DPB induced G2/M cell cycle arrest of both cancer cell lines and prompted cell death through apoptosis. We observed that PC-3 and DU145 cells stimulated with DPB increased the levels of APP, ferritin H and ferroportin, which are proteins related to iron storage and export. What is important, these alterations were less evident in PNT1A cells. The iron chelator – Desferrioxamine (DFO), partially protected PC-3 cells from DPB toxicity, which suggest the role of iron in this process.

Conclusion: In conclusion our data indicates that cytotoxicity of DPB is related changes in iron metabolism and possibly labile iron pool participates in the mechanism of DPB induced cell death. Changes in proteins of iron metabolism indicates for adaptive response of cancer cell against iron toxicity.

Biography

Jędrzej Antosiewicz works at the Medical University of Gdansk. For many years, he has been conducting research on iron metabolism, both at the cellular level and the whole organism. In his works, he showed, among others, that stress-activated kinases regulate the process of ferritin degradation, and thus the bioavailability of iron for metabolic processes and reactions responsible for the formation of reactive oxygen species. His professional career is related to scientific internships in renowned research centers such as the University of Ancona, Italy, Nagoya (Japan), Pittsburgh (USA).

EFFECTS OF NOVEL USNIC ACID DERIVATIVE ON WNT SIGNALING-PATHWAY IN BREAST CANCER CELLS

Klaudia Żuczek[1], Elwira Smolińska[2] and Anna Herman-Antosiewicz[1]

[1]University of Gdańsk, Gdańsk, Poland
[2]Medical University of Gdańsk, Poland

Abstract:

Objectives: The main aim of this project was to verify the hypothesis of the downregulation of the Wnt signaling pathway by 2b – a new derivative of usnic acid - in breast cancer cells. Breast cancer is still the first leading cause of cancer-related deaths. Development of metastatic disease, poor response to standard therapy, and relapse of the disease still constitute the major clinical problems preventing the cure of high-grade breast cancer patients. Thus, there is a strong need for the continuous development of novel therapeutic agents to improve breast cancer therapy. To date, evidence suggests that the Wnt signaling pathway is the key factor in breast cancer chemoresistance, stem cell features and metastasis.

Methods: MCF-7 and MDA-MB-231 breast cancer cells were used. The impact of 2b on elements of Wnt pathway on the transcription level was investigated using RNA-seq and qPCR techniques. The levels of selected proteins were investigated by immunoblotting.

Results: Exposition of MCF-7 cells to 2b for 6 or 24 h resulted in changes in the expression of genes encoding multiple components of the Wnt signaling including the ligands, receptors and intracellular components. To further explore the Wnt/β-catenin activity, we determined the mRNA levels of the specific Wnt/β-catenin target genes: LRP5, LRP6, CCND1, CD44, CTNNB1, LEF1, Wnt3, Wnt10B, Fzd7, ALDH4A1. All of them were downregulated in MCF-7 cells; however, in MDA-MB-231 reduction of transcripts was observed only after 24-h treatment in the majority of tested genes. Interestingly, levels of LRP5 and LRP6 were heavily reduced after 6 and 24 h of treatment with 2b in both cell lines. LRPs are essential Wnt signaling coreceptors and LRP5 is significantly up-regulated in 20–36% of human breast carcinomas which makes it a promising cancer therapy target.

Conclusion: Collectively, these data show that 2b downregulates the Wnt signaling pathway in breast cancer cells which makes it a promising therapeutic acting at different levels of breast cancer progression.This research was funded by the National Science Centre, Poland, Project Number: 2017/26/ M/ NZ7/ 00668.

Biography

Klaudia Żuczek, received her master's degree from the University of Gdańsk in 2021 (specialization Medical biology). She is a student at the Doctoral School of Exact and Natural Sciences of the University of Gdańsk carrying out research in the project on new derivatives of usnic acid as anticancer drugs. Her main fields of interest include the molecular basis of therapeutic approaches in breast cancer. She has actively taken part in conferences and workshops. She is also interested in preclinical studies and clinical trials.

THE ISOXAZOLE DERIVATIVE OF USNIC ACID DISTURBS BREAST CANCER CELL METABOLISM

Anna Herman-Antosiewicz[1], Agnieszka Pyrczak-Felczykowska[2], Anna K Kaczorowska[1], Jędrzej Antosiewicz[2] and Tristan A Reekie[3]

[1]*University of Gdańsk, Poland*
[2]*Medical University of Gdańsk, Poland*
[3]*Australian National University, Australia*

Abstract:

Objectives: Usnic acid (UA) is a secondary metabolite found in lichens with documented multiple activities, including antiproliferative and cytotoxic against cancer cells. As anticancer activity is observed for rather high UA concentrations, which are otherwise toxic to healthy cells, synthetic derivatives are designed with a more favorable biological profile. One of them is a recently obtained isoxazole derivative of UA, named 2b, that was shown to induce paraptosis-like death of breast cancer cells. In this work, the impact of 2b on the metabolism of breast cancer and noncancerous cells was investigated.

Methods: MCF-7 breast cancer cells and HB-2 breast epithelial cells were used. They were treated with 2b (3 µg/ml) or UA (40 µg/ml) for 6 or 24 h. ATP level was measured spectrophotometrically, cell bioenergetics - using Seahorse XF96 extracellular flux analyzer, and mitochondrial functionality - using BIOLOG system.

Results: 2b compound reduced ATP level in MCF-7 cells and it was connected with a drop in oxygen consumption rate (OCR), especially basal and maximal respiration. Statistically significant changes were also observed for the ATP-linked respiration, spare capacity and proton leak already after 6-h treatment, although this effect was more pronounced after the longer exposition, and 2b was much more effective than the parent compound. Subsequent experiments showed that 2b disturbs mitochondrial functioning: electron flow into and through the electron transport chain was stimulated by the addition of the majority of metabolic substrates that produce NADH or FADH2 but treatment with 2b significantly inhibited this flow in MCF-7 but not HB-2 cells.

Conclusion: New derivative of UA is a more potent inhibitor of breast cancer progression. Its mechanism of action partly relies on the inhibition of mitochondria activity and thus disturbance in cancer cell metabolism.

This research was funded by National Science Centre, Poland (Project No. 2017/26/M/NZ7/00668)

Biography

Anna Herman-Antosiewicz is a molecular biologist. She received her PhD at the University of Gdańsk. Poland. She completed postdoctoral training at the University of Pittsburgh Cancer Institute, Pittsburgh, USA. In her research, she concentrates on chemopreventive and therapeutic agents from natural sources as well as their chemically modified derivatives for the treatment of cancer or bacterial infections.

CONSECUTIVE STEPS OF THE FIRST KAZAKHSTANI PROGRAM ON EARLY DIAGNOSIS OF CHEMOTHERAPY-ASSOCIATED CARDIOTOXICITY IN BREAST CANCER PATIENTS: WHERE WE ARE?

Zhenisgul Tlegenova
West Kazakhstan Marat Ospanov Medical University, Kazakhstan

Abstract:

A multidisciplinary team consisting of cardiologists and chemotherapists becomes the compulsory component of oncologic service due to cardiotoxicity associated with anticancer treatment. Currently, a cardio-oncological service is being created in Kazakhstan based on the provisions of the European Society of Cardio-oncology Guidelines. In frames of a pilot project, we formed a multidisciplinary team at the Aktobe Cancer center and initiated a cohort study on CTRCD (Cancer Treatment-Related Cardiac Dysfunction) conditions.

The Program Details: Between September 2021 and August 2022, we recruited 128 newly diagnosed breast cancer patients started on doxorubicin and/or trastuzumab. Echocardiography with global longitudinal strain (GLS) assessment, six-minute walk test, ECG with Holter monitoring, biomarkers panel (cTnI, BNP, MPO, Gal-3, D-dimers, CRP), and other tests were performed at baseline and every three months.

The Cardiovascular Risks Stratification Stage: Patients were allocated into risk groups during the pre-treatment visit according to the ESC recommendations. 7.8% of patients were assigned to the high-risk group, 37.5% - to the medium-risk group, and 54.7% - to the low-risk group. High-risk patients have been receiving their cardioprotective treatment from the outset.

Adherence to Cardioprotective Medications Control: we practice monthly encouraging calls to patients under observation to ensure adherence to protocol activities. During the baseline examination, we assisted willing participants who were prescribed cardiac protectors in installing appropriate apps on their telephones to remind them of pill intake.

Current Stage: By the end of January 2023, 67 patients out of 128 had been followed up for 12 months or more. Mild symptomatic CTRCD was revealed and treated in 2 (1.6%) participants and a mild asymptomatic variant - in 26 (20.3%). Mild asymptomatic conditions are defined as LVEF $\geq$ 50% and further relative reduction in GLS by >15% from baseline and/or a further rise in cardiac biomarkers. No cases of chemotherapy discontinuation due to cardiotoxic complications have been recorded so far.

Biography

Zhenisgul Tlegenova is an Associate Professor at the Internal Diseases-2 Department. Designer and Coordinator of scientific projects of republican importance on cardiovascular diseases. Professional areas: general cardiology, instrumental cardiology. Research focus: cardiotoxicity of chemotherapy; heart failure; arterial hypertension; atrial fibrillation; Echocardiographic techniques. Currently she is a Coordinator of the project on breast cancer chemotherapy-linked cardiotoxicity.

THE SARS-COV-2 SPIKE PROTEIN HIJACKS THE EPIDERMAL GROWTH FACTOR RECEPTOR- MEDIATED SIGNALING IN CANCER CELLS

Rabah Iratni[1], Abdulrasheed Palakkott[1], Aysha Alneyadi[1], Khalid Muhammad[1], Ali H. Eid[3], Khaled Amiri[1] and Mohammed Akli Ayoub[4]

[1]United Arab Emirates University, UAE
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[4]C Khalifa University, UAE

Abstract:

Since December 2019, the world is facing a global health threat by the coronavirus disease-19 (COVID-19) pandemic caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). At the molecular and cellular levels, the SARS- Cov-2 uses its envelope glycoprotein, the spike S protein, to infect the target cells in the lungs via binding with their transmembrane receptor, the angiotensin-converting enzyme 2 (ACE2). Here, we investigated the possibility for the spike 1 S protein and its receptor- binding domain (RBD) to target the epidermal growth factor receptor (EGFR) and its downstream signaling pathway *in vitro* using ACE expressing and non-expressing cancer cell lines. Our data demonstrate for the first time the activation of EGFR by the Spike 1 protein associated with a significant phosphorylation of the canonical ERK1/2 and AKT kinases and an increase of survivin expression controlling the proliferative and survival pathways. Strikingly, the RBD although it had no effect on the activation of EGFR, still, it significantly promoted AKT and ERK1/2 phosphorylation as well as survivin expression and hence suggesting different mode of activation and/or molecular pathways involved between Spike 1 and its RBD. Our data suggest the implication of EGFR and its proliferative/survival pathways in SARS-CoV-2 infectivity and Covid-19 pathology. This may open new perspectives in the treatment of Covid-19 patients by targeting EGFR.

Biography

Rabah Iratni obtained his PhD from University Joseph Fourier, Grenoble 1 in December 1994. After completion of his PhD he joined, as postdoctoral fellow, the laboratory of Prof. Dany Reinberg at the University of Medicine and Dentistry of New Jersey (UMDNJ). In 2002, he joined the University Joseph Fourier, Grenoble 1 as "Maitre de conference). In 2005 he obtained his "Habilitation a Diriger la Recherche" (HDR) from the same university. In 2007, he joined the United Arab Emirates University first as an Associate professor and then as professor. My main research interests focus on (i) drug discovery through screening of new potential anti-cancer natural compounds using in vitro and in vivo assays and determine their mechanism(s) of action by combining cellular and Molecular and biochemical approaches (ii) preclinical evaluation of the role of the human Drap1(NC2α), the inhibitor of member of the TGF-β signalling pathway Nodal, as potential tumor suppressor of breast cancer and (iii) understanding of the epigenetic basis of cancer. He has co-authored a number of publications in prestigious scientific journals such as Cell, Science, Genes and Development, PNAS.

NUCLEOPHOSMIN-1 INTERACTION IS INVOLVED IN NUCLEAR HER2-MEDIATED TUMOR PROGRESSION AND DRUG RESISTANCE

Yun-Ju Chen, Pei-Hsuan Chien, Wen-Ling Wang, Ya-Ling Wei and Wei-Chien Huang

I-Shou University, Taiwan

Abstract:

Overexpression of HER2 occurs in approximately 20% of breast cancer cases. Despite significant efficiency in clinical outcomes, overcoming drug resistance remains the unmet need for the clinic. The somatic mutations or acquired mutations of HER2 attenuate therapeutic effects of HER2-targeted therapies. L755 in exon 19, comprising 22% of HER2 mutations, is the most common somatic HER2 mutation in breast cancers and highly associates with lapatinib resistance. Quarter patients developed L755S mutation in response to HER2-targeted therapies. The site chain of L755 is in close proximity to the drug binding pocket and L755 mutation thereby changes the drug-binding pocket volume, leading to drug resistance and even cross-resistance. We investigated the role of HER2 L755 mutation in drug resistance. Our results showed that L755P/S mutants displayed hyper-active HER2 signaling pathways. Interestingly, L755 locates near a putative nuclear export signal, and L755P/S mutants induced nuclear translocation of HER2. We found that breast cancer cells ectopically expressing L755P mutant showed more resistance to tyrosine kinase inhibitors than those expressing L755S mutant. These findings lead us to address the functions of nuclear HER2 L755 mutants in drug resistance and tumor progression. Our results further demonstrated the specific interaction between HER2 L755P mutant and NPM1, which mainly localizes in nucleolus and functions as a histone chaperon to mediate genomic stability, DNA repair, and anti-apoptosis. Depending on the cancer type, NPM1 controversially acts as an activating oncogene or a tumor suppressor. However, the role of NPM1 in breast cancer is unclear. Our results suggest that NPM1 acts as an oncogene and is highly associated with lapatinib resistance. Collectively, NPM1 interaction with HER2 L755 mutation is involved in nuclear HER2-mediated tumor progression and drug resistance. In the future, we will evaluate whether targeting NPM1 as a promising strategy suppresses tumor progression and overcomes drug resistance.

Biography

Yun-Ju Chen has her expertise in evaluation and passion in improving the health and wellbeing. Her research is on cancer research, especially the aspect of the mechanism underlying resistance to targeted therapy. She tries to identify not only the predictive unknown biomarkers for targeted therapy in order to extend the application of targeted therapy, but also the predictive biomarkers for resistance in order to provide clues to overcome resistance. She has built this model after years of experience in research and evaluation in education institutions.

PHOSPHATASES ARE INVOLVED IN CELECOXIB-MEDIATED CANCER STEMNESS INHIBITION OF COLORECTAL CANCER CELLS

Yueh-Ming Lin, Pei-Hsuan Chien and Yun-Ju Chen

Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Taiwan

Abstract:

Several lines of evidence demonstrate that cancer stemness inhibition acts as a predictive factor for cancer relapse. Our previous study indicates that celecoxib owns the most potent inhibitory activity against cancer stemness property of colorectal cancer (CRC) cells among a variety of non-steroidal anti-inflammatory drugs (NSAIDs). Analysis of underlying mechanism reveals that celecoxib inhibits both cyclooxygenase-2 (COX-2) activity and c-Met activity. Furthermore, c-Met is a critical factor for the cancer stemness property of CRC cells. In this study, we further investigated the mechanism underlying celecoxib-mediated inhibition of c-Met activity in CRC cells. The results showed that c-Met kinase activity was only slightly inhibited by celecoxib whereas totally blocked by well-known classical c-Met kinase inhibitors as shown by *in vitro* kinase assay, suggesting that celecoxib did not directly bind to c-Met to inhibit its kinase activity. Furthermore, we found that tyrosine 1234/1235 phosphorylation of c-Met was attenuated in celecoxib-treated CRC cells. We further examined the involvement of c-Met phosphatases in this regulation. The results showed that the expression of protein tyrosine phosphatase 1B (PTP1B) was increased by celecoxib in dose- and time-dependent manners. Furthermore, we found that spheroid formation was slightly increased in CRC cells without PTP1B expression. On the other hand, it is known that protein phosphatase 2A (PP2A), a serine/threonine phosphatase, is reported to mediate serine 985 dephosphorylation of c-Met and in turn to enhance tyrosine 1234/1235 phosphorylation of c-Met. The results showed that serine 985 phosphorylation of c-Met was obviously increased at 30 minutes of celecoxib treatment and lasted for 12 hours, which negatively corresponded to the pattern of tyrosine 1234/1235 phosphorylation of c-Met. Collectively, these results suggest that c-Met-related phosphatases are involved in celecoxib-mediated CRC cancer stemness inhibition.

Biography

Yun-Ju Chen has her expertise in evaluation and passion in improving the health and wellbeing. Her research is on cancer research, especially the aspect of the mechanism underlying resistance to targeted therapy. She tries to identify not only the predictive unknown biomarkers for targeted therapy in order to extend the application of targeted therapy, but also the predictive biomarkers for resistance in order to provide clues to overcome resistance. She has built this model after years of experience in research and evaluation in education institutions.

THE ISOXAZOLE USNIC ACID DERIVATIVE INDUCES RETICULAR STRESS IN BREAST CANCER CELLS WHICH LEADS TO ER-PHAGY AND CELL DEATH

Agnieszka Pyrczak-Felczykowska[1], Anna Herman-Antosiewicz[2], Anna Pawlik[2], Aleksandra Hać[2] and Tristan A Reekie[3]

[1]*Medical University of Gdańsk, Poland*
[2]*University of Gdańsk, Poland*
[3]*Australian National University, Australia*

Abstract:

Objectives: Usnic acid (UA) is a known lichen metabolite with anticancer, antibacterial and antiinfective activity. However, the use of UA as a potential anti-cancer drug is limited by its low solubility in aqueous solutions and hepatotoxicity. In order to avoid these disadvantages a number of usnic acid derivatives was obtained by chemical synthesis. One of them, named 2b, showed a strong anti-proliferative activity toward breast cancer cells with minimal effect on normal fibroblasts. Herein, the molecular mechanisms underlying 2b activity derivative on breast cancer cells were investigated.

Methods: In this study MCF-7 breast cancer and 1-7HB2 non-cancerous cell lines were utilized. The viability of breast cancer and normal cells was tested using an MTT assay. Cell and organelle morphology was analyzed using light, electron and fluorescence microscopy. Gene expression was evaluated by RNAseq. The IR-phagy has been investigated using the TetOn-eGFP-mCherry-RAMP4 construct which allows to track the degradation of endoplasmic reticulum fragments in lysosomes in fluorescence microscopy. *In vivo* anticancer activity was evaluated on a mice xenograft model.

Results: We found that 2b induced massive vacuolization which originated from the endoplasmic reticulum (ER). ER stress markers were upregulated both at the mRNA and protein levels. ER stress was caused by the release of Ca^{2+} ions from the ER by IP3R channels which was mediated, at least partly, by phospholipase C (PLC)-synthetized 1,4,5-inositol triphosphate (IP3). ER stress induced the ER-phagy process. Prolonged ER stress led to the cell death with features of apoptosis and paraptosis. When applied to nude mice with xenografted breast cancer cells, 2b stopped tumour growth.

Conclusion: This study shows that the antiproliferative activity of 2b relates to the induction of ER stress in cancer, not in healthy, cells and it leads to breast cancer cell death both *in vitro* and *in vivo*.

Biography

Agnieszka Pyrczak-Felczykowska, privately, mother of two urchins, graduated the Biotechnology at the Gdańsk University of Technology. Then she completed her PhD at the Faculty of Biology of the University of Gdańsk, where she participated in an international project investigating potential new anti-cancer compounds derived from marine organisms. Currently involved in the study of newly synthesized usnic acid derivatives for potential use in anticancer therapy. Additionally, she fills her time teaching physiology to medical students.

PYRAZOLE USNIC ACID DERIVATIVE AS AN ANTIPROLIFERATIVE AGENT TOWARDS PANCREATIC CANCER CELLS

Mariola Gimła[1], Tristan Reekie[2] and Anna Herman-Antosiewicz[1]

[1]*University of Gdańsk, Poland*
[2]*Australian National University, Australia*

Abstract:

Objectives: The incidence of neoplastic diseases is constantly increasing, therefore new methods of prevention and treatment of these diseases, including new drugs, are constantly being sought. For this purpose, naturally occurring compounds are used or their derivatives with more favorable chemical and biological properties are synthesized. Such compounds include usnic acid (UA) - a secondary metabolite of lichens, a derivative of benzofuran. Reports indicate that it has a cytotoxic effect on cancer cells of various origins, both *in vitro* and *in vivo*, but it should be used in relatively high concentrations. They may, in turn, be toxic to normal cells and there are indeed reports of hepatotoxic effects of this compound in rodents and humans.

Methods: In this research, a new synthetic pyrazole derivative of UA has been obtained and its antiproliferative potential against two pancreatic cancer cell lines, PANC-1 and MIA PaCa-2, was investigated. Effects of the UA derivative on cancer cells viability, changes in cell morphology, cell cycle progression and apoptosis have been tested using colorimetric or microscopic methods and flow cytometry.

Results: The obtained results demonstrate the quite potent antiproliferative activity of the tested UA derivative against both pancreatic cancer cell lines. It induces cell cycle arrest, cytoplasm vacuolization and apoptosis as well as inhibits migration of cells; however, the extent of affected processes is cell-line specific. In addition, it is less cytotoxic for healthy than for cancer cells. To fully evaluate the anticancer potential of the tested compound additional experiments need to be performed.

Conclusion: Based on the presented results it seems that modification of usnic acid structure is a promising strategy to obtain compounds with a higher than parent compound anticancer potential.

This research was funded by National Science Centre, Poland (Project No. 2017/26/M/NZ7/00668)

Biography

Mariola Gimła, received her master's degree from the University of Gdańsk. She is a student at the Doctoral School of Exact and Natural Sciences of the University of Gdańsk. On a daily basis, she works in the Laboratory of Cell Signaling of the Department of Medical Biology and Genetics, Faculty of Biology, University of Gdańsk. She works with cancer cells investigating how potential chemotherapeutics influence their processes and molecular pathways that play a role in cancer progression. Her research focuses on the anticancer potential of natural compounds, as well as their synthetic derivatives, to uncover new therapeutic options for cancer patients. She is also interested in understanding the mechanisms of action behind each compound and determining optimal doses for effective treatments.

SIGNIFICANCE OF SERUM SURVIVIN AND -31G/C GENE POLYMORPHISM IN THE EARLY DIAGNOSIS OF EGYPTIAN BREAST CANCER PATIENTS

Tarek Mohamed Kamal Mohamed Metawie
Cairo University, Egypt

Abstract:

Background: Breast cancer is one of the most relevant malignancies among women. Molecular abnormalities in promotor region of survivin gene may account for overexpression of survivin and increased breast cancer risk. This study aimed to explore the potential association between survivin promotor gene -31G/C SNP (rs9904341) and its serum level alteration on one hand, and the risk of breast cancer in Egyptian patients on the other hand. It also aimed to assess the usefulness of survivin as an early non-invasive diagnostic biomarker and in breast cancer staging.

Subjects and Methods: A total of 135 patients with physically and pathologically confirmed breast cancer and 40 unrelated controls as well as 40 patients with benign breast mass were recruited from the early detection unit at National Cancer Institute, Cairo University. Genotyping was performed using allelic discrimination probes by qPCR and serum survivin by ELISA.

Results: The minor allele C of -31G/C survivin SNP was more frequent in breast cancer patients (19.3%) compared to the control group (7.5%). Furthermore, subjects with GC+CC genotype were at increased risk of breast cancer compared with the GG genotype of control group and also with benign group. Moreover, those patients exhibited higher serum levels of survivin when compared with GG genotype. There were also significant elevation of serum survivin in different breast cancer stages.

Conclusion: Genetic variation in -31G/C of survivin gene may contribute to the disposition of breast cancer in Egyptian population. Serum survivin alteration displayed a pivotal role in the pathogenesis of breast cancer.

Biography

Tarek Mohamed Kamal Mohamed Metawie, Professor of Biochemistry, Faculty of Pharmacy, Cairo University. Egyptian, date of birth 6/3/1955. Ph.D. in Pharmaceutical Sciences, 1984; M.Sc. in Pharmaceutical Sciences, 1979; B.Sc. in Pharmaceutical Sciences, Faculty of Pharmacy, Cairo University, Egypt.

Day 2

Oncology Congress 2023

e-Poster

A RARE CASE REPORT OF PANCREATIC CANCER INITIALLY MANIFESTED AS PORTAL VEIN THROMBOSIS

Jingfen Shi[3], Haiyan Xu[1], Wei Hong[1], Shanhong Tang[2], Wuxiu Yao[1], Wei Li[1] and Lan Peng[1]

[1]*Wenjiang District People's Hospital, China*
[2]*The People's Liberation Army Western Theater General Hospital, China*
[3]*University of Electronic Science and Technology of China, China*

Abstract:

Background: Malignant tumors initially presenting with portal vein thrombosis (PVT) are extremely uncommon.

Methods: In this rare case, a 61-year-old male was admitted with pancreatitis-like symptoms and initial imaging manifestations of PVT. The initial abdominal enhanced computed tomography (CT) scan and pathology examination did not show obvious signs of pancreatic cancer.

Results: After 3 months, both the enhanced CT scan and intraoperative frozen section examination indicated pancreatic cancer with liver metastasis, while thrombosis was ruled out. Chemotherapy was administered following the operation.

Conclusion: For unexplained PVT, doctors need to be highly vigilant about the possibility of pancreatic malignant tumors to avoid clinical missed diagnosis.

Biography

Jingfen Shi, Doctor of Management, Associate professor of Health management, master supervisor, research field covers medical education, health policy and hospital management. She is now the deputy director of Health Policy and Hospital Management Institute of Sichuan Academy of Medical Sciences and Sichuan Provincial People's Hospital, and the Deputy director of Wenjiang District People's Hospital of Chengdu.
current affiliation:1.Institute for Health Policy and Hospital Management, Sichuan Academy of Medical Science and Sichuan Provincial People's Hospital, University of Electronic Science and Technology of China, Chengdu, China.2.Wenjiang District People's Hospital, Chengdu, China.

Day 2

Oncology Congress 2023

Video Presentation

DOES ORAL CARE WITH PROPOLIS A¬ECT THE DEVELOPMENT OF ORAL MUCOSITIS IN PEDIATRIC ONCOLOGY PATIENTS: A RANDOMIZED CONTROLLED CLINICAL STUDY

Aslı Elif Tanugur Samancı[5], Beste Özgüven Öztornacı[1], Esra Ardahan Akgül[1], Pınar Dogan[1], Hatice Yıldırım Sarı[1], Gülah Kapkın[2], Deniz Kızmazoglu[3], Zuhal Önder Sivi[4] and Ali Timuçin Atayoglu[6]

[1]*Izmir Katip Celebi University, Turkey*
[2]*University İzmir Tepecik Educationand Research Hospital, Turkey*
[3]*Health Sciences University İzmir Tepecik Educationand Research Hospital, Turkey*
[4]*Ege University Turkey*
[5]*Bee&You / Bee'o Research Center, SBS Bilimsel Bio Cozumler, Turkey*
[6]*Istanbul Medipol University, Turkey*

Abstract:

In chemotherapy, the target is cancerous cells, yet high doses of chemotherapeutic agents do not have selectivity. Intact tissue cells are also affected by this cytotoxicity and causes mucositis development in the patient, especially as a result of mucosal cells being affected. Mucositis is a condition that is expected to begin on the third to fourth day following the start of high-dose chemotherapy, and to peak in terms of severity and depth between seventh and fourteenth days and heals after 21 days. Treatment of more than one third of patients mire down due to oral mucositis. Furthermore, this condition cause increase of hospitalization time and mortality.

Aim of the study: In this study, it was aimed to determine whether oral care with Anatolian Propolis, which is anti-inflammatory, antibacterial, antifungal, antioxidant, antiviral and anticarcinogenic and has an immune-enhancing effect, prevents the formation of oral mucositis due to multiple use of chemotherapeutic drugs on pediatric oncology patients.

Results: The mucosal changes and the effectiveness of propolis extract for preventing oral mucositis were evaluated. 28 patients (77.77%) did not develop oral mucositis. Two patients (5.55%) developed grade 1 mucositis. 2 patients (5.55%) had mucositis grade 2. Patients did not report any pain during the use of the propolis extract. Candidosis was not observed in any patient during the use of propolis extract.

Conclusion: In conclusion, it was determined that oral care solution including 15% water-soluble propolis was significantly effective on the prevention of oral mucositis in paediatric oncology patients.

Biography

Asli Samanci and her Brand: Bee&You Asli Samanci is a renowned and award-winning food scientist committed to creating natural and healthy products for the educated consumer. Asli Samanci graduated from the Department of Food Engineering at Istanbul Technical University in 1996 and received her Master of Science degree from the same university in 2006. Her thesis involved research on "Determination of Origin in Honey". Asli Samanci has many years of experience working as a manager in the beekeeping and bee products industry, where she specialized in quality and food safety management systems, R&D projects, and product authenticity. Her expertise includes determining quality characteristics, identifying contaminants and residues, analyzing sensory qualities, developing new products, and determining geographical and botanical origin.

Virtual Presentations

Virtual
Day-01

Oncology Congress 2023

Keynote Presentation

COMBINING ANTIANGIOGENIC AND IMMUNOTHERAPEUTIC APPROACHES TO ACHIEVE SYNERGISTIC EFFICACY IN CANCER TREATMENT

WenQing Yang[1], Liting Xue[2], Kun Wang[2], Jianxing Tang[2], Janine Y Yang[3], Xinxin Li[2], Wenjie Song[2] and Renhong Tang[2]

[1]Founder and Chief Scientific Officer, ClinBridge Biotech Ltd., China
[2]Jiangsu Simcere Pharmaceutical Co. Ltd, China
[3]Massachusetts Eye and Ear, Harvard Medical School, USA

Abstract:

In the past decade, cancer immunotherapy has demonstrated remarkable progress in clinics, however, the response rate remains relatively low. Cancer immunotherapy as a monotherapy may not be enough. Development of combinatorial cancer immuno-therapies engaging multiple MOAs or drug modalities is required to improve clinical outcome and ultimately benefit cancer patients An increasing number of studies have focused on combining antiangiogenic agents and immune checkpoint inhibitors (ICIs) to treat cancer in preclinical and clinical settings. Sevacizumab (BD0801) and Endostar are both antiangiogenic agents with different characteristics. This work investigated MOA and potential clinical benefits resulting from combing Sevacizumab (BD0801) or Endostar with ICIs. Sevacizumab exhibited dose-dependent tumor growth inhibitory activities in xenograft and murine syngeneic tumor models. Notably, combining Sevacizumab with either anti-PD-1 or anti-PD-L1 antibody showed synergistic antitumor efficacy in both lung and colorectal cancer mouse models. Furthermore, the mechanistic studies suggested that the mechanism of action (MOA) of the synergistic antitumor efficacy involving improved tumor vasculature normalization, reduced exhausted effect cells and enhanced T-cell mediated immunity. In addition, our data showed that Endostar, an antiangiogenic agent with numeral targets, could bind to both VEGF and basic Fibroblast Growth Factor (bFGF) with high affinity and block the signaling through bFGF/FGFR and VEGF/VEGFR. As expected, Endostar showed synergistic antitumor effects in combination with anti-PD-L1 antibody in both colorectal cancer and melanoma mouse models. These data provide a solid rationale testing antiangiogenic agent Sevacizumab or Endostar in combination with ICIs in clinical development. The recent progress of combinatorial therapies using antiangiogenic agents and immunotherapy approaches at preclinical and clinical stages will be also reviewed and discussed.

Biography

WenQing Yang gained a Ph.D. degree on Cell Biology and finished Post-Doctoral training in Cancer Biology at University of Calgary, Canada. He has ~30 years of translational and innovative drug development experience on cancer and inflammatory diseases from a range of leading academic institutions or pharmaceutical organizations, including Celgene, Amgen, Crown Biosciences, UCLA, Kosan Biosciences, ImaginAb Inc and Simcere Pharma Group. As a translational scientist and leader in the field, he led or crucially contributed to drug discovery programs involving >20 novel targets in the areas of gene therapy, epigenetics, targeted therapy and I/O, which led to 15 INDs or Phase-II/III development. He held several management positions in the biotech industry including Executive Director, Cancer Biology, Global Scientific Research Innovation Organization, Senior Director of Cancer Pharmacology, Crown Biosciences, Head of Pharmacology at ImaginAb Inc. and Head of Translational Sciences, State Key Laboratory of Translational Medicine and Innovative Drug Development, Simcere Pharma Group. Dr. Yang's expertise focuses on translational medicine and translational research in cancer and inflammatory diseases using innovative drug candidates including small molecules, biologics, nanoparticles or polymeric micelles. His long-term research and effort have resulted in >100 publications in peer-reviewed Journals or top international conferences in the field including J Natl Cancer Inst, Cancer Res, Clin Cancer Res, Gene Therapy, Front Onc and Front Pharm, etc. Dr. Yang serves as an editorial board member or reviewer/editor for several international scientific journals including Front Imm, Front Onc, Cancer Res J, Cancer Res Cell Ther, J Onco Res Ther, and Int J Mol Onc.

Virtual
Day-01

Oncology Congress 2023

Oral Presentations

ANTITUMOR EFFICACY OF THE PROTEASOME INHIBITOR BORTEZOMIB ON MALIGNANT MESOTHELIOMA: EVIDENCE FROM IN VITRO STUDIES AND FROM A SYNGENEIC MOUSE MODEL

Camilla Palumbo, Monica Benvenuto, Valentina Angiolini, Chiara Focaccetti, Daniela Nardozi, Raffaele Carrano, Laura Masuelli and Roberto Bei

University of Rome 'Tor Vergata', Italy

Abstract:

Malignant mesothelioma (MM) is a rare and highly aggressive tumor arising from the mesothelial cell lining of serous membranes, most often occurring at the pleural level and mainly associated with asbestos exposure. This tumor, characterized by high local invasiveness and low metastatic efficiency, is seldom amenable to surgical eradication and highly resistant to conventional therapies. Further, MM is poorly immunogenic and creates an immunotolerant microenvironment, and relatively modest response rates have been obtained with immunotherapy approaches, including those based on the recently introduced Immune Checkpoint Inhibitors (ICIs). Accordingly, MM has presently a dismal prognosis, with a 5-year overall survival of about 10%. Bortezomib (BTZ), a proteasome inhibitor approved for the treatment of multiple myeloma and mantle cell lymphoma, is reported to have limited effects on solid tumors, due to its low penetration and accumulation into solid tissues following IV or SC administration. On the other hand, in MM this limitation could be overcome through intracavitary BTZ delivery, with the advantage of increasing local drug concentration and decreasing systemic toxicity.

We investigated the effects of BTZ on cell survival, cell cycle distribution and modulation of apoptotic and pro-survival signal transduction pathways, in human MM cell lines of different histotypes cultured *in vitro*. Further, using a mouse MM cell line which reproducibly forms ascites when intraperitoneally injected in syngeneic C57BL/6 mice, we investigated the effects of intracavitary BTZ administration *in vivo* on both tumor cell growth and the modulation of the tumor immune microenvironment. The latter was evaluated by characterizing the phenotype and functional status of immune cells present in the peritoneal ascites of mice transplanted with the syngeneic MM cells. The results of our study support the use of BTZ in MM and advocate future studies aimed at defining the therapeutic potential of BTZ/ICIs-based combination regimens for this treatment-resistant, aggressive tumor.

Biography

Camilla Palumbo has a PhD in Experimental Medicine and is Assistant Professor of General Pathology at Tor Vergata University in Rome. Her main research interests include molecular aspects of oncology, anticancer drugs sensitivity and resistance, combination therapies in cancer treatment, with a special focus on malignant mesothelioma.

INCISIONAL METASTATIC BREAST CARCINOMA DEPOSIT IN A TOTAL KNEE REPLACEMENT PRESENTING AS PERI-PROSTHETIC JOINT INFECTION—A CASE REPORT

Ahmed Elzawahry, AyshaRajeev, Simren Rakhra and Kiran Singisetti
Gateshead Health NHS Foundation Trust, United Kingdom

Abstract:

Cutaneous metastasis from the primary breast carcinoma occurs when the disease is widespread and can present as skin infection especially in a previous well-healed scar. If the secondary deposit is over a total knee incisional site it can mimic peri-prosthetic joint infection. We report a rare and unusual case of a woman who presented with clinical signs and symptoms of a peri-prosthetic total knee replacement which on biopsy turned out to be cutaneous metastasis from a previously treated breast cancer. Chronic granulation tissue in a total joint incisional scar may present as peri-prosthetic joint infection. A good history taking and clinical examination with specimens from the skin lesions sent for both microbiology and histopathology is recommended to arrive at an early and accurate diagnosis.

THE LONG NON-CODING RNA REGULATES RBFOX2-MEDIATED ALTERNATIVE SPLICING IN COLORECTAL CANCER

Maria Magdalena Barreca, Aurora Cordaro, Marco Loria, Chiara Zichittella, Claudia Moltalto, Marco Tripodi, Simona Fontana, Riccardo Alessandro and Alice Conigliaro

University of Palermo, Italy

Abstract:

In various cancer types, long non-coding RNA H19 (lncH19) has been shown to play critical roles in tumor development, proliferation, and metastasis. It is, also, known that lncH19 is highly expressed in colorectal cancer (CRC) cells. Several studies highlighted that LncRNAs are involved in regulating gene expression at the epigenetic, transcriptional, and translational levels. To date is known that LncRNAs can coordinate with miRNA or RNA-binding proteins (RBPs) to regulate the stability of mRNA, thus playing an important role in post-transcriptional regulation.

RBPs are a group of proteins that binds to different classes of RNAs, including lncRNAs, through structural motifs and domains. This interaction may facilitate the RBPs' role in a variety of cell processes, such as gene alternative splicing (AS), contributing to tumor development and progression. RBFOX2 is an RBPs protein widely expressed in many tissues throughout life, and it is an important signal-responsive alternative mediator. As a splicing factor, RBFOX2 is involved in epithelial-mesenchymal-transition (EMT) and invasiveness of cancer cells including CRC cells.

Given that RBFOX2 is a regulator of AS and that lncRNAs can be involved in the regulation of this process, we have investigated in CRC cell lines (SW620, SW480, HCT116) whether lncH19 might affect RBFOX activity acting as a molecular platform for RBFOX2 transport to target genes thus modulating its role in AS.

Through the online database RBPmap, we identified RBFOX2 binding motifs (GCAUG) in the lncH19 sequence. By LS-MS analysis from lncH19 pull-down, we confirmed RBFOX2 as a protein binding the lncH19 in CRC cell lines. Moreover, we validated this data with RNA-Immunoprecipitation assay, RT-PCR results showed that lncH19 was enriched in the complexes immunoprecipitated with anti-RBFOX2 compared with that in the complexes immunoprecipitated with anti-IgG.

Recently it was demonstrated that RBFOX2 functions within a Large Assembly of Splicing Regulators complex (LASR) containing a distinct set of other splicing factors. Interestingly, LS-MS analysis identified, in addition to RBFOX2, other LASR proteins binding lncH19 in CRC cells such as SRSF1, U2AF, hnRPM1-M4, hnRPC1-C2. Formal proof of physical interaction among the lncH19 and LASR proteins, SRSF1 and hnRPM1-M4, was obtained through an lncH19 pull-down assay followed by protein investigation.

To study if lncH19 works as a shuttle for RBFOX2/LASR-complex we performed lncH19 pull-down assay and analyzed the binding between lnH19 and LASR targets. We focused our attention on RBFOX2-targets involved in EMT and cancer progression, such as ENAH1, PARD3A, and RAC1. Interestingly we found that in CRC

cell lines these mRNAs were bound to lncH19. Moreover, the pro-EMT splicing variants were down-regulated in CRC cells silenced for the lncH19 thus supporting its pivotal role in RBFOX2-mediated AS.

Biography

After Maria Magdalena Barreca master's degree in Cellular and molecular biology, she was involved in a Ph.D. program in "Cell biology and drug's science and technology". During her Ph.D. training, she was mainly focused on understanding the role of specific KRAS mutations in colorectal cancer (CRC) cell response to chemotherapy. After my Ph.D., she was involved in a project about the role of Extracellular Vesicles (EVs) in intercellular communication by using mesoangioblast stem cells as a model system. Thanks to the "Post-Doc AIRC Fellowship", she is working as a researcher at the Dept. of BioMedicine, Neuroscience and Advanced Diagnostics (Bi.N.D) of the University of Palermo. Her research project concerns the field of cancer progression with a focus on the molecular mechanism by which the non-coding RNA affects cell behavior. In particular, my interest is focused on evaluating the possible roles of lncRNA H19 and RNA binding protein in colon cancer biology. She was the the author/ co-author of several research articles, reviews, and chapter books in the tumor and extracellular vesicles field.

POSTOPERATIVE CHEMOTHERAPY AFTER SURGICAL RESECTION OF METACHRONOUS METASTASES OF COLORECTAL CANCER

Evdokimova Sevindzh P

Hertsen Moscow Oncology Research Institute, Russia

Abstract:

The incidence of colorectal cancer (CRC) is steadily increasing worldwide, so in 2020 more than 1.93 million cases were newly identified. Despite advances in screening programs and treatment of precancerous conditions, 20-30% of all patients with CRC have metastatic disease at the time of diagnosis, and 30-40% of patients with cured locally advanced stages of CRC develop metachronous metastases during follow-up.

The study showed that patients with radically resected metastatic foci had significantly improved long-term survival by increasing the overall 5-year survival rate by 60%.

Clinical guidelines suggest that patients with metachronous resectable metastases may undergo surgical treatment followed by adjuvant therapy or receive perioperative chemotherapy for six months if ACT has not been performed previously or after 12 month-period after they finished ACT. However, trials that studied the efficacy of ACT have controversial results with some limitations such as inappropriate study design, chemotherapy regimen, a small number of patients, and retrospective analysis.

Thus, the rationale and duration of adjuvant treatment after removal of solitary metachronous metastases still remain unclear, especially in patients with certain prognostic factors. It is worth stratifying patients by the presence of risk factors to determine further treatment strategy, because patients belonging to the high-risk group have advantages from the appointment of systemic chemotherapy.

Also ctDNA could be used as a prognostic marker in patients after radical resection of colorectal liver metastases.

Biography

Evdokimova Sevindzh was completed her graduation at The First Sechenov Moscow State Medical University under Ministry of Health of the Russian Federation in 2019. Then graduated from the residency in P.Hertsen Moscow Oncology Research Institute. Since 2022. She was in graduate school and her research work is dedicated to Adjuvant chemotherapy after surgical resection of metachronous metastases of colorectal cancer.
She is specializing in colorectal, pancreatic, breast and other malignant tumors involve new drug evaluation and chemotherapy, development of new therapeutic regimens.

THE UNIVERSALITY OF TRIM28 ASSOCIATION WITH CANCER STEMNESS IN SOLID TUMORS

Patrycja Czerwinska and Mackiewicz Andrzej Adam
Greater Poland Cancer Centre, Poland

Abstract:

Stem cell-associated molecular features of solid tumors, collectively known as cancer stemness, are essential in tumor development, progression, and relapse. Both cancer dedifferentiation and stemness acquisition are mediated by transcriptional and epigenetic dysregulation. Here, we characterized the association between the Transcriptional Intermediary Factor 1 (TIF1) family members, namely TIF1α/TRIM24, TIF1β/TRIM28, TIF1γ/TRIM33, and TIF1δ/TRIM66 transcriptional co-factors and cancer stemness in 27 distinct types of solid tumors.

We used transcriptomic, genomic, and clinical cancer data (publicly available from TCGA and GEO databases) and harnessed several bioinformatic tools to determine the association between TIF1 members and cancer stemness. The level of cancer dedifferentiation was assessed by previously reported transcriptome-based stemness score (mRNA-SI) or stem cell-derived gene expression signatures. In silico analyses were further validated with *in vitro* 3-dimensional cell cultures, including the soft agar assay, limiting dilution cultures, migration, and invasion assays.

Our results demonstrate that TRIM24 and TRIM28 are positively, while TRIM33 and TRIM66 are negatively associated with tumor stemness. However, only for TRIM28, the correlation between high expression and cancer stemness is very robust and universal regardless of the tumor type, resulting in a worse prognosis for cancer patients. TRIM28 is highly expressed in higher-grade tumors that exhibit stem cell-like traits. Also, the transcriptome profiles of TRIM28 high-expressing solid tumors are significantly enriched with stem cell markers. In contrast to other TIF1 members, TRIM28 possesses potential diagnostic value in predicting the stemness high phenotype (that corresponds to the worse patients' survival). TRIM28's involvement in regulating cancer stem cell-like phenotype was further confirmed *in vitro.*

Our work demonstrates that TIF1 family members exhibit distinct expression patterns in stem cell-like tumors, despite their structural and functional similarity. The association between high TRIM28 expression and enriched cancer stem cell-like phenotype is a universal phenomenon across solid tumors.

Biography

Patrycja Czerwinska is a young scientist currently working at the Department of Cancer Immunology, Poznan University of Medical Sciences. She completed her Ph.D. at the Medical University of Warsaw. Her research focuses on characterizing the molecular mechanisms that facilitate cancer stem cell-like phenotype acquisition to identify novel therapeutic targets. Her work also aims to delineate the anti-tumor immune responses against stem cell-like cancer cells to improve the efficacy of current therapeutic strategies. She has been published extensively as an author and co-author of more than 20 papers in highly regarded, peer-reviewed journals. The promoter of several bachelor, engineering, and master theses. Chairman of the Undergraduate Research Club at Poznan University of Medical Sciences, improving skills in bioinformatics.

THE ROLE OF EXTRACELLULAR VESICLES SECRETED BY COLON CANCER CELLS IN MEDIATING THE NUCLEAR TRANSLOCATION OF PD-L1 IN A MODEL OF HUMAN HEALTHY HEPATOCYTES: NEW INSIGHTS ON IMMUNE CHECKPOINT PATHWAYS.

Marzia Pucci, M Loria, E Costanzo, M Moschetti, O Urzi', R Gasparro, R Alessandro and S Fontana

University of Palermo, Italy

Abstract:

Evasion of immune surveillance is one of the most features of tumor progression and is mainly caused by the activation of immune check-point PD-L1/PD-1. PD-L1 is an immunosuppressive protein highly expressed on surface of several types of tumor cells that binds directly to receptor PD-1 on T cell inducing anergy and exhaustion thus allowing tumors to escape from immune attack. Emerging data in the literature reports that beyond the well-known localization on cell surface and in cytoplasm, PD-L1 is also present in the nucleus (nPDL1) where could work as crucial effector in transducing intrinsic signals responsible of the activation of alternative pathways supporting tumor progression which are not targeted by immune checkpoint inhibitors, thus leading to a possible acquired immunotherapy resistance. Recently, in our paper we demonstrated that colorectal cancer (CRC) derived EVs significantly upregulate the expression of PD-L1 in M0 macrophages mediating inhibition of the local immune system. The central hypothesis of our research project is that EVs derived from colorectal cancer (CRC/SEVs) can support liver metastasis inducing an early alteration of hepatocytes (Heps) immunomodulatory properties within the pre-metastatic niche, inducing tumor-associated escape from antitumoral immunity.

Material and Methods: SW480 CRC cells were used as source of CRC-EVs and immortalized normal human Heps (THLE-2 cells) were used as target cells. Western Blot, confocal microscopy, qRT-PCR and cytofluorimetry were applied to analyze how CRC-EVs modulated the expression and the cellular localization of PD-L1 in Heps. Moreover, we showed that nPD-L1 should promote the establishment of an immunosuppressive microenvironment by regulating GAS6, VISTA and PDL2 expression in treated hepatocytes.

Results: For the first time our study demonstrates that the CRC-EVs induce in Heps the increase of PD-L1 expression also promoting its nuclear translocation. Interestingly, this observation is associated with the increase of GAS6 expression and TAM receptor-mediated release of TGFβ, power inducer of the fibrotic environment considered a targetable driver of metastasis. Moreover, conditioned medium (CM) of hepatocytes treated with CRC-EVs polarized THP-1 toward M2 phenotype showing a significant induction of the expression of M2 cytokines as well as the increased release of TGFβ.

Conclusion: the obtained results highlighted that CRC-EVs elicit in Heps alternative activities of PD-L1 able to switch the behavior of the surrounding macrophages toward a pro-tumoral phenotype. These data could open new avenues to better understanding the mechanisms of the immune checkpoint pathways, in order to

develop new potential therapies for the early treatment of liver metastatic disease and improve the response rate to therapies.

Biography

Marzia Pucci, from December 2021 researcher RTDA PON GREEN at the University of Palermo. After graduating She won a scholarship at the San Raffaele Giglio Hospital in Cefalù and the research project She followed was focused on the study of innovative technologies for the therapy of selective and radical destruction of neoplastic pathologies. After this experience I started the International PhD in Experimental Oncology and Surgery at the Department of Biomedicine, Neuroscience and Advanced Diagnostics (Bi.N.D., UNIPA). In July 2018, She won a PostDoc fellow research and the research project She followed was focused on molecular analysis and functional role of bioactive compounds obtained from Sicilian citrus fruits. In April 2019, I won an AIRC (Italian Association for Cancer Research) scholarship for research activities related to the study of the effects of colon cancer-derived exosomes in inducing early phenotypic transformation in Heps in order to highlight new insight into pre-metastatic niche formation in the liver.

OVERVIEW OF CARDIO-ONCOLOGY AND CARDIOVASCULAR TOXICITY RISK STRATIFICATION BEFORE ANTICANCER THERAPY

Jassim Zaheen Shah
Qatar University, Qatar

Abstract:

My Presentation will focus on introduction of Cardio oncology, structure and function of cardio oncology service, burden of Cancer and Cardiovascular disease in cancer survivors and how to risk stratify patients for cardiovascular toxicity before starting cancer treatment

Agenda:

- Cancer burden and trends in mortality
- Introduction to Cardio oncology
- Cardiovascular side effects of common Chemotherapeutic agents
- Cancer therapy-related cardiovascular toxicity definitions
- Cardiovascular toxicity risk stratification before anticancer therapy

Biography

Jassim Zaheen Shah, MBBS, FRCP(Edin) Certification in Cardio-Oncology from International Cardio-Oncology Society (ICOS). Certification in Acute Cardiovascular Care by Association of Acute Cardiovascular Care (ACVC) of European Society of Cardiology (ESC). Certification in Heart Failure from HFA of ESC in May 2018. Consultant Cardiologist, Cardio Oncology, Heart Failure and Heart transplant. MBBS in 2006 from Pakistan, followed by Residency in Internal medicine at Hamad medical Corporation, Doha, Qatar, fellowship in General cardiology at Heart Hospital, HMC, Doha, Qatar. Fellowship in Advanced heart failure and Heart transplant at Wythenshawe Hospital, Manchester, UK. Currently working as consultant at heart hospital, Doha, Qatar. Covering Cardio oncology and heart failure and Transplant clinic. Lecturer of clinical medicine at college of medicine at Qatar University. Instructor of clinical medicine at weill cornell medicine, Qatar.

CHARACTERIZATION OF THE ROLE OF STRA6 IN TUMOR SUPPRESSION MECHANISMS

Marwah Suliman Maashi and Salvador Macip
King Abdulaziz University, Saudi Arabia

Abstract:

Stra6 is a protein that is upregulated in response to retinoids. Interestingly, we have found that Stra6 can induces p53 independently of DNA damage through ROS generation. Stra6 have shown a great induction of p53 protein levels with high stability as well. p53 stabilization through Stra6 leads to stimulate downstream proapoptotic events such as increase the activation of caspase-3, caspase-9 and PARP cleavage. Stra6 have shown the capability of driving tumor cell to apoptosis after cell sensitized with ATRA and stimulated with DNA damaging agents. However, both Stra6 and p53 were important to achieve maximum percentage of cell death, as this was observed by detecting a positive feedback loop between Stra6 and p53. Pull-down assay of Stra6 protein have shown truncated forms of the Stra6 protein with molecular weights of 25 and 15 kDa. Basically, we have found that the small form of Stra6 with 25 kDa was translocated from cell membrane to cytosol in the absence of DNA damage and it was found to be located within the nucleus in response to DNA damage. Furthermore, this shorter form of Stra6 was capable of generating ROS and enhancing p53 dependent apoptotic cell death *via* the upregulation mechanism of the downstream cascade of p53 signaling pathway. Additionally, mass spectrometry data have identified some of cytosolic and nuclear proteins as Stra6's protein binding partners. Remarkably, several of these identified proteins were related to apoptosis, as well were associated in the regulation of important cellular mechanisms. We propose that Stra6 can sensitize tumor cells to DNA damaging agents and function as an apoptotic protein in a p53 dependent manner.

Biography

Marwah Maashi is Assistant Professor of Clinical Biochemistry in the Medical Laboratory Sciences Department. Her PhD was in Cancer Research from the University of Leicester - United Kingdom. She is interested in the field of caner biomarkers, stem cell research and regenerative medicine. Maashi has published research in prestigious scientific journals in this field. Maashi has participate as Referee and reviewer in scientific journals and representative of the European Association of Cancer Research.

DOSIMETRIC COMPARISON OF INTENSITY MODULATED VERSUS 3DCRT IN TREATMENT OF LOCALLY ADRENAL CARCINOMA CERVIX

Seema Devi
IGIMS, Bihar

Abstract:

There are an estimated 18078957 new cancer cases and 9,555027 cancer death worldwide withan incidence rate of 197.9 and mortality of 101.1 per 100000 population. Cervical Cancer was second most common cancer. In India there are 96,922 new cervical cancer (9.2%) cases with an age standardized incidence rate of 14.7 per 100000 population. The definitive treatment of locally adverted cervical cancer with external beam radiotherapy (EBRT) and concurrent chemotherapy followed by brachy therapy has been established. Three-dimensional conformal Radiation Therapy (3DCRT) is the most commonly used method of EBRT but this technique has been associated with significant side effects including genital urinary symptoms gastrointestinal symptoms and bone marrow suppression when radiotherapy combined with concurrent chemotherapy.

Material and Method: Carcinoma cervix treated with radiotherapy at department of radiation at State cancer Institute at Indira Gandhi Institute of Medical Science, Patna between Jan 2022 to July 2022.We analysed the 50 cases who received 3DCRT(FIF) techniques and 50 cases of carcinoma cervix treated with Intensity modulated radiotherapy technique. All the patient were treated with curative intent. We analysed the patients who were received EBRT with chemotherapy and patients had karnofsky score >70 we reviewed clinical record of the patient.

Result: Mean age of the patients were over 50 years of age with majority of cases had squamous cell carcinoma. According to the FIGO (International Federation of gynecology and obstetrics staging majority of patients were IIIA, IIIB. Hemoglobin level was range of 7.5-9.5gm %. During treatment about 17% of patients required blood transfusion.

Conclusion: IMRT intensity modulated radiotherapy is associated with more accurate dose distribution to tumors and reduce dose to normal time (OAR) thus reducing the side effects of bladder, rectum, bowel and bones.

Biography

Seema Devi is a versatile Radiation Oncologist with a total of 23 years of exemplary service in the medical field. She is currently working as Additional Professor in the Department of Radiation Oncology at Indira Gandhi Institute of Medical Science, Patna. She has done her M.DRadiotherapy from S N Medical College Agra. She has already worked in several prominent Institutions across the country. She had published around 20 research papers in various national as well as International Journals. She has also been a recipient of Dr Arpita Roy Award in 2015.She has got experience in a variety of radiological healthcare settings and with many different patient age ranges. She is effective at multi-tasking and organizing duties, which has helped her to be successful in the nonstop pace of a busy medical exigencies. She provides oncology evaluations, management, treatments and second opinions to patients from diverse background, she has got strong exposure in treatments such as chemotherapy, and targeted therapies. She has also counselled and educated patients and family members on pre and post palliative care treatment. She had also mentored medical interns and residents on emergency procedures to support career growth. She is continuous conducting research to further enhance skills and develop new treatment innovations.

TOXICOLOGICAL RISK ASSESSMENT OF POLYCYCLIC AROMATIC HYDROCARBONS IN GROUNDWATER RESOURCES OF ABIDJAN, SOUTHERN IVORY COAST.

Brou Richmond Konan, Bernard Adiaffi, Véronique Yoboue and Yéï Marie Solange Oga

University Felix Houphouet-Boigny Abidjan, Cote d'Ivoire

Abstract:

Anthropogenic pollution of groundwater has been increasing for several decades. Abidjan, like other capitals in the world and particularly in developing countries, is not spared. This study aims to assess the levels of contamination of groundwater in Abidjan by Polycyclic Aromatic Hydrocarbon (PAHs), from frequently used indexes but also, to highlight the risks of cancer to which the population would be exposed. Twenty (20) points (14 boreholes and 6 wells) were sampled in 2019. The PAHs give concentrations ranging from nd to 1.833µg/l. The hazard index by ingestion route (HIing) obtained with non-carcinogenic PAHs ranged from nd to 10^{-3} while the hazard index by dermal route (HI der) ranged from nd to 2.83. The risk of cancer by ingestion (RIing) varies between nd and 10^{-3} and the risk of cancer by dermal route (RIder) varies between nd and 2.34. However, the values remain higher in children than in adults.

Biography

Brou Richmond Konan is an Ivorian PhD student. His field of study takes into accounts air-rainwwater-groundwater. For his research work, he Works on the Heath impact of PAH and Heavy metals from these environment on the population of Abidjan. His first result shown that air and water contain fairly toxics substances that are defined as carcinogens by US-EPA and IARC. It has shown that childrens are more exposed to cancer than adults. These results have been published in the Journal of Water and Health and he participated in an international symposium in Yamoussoukro and another in Benin. Brou participated in several study missions aimed at raising awarness of protection measures and treatment of water.

CONTACT X-RAY BRACHYTHERAPY (CXB): A RELEVANT NICHE FOR RECTAL, SKIN, BREAST CANCER

Syrine Ben Dhia, Mitrea D, Barbet N, Pace Loscos T, Scouarnec C, Baron D, Evesque L, Sun Myint A and Gerard JP

Antoine Lacassagne Center, France

Abstract:

Contact X-ray brachytherapy has a rich history that dates back to the 1930s when it was first introduced with the Siemens unit. However, it was in the 1950s that the technique gained significant popularity with the advent of the Philips unit. Over time, advancements in technology have led to the development of the modern PapillonTM systems, which have revolutionized the field of contact X-ray brachytherapy. The PapillonTM systems, with a high dose rate, allows an effective treatment with shorter treatment times. These systems have demonstrated success in treating breast, skin, eyelid, and rectal cancer. Organ preservation has emerged as a crucial consideration in the treatment of rectal cancer, particularly in cases of early and good intermediate rectal cancers. The importance of organ preservation has been further underscored by the results of the randomized phase III Trial OPERA for early and good intermidiate rectal cancers comparing a dose escalation using contact therapy versus standard of care.During the presentation, the OPERA trial will be discussed, highlighting the results pertaining to organ preservation at 4 years. This trial has provided valuable insights into the potential benefits of contact x-ray brachytherapy in achieving organ preservation in rectal cancer patients. Additionally, the role of contact x-ray brachytherapy in intraoperative irradiation of breast cancer with the Papillon plus machine will be explored, with a focus on the learning curve associated with this technique. The use of contact x-ray brachytherapy in treating skin tumors will also be discussed. Furthermore, the talk will cover current trials and future prospects of development for contact x-ray brachytherapy. Two notable trials will be highlighted the TRESOR trial and the STRASS trial.

Biography

Syrine Ben Dhia is an accomplished radiation oncologist who has undergone training in Tunisia. Following her education, she served as a university hospital assistant in Tunisia, where she gained clinical experience and enhanced her skills in radiation oncology. After successfully completing the equivalence examination, Syrine Ben Dhia ventured into new professional territory and works actually at Antoine Lacassagne Center in Nice, France. Prior to her current role, she had the opportunity to expand her expertise at the renowned Institut Curie in Paris, France. These experiences at prestigious institutions have provided her with a broad and diverse perspective on radiation oncology practices. Syrine Ben Dhia's professional interests lie primarily in the management of digestive tumors, breast and skin cancer. She is dedicated to develop effective treatment strategies to improve patient outcomes. Furthermore, Syrine Ben Dhia has a profound interest in clinical research. Currently, she is fortunate to be working under the guidance of Professor Jean Pierre Gérard, a distinguished figure in radiation oncology. This collaboration enables her to gain knowledge, and expand her expertise in the field of contact therapy.

COMPARATIVE ANALYSIS OF MACHINE LEARNING ALGORITHMS FOR CANCER PREDICTION AND FEATURE SELECTION

Loai AbdAllah, Ibrahem Zoabi and Afefe Shibli
The Max Stern Yezreel Valley College, Israel

Abstract:

The goal of this research is developing an accurate machine learning-based classifier for predicting cancer and identifying the most significant factors contributing to the prediction. The dataset used for this study consists of 1000 positive samples obtained from the internet and 72 negative samples collected from online forums.

To build the classifier, the dataset is divided into groups. Then, a total of 144 samples are used to build the classifier, with 72 positive and 72 negative samples in each group. This approach ensures that the classifier is trained on an equal number of positive and negative samples, thereby avoiding any bias towards either class.

Several classifiers are employed, including decision trees, support vector machines, logistic regression, naive Bayes, and K-nearest neighbors. The performance of each classifier is evaluated using standard metrics such as accuracy, precision, recall, and F1-score. The mean and variance of the accuracies of each classifier are computed based on the different groups to select the best one.

The study also focuses on feature selection research to identify the most informative features that distinguish between positive and negative patients. The researchers employ various feature selection techniques, including principal component analysis (PCA) and recursive feature elimination (RFE).

The proposed approach has the potential to enhance cancer diagnosis and improve patient outcomes. By identifying the most significant features, the classifier can be optimized for accuracy and speed, making it a useful tool for healthcare professionals. Moreover, the results of this study may provide insight into the factors that contribute to cancer diagnosis, potentially leading to new discoveries in cancer research.

In conclusion, this research aims to develop a highly accurate classifier for predicting cancer in patients using machine learning algorithms. The results of this study may have a significant impact on improving cancer diagnosis and treatment.

Biography

Loai AbdAllah Introducing Loai, an esteemed expert in data analysis and data science with over 15 years of experience in artificial intelligence, business intelligence, computer vision, and big data. He is a senior lecturer at The Max Stern Yezreel Valley Academic College, where he leads research projects on data mining, big data, and business analytics, and teaches courses on the latest techniques and trends in data analysis. As the founder and CEO of xBiDa, Loai has successfully implemented algorithms for various industries, including medicine, healthcare, e-commerce, and bioinformatics.

CHEMOTHERAPY PROLONGS SURVIVAL OF PATIENTS WITH RESISTANT CANCERS AND UNFAVORABLE PREDICTIVE BLOOD TESTS

Howard Bruckner, Elisheva Dusowitz, Robert De Jager, Fred Bassali and Azriel Hirschfeld

MZB Foundation for Cancer Research

Abstract:

Background: New treatments, rechallenge, with 1/3 (1/4–1/2) of standard dosages, and the simultaneous use of 4–7 drugs may prolong median survival (MSTs) by 6–18 months. Patients with standard therapy and unfavorable predictive blood tests (PBTs) have MSTs of 6 (4–8) months in meta-analyses.

Methods: Patients have advanced resistant (R) colorectal (CRC, N=50, 3-4 prior lines of treatment), ovarian (OC, N=102, 4–5 prior lines of treatment), and pancreatic (APC, N=53, 2 prior lines of treatment) cancers. Eligibility requires: measurable metastatic cancer; performance status of 0-2; reliability for office visits; > 6 weeks to live; intention-to-treat; written consent; and use of Helsinki, IRB, and HIPPA protocols. Ineligibility includes: a hospitalization within 14 days; severe organ failure; or irreversible cytopenia.

Kaplan Meier and Cox analyses characterize the survival of patients with unfavorable tests. These include: serum albumin < 3.5 g/dl; neutrophil-lymphocyte ratio > 3 or 5; lymphocyte monocyte ratio < 2.1; absolute lymph count < 1.5/μl; absolute neutrophil count > 10,000/μl; platelet counts > 300,000/μl; alkaline phosphatase ≥ 135/IU; and white blood count of > 10,000/μl.

Biweekly treatment, in mg/M^2, includes: Gemcitabine 500; 5-Fluorouracil 1200 over 24 hours; Leucovorin 180; Irinotecan 80 and on day 2, Oxaliplatin 40, or for OC patients Carboplatin AUC 2. On progression, drugs are added: first, Docetaxel 25 with or without Mitomycin C 6 for gastrointestinal cancers; second, Cetuximab for CRC, 400 total mg then 200 mg weekly; and third, Bevacizumab 10 mg/kg is substituted for Cetuximab. For ROC patients, Bevacizumab and Cyclophosphamide 150 mg IV (x1) are added from day 1.

Results: Patients with R CRC, OC, and APC have overall MSTs of 16.3, 15, and 10.3 months, respectively. Unfavorable groups with strong MSTs include: 5 ROC, MST ~ 12–19.8 months; 7 RCRC, MST ~ 12 – > 24 months; 1 RAPC, MST 14.3 months. There are curve breaks, ~ 40% of patients alive in spite projected short MSTs: 6 OC groups, 14.5–22.5 months; 1 APC group, 12–18.2 months; 6 CRC groups, 12 – ≥ 24 months. Only unfavorable lymphocytes meet milestone criteria in each series.

Conclusion: For the first time, treatments often produce useful survival for many groups with unfavorable tests. Tests as surrogate biomarkers may facilitate personalized therapy to identify, reverse, and avoid the underlying mechanisms of lethality associated with the tests: immunosuppression, cytokine drivers, inflammation, and resistance to apoptosis. PBTs and high-risk patients warrant investigation.

Biography

Howard Bruckner was a experienced chief researcher with a demonstrated history of working in the hospital and healthcare industry. Skilled in Clinical Research (resistant and difficult tumors), Consulting, Medical Education, Manuscript Review, Coaching, Translational Medicine (drug interactions and the next generation of personalized medical tests), and Medical Devices. Strong research professional with experience at the NIH, Yale, and Sinai. International cooperative group consultant. Authored 150+ papers.

TREATMENT MODALITIES FOR METASTATIC UVEAL MELANOMA: WHERE ARE WE NOW?

Hannah Riva, Fabiola Ramirez, Lorena Fernandez, Sarah Mazal, Jessica Chacon, and Ioannis Konstantinidis

Texas Tech University Health Sciences Center, USA

Abstract:

Uveal melanoma, although rare, is the most common primary ocular neoplasm and is a potentially devastating malignancy. Uveal melanoma has characteristics, clinical course, and response to treatment distinct from cutaneous melanomas. In spite of primary radiation or surgical treatment, up to 50% of patients will develop metastases. Effective systemic treatment for metastatic uveal melanoma has yet to be determined, and further research in targeted therapies, including immunotherapy, is needed.

Current and upcoming treatment modalities for uveal melanoma including radiation, surgery, and potential for targeted therapies, including immunotherapeutic agents are discussed in this review. Hepatic metastasectomy, and in certain cases, radiofrequency ablation of hepatic metastases, have shown efficacy for metastatic uveal melanoma. Therapeutic agents showing efficacy include the newly FDA-approved tebentafusp for HLA-A*02:01- positive patients. Combination immune checkpoint inhibitor therapy has shown promise in treating metastatic uveal melanoma and is being studied further in clinical trials. Also, vaccines involving dendritic cells are under investigation for patients with primary uveal melanoma in an effort to decrease risk of metastasis.

Recent advances, such as seen in the FDA approval of tebentafusp in March 2022 for HLA-A*02:01-positive patients, show promise for patients with metastatic or unresectable uveal melanoma. Further research development in targeted therapies for metastatic uveal melanoma, including T-cell therapy, combination immune checkpoint inhibitor therapy, and vaccines, is essential to improve our understanding and treatment of this difficult-to-manage disease

Biography

Hannah Riva is a medical student at Paul L. Foster School of Medicine at Texas Tech University Health Sciences Center El Paso, TX, USA.

Virtual
Day-01

Oncology Congress 2023

Poster Presentations

DMBC11 MELANOMA CELL LINE RESPONSE TO DNA DOUBLE STRAND BREAK REPAIR

Małgorzata Drzewiecka[1], Tomasz Skorski[2] and Tomasz Śliwiński[1]

[1]*Uniwersytet Łódzki, Poland*
[2]*Lewis Katz School of Medicine, Temple University, USA*

Abstract:

Synthetic lethality is a clinically promising phenomenon, offers the potential to selectively eradicate cancer cells by inhibiting backup pathways when essential mechanisms are compromised due to genomic instability. DNA repair pathways, particularly those involved in DNA strand break repair, represent ideal targets for inducing synthetic lethality. In our study, we analyzed the expression level of genes involved in repair of the DNA strand breaks in cancer cells compared to normal cells. After treatment with alkylating compound (DTIC) and inhibitors (BMN 673), we correlated the gene expression profile and cell viability.

Based on the acquired data, we have noticed that the DMBC11 cell line is characterized by down regulation of few genes essential for both HR and NHEJ repair mechanism. In addition, observation of melanoma cell survival after incubation with analyzed compounds showed that the most effective variant for cancer cells elimination was dacarbazine. Combined therapy of dacarbazine and PARP1 inhibitor gave similar effect to the monotherapy with alkylating agent.

PD-1 BLOCKER BOOSTS IL-15-MEDIATED NK CELLS ACTIVITY INDUCTION IN RELAPSED ACUTE MYELOID LEUKEMIA (AML) PATIENTS

Javad Firouzi[1,2], Alireza Khosravani[1], Masoumeh Azimi[1], Fatemeh Ghaemi[1], Niloufar Shayan asl[1], Majid Safa[2] and Marzieh Ebrahimi[1,3]

[1]Royan Institute , Iran
[2]Iran University of Medical Sciences, Iran
[3]Royan Institute for Stem Cell Biology and Technology, ACECR, Iran

Abstract:

Objective: Natural killer (NK) cells are critical immune cells for acute myeloid leukemia (AML) targeting. However, little is known about the relationship between using checkpoint inhibitors and Heat shock protein 70 (Hsp70) as NK cell activators to control AML. Therefore, the study aims to find the best formulation to activate NK cells in AML patients.

Materials and Methods: In this experimental study, we aimed to investigate the antitumor effects of activated NK cells pre-treated with ex-vivo Hsp70, human PD-1 (Programmed cell death protein 1) blocker, and interleukin 15 (IL-15) against AML. The NK cells were isolated from Mononuclear cells (MNCs) by using magnetic activation cell sorting (MACS) and were activated using the different combinations of Hsp70, PD-1 blocker, and IL-15 and then followed by immunophenotyping, functional assays to estimate their killing potential, and evaluation of expression pattern of PRF1, PIK3CB, PD-1, AKT-1, FAS-L, TRAIL, and GER A & B.

Results: The expression of PD-1 was significantly ($P<0.05$) reduced after NK cell activation by the different formulas of IL-15, Hsp70, and PD-1 blocker. The expression of NKG2A in the treated NK cells was reduced particularly in the IL-15 ($P<0.01$) and IL-15 + PD-1 blocker ($P<0.05$) groups. The addition of Hsp70 increased its expression. The cytotoxic effect of NK cells increased in all groups, especially in IL-15 + PD-1 blocker besides increasing interferon-gamma (IFN-γ), Granzymes, and perforin expression ($P<0.05$). All IL-15 + PD-1 blocker group changes were associated with the up-regulation of PIK3CB and AKT-1 as key factors of NK cell activation.

Conclusion: We suggested the Hsp70 in combination with IL-15 did not show a remarkable effect on AML-NK cells. Moreover, the combination of IL-15 and PD-1 blocker could enhance the activity and killing potential of AML-NK cells.

Biography

Dr. Javad Firouzi received his Ph.D. in Applied Cell science from the Iran University of Medical Sciences and currently serves as the director of stem cell laboratories at Royan Research Institute. His specialty is NK cell expansion and therapy. He has published articles in various journals and has an H-index of 8.

ADDRESSING SURVIVORSHIP AND SUPPORTIVE CARE FOR WOMEN AND MEN WITH BREAST CANCER IN WESTERN KENYA.

Jane Kinuthia, Mercy Osor, Kapten Muthoka, Lucy Wabende, Nicholas Kisilu, Jenniffer Morgan and Naftali Busakhala

Academic model providing access to health care-AMPATH, Kenya

Abstract:

The increased number of women with breast cancer in Western Kenya and the recognition of the physical and psychosocial challenges cancer poses led to the discipline of cancer survivorship and supportive care. As breast cancer survivors continue to rise, Western Kenya becomes more ethnically and socially diverse. There is a need for new models of survivorship care to ensure the support of self-management through culturally appropriate methods across diverse populations. This study explored the supportive care experiences of a multi-ethnic sample of breast cancer survivors and aimed to understand the potential barriers to receiving care.

Methods: This was a qualitative descriptive study that was done at the Moi Teaching and Referral Hospital in Eldoret. In-depth interviews were conducted with 40 breast cancer survivors in the Western Kenya region. These participants were still on treatment or receiving follow-up in the 12 months before the study. The interviews were transcribed verbatim, cleaned and analyzed using thematic analysis.

Results: Six main themes emerged from the qualitative data that explain potential barriers to receiving care among breast cancer survivors in western Kenya. These include variable knowledge of breast cancer, limited autonomy for women, a preference for traditional healers, lack of trust in the health care system, inadequate access to services and limited finances among the respondents.

Conclusion: Determining the level of breast cancer awareness and the perceived barriers to care are the first steps in establishing locally relevant intervention programs. There is a need for improved and coordinated breast cancer education for members of the community. Future research should identify successful strategies to achieve this goal in more culturally relevant ways, particularly in rural communities. There is also a great need for standardized patient management guidelines, decentralized early detection and diagnostic services, and better access to treatment services.

Virtual
Day-02

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Oral Presentations

EV-MEDIATED NME1 AND NME2 MODIFY LIPID METABOLISM IN FIBROBLASTS

Krisztina Takacs-Vellai
Eotvos Lorand University, Hungary

Abstract:

Communication between cancer and stromal cells involves paracrine signalling mediated by extracellular vesicles (EVs). EVs derived from both cancer and stromal cells have been implicated in tumor progression. In this study, we focused on the first identified metastasis suppressor NME1, and on its close homolog NME2, and investigated their function in EVs in the interplay between cancer and stromal cells.

As a model, we used human invasive breast carcinoma cells overexpressing NME1 or NME2, and first analysed in details the presence of both isoforms in EV subtypes by capillary Western immunoassay (WES) and immuno-electronmicroscopy. Data obtained by both methods showed that NME1 was present in medium-sized EVs or microvesicles, whereas NME2 was abundant in both microvesicles and small-sized EVs or exosomes. Next, human skin-derived fibroblasts were treated with NME1 or NME2 containing EVs, and subsequently mRNA expression changes in fibroblasts were examined. RNAseq results showed that the expression of fatty acid and cholesterol metabolism-related genes was decreased significantly in response to NME1 or NME2 containing EV treatment. We found that FASN (fatty acid synthase) and ACSS2 (acyl-coenzyme A synthetase short-chain family member 2), related to fatty acid synthesis and oxidation, were under expressed in NME1/2-EV treated fibroblasts. Our data show an emerging link between NMEs-containing EVs and regulation of tumor metabolism.

Biography

Krisztina Takacs-Vellai has expertise in tumor genetics and developmental genetics. Her lab uses the nematode Caenorhabditis elegans as a model to investigate questions related to tumor genetics. The lab also investigates processes of tumor progression on different tumor cell lines.

BREAST CANCER FREQUENCY : A REVIEW

Trivikram Madhusoodan Deshpande and Hanmantrao D. Kanase
Kisan Veer Mahavidyalaya, India

Abstract:

As per Globocan 2000, breast cancer is the second most common cancer overall with 10, 50, 000 new cases reported and 3,73,000 deaths. The frequency of breast cancer in Goa, India was reported to be 27 % in 2003 [Deshpande et al 2017]. As per globocan 2020, 22,61,419 were new cases of female breast cancer and 6,84,996 were deaths [Sung 2021].

In India, Hyderabad district (48.0 per 100,000) among all PBCRs (Population Based Cancer Registries) had the highest incidence rate. Cancer of breast followed by cervix uteri was the leading site of cancer in Delhi and Mumbai over the years. There was a significant increase in incidence rates of breast cancer across all PBCRs over the years, except in Nagpur PBCR. The incidence rate of breast cancer increased significantly by 3% annually over the time period (1988-2016). Breast cancer among females showed a significant increase in incidence rate (4.7%) over the years. The incidence rate of breast cancer increased significantly by 8.4% annually from 2005 to 2016 [ICMR Report 2020].

Among women, breast cancer accounts for 1 in 4 cancer cases and for 1 in 6 cancer deaths, ranking first for incidence in the vast majority of countries (159 of 185 countries). Incidence rates of breast cancer are rising fast in transitioning countries in South America, Africa and Asia as well as in high-income Asian countries (Japan and the Republic of Korea), where rates are historically low [Sung et al 2021].

Hence, further research on genetic etiology and other diet and lifestyle factors may help in diagnosis, prognosis of breast cancer and develop new treatments based on individual genome. It may be even hoped to prevent breast cancer depending on gene therapy research. Accordingly, genetic counseling may be suggested for sporadic and familial breast cancer patients and normal women.

Biography

Trivikram M. Deshpande did his PhD on the topic entitled 'human leucocyte culture and genetic studies of human breast cancer.' He studied frequency of breast cancer in Goa India, cytogenetic studies, family history studies, dietary habits and other habits such as consumption of pan masala, gutkha, smoking and alcohol in Goan breast cancer patients. He was awarded Indian council of Medical Research fellowship on 'cytogenetic and molecular biological study of sporadic and familial breast cancer patients from Goa.' After 2 years of work, he also worked in cancer research and development department of pharmaceutical company Nicholas and Piramal in Mumbai. He wrote research proposal 'Molecular therapy of breast cancer with microRNAs.' Then, taught graduate and postgraduate students in biotechnology and guided and worked for their dissertations. Published 15 research papers and presented in 16 conferences and in 1 webinar.

Presently he is teaching zoology to undergraduate students. He is interested to continue the latest research in breast cancer research abroad and get the funds or fellowship and develop further career in breast cancer research. Areas of interest are molecular genetics, next generation sequencing, nude mice, cancer cell lines, bioinformatics, publish in nature and high impact factor journals, obtain patents.

THE USE OF KERATIN-7 ANTISENSE, IN CONJUNCTION WITH KRT7-AS OVEREXPRESSION, REPRESENTS A NOVEL AND HIGHLY EFFECTIVE STRATEGY TO SUPPRESS TUMORIGENESIS AND PROMOTE APOPTOSIS IN CASES OF BREAST CANCER.

Hamed Hosseinalizadeh, Mohammad Rahmati and Mohamad Eftekhary
Guilan University of Medical Sciences, Iran

Abstract:

Expression of the keratin-7 (KRT7) is upregulated in breast cancer, and has been shown to correlate with cancer's poor prognosis; however, the precise mechanisms underlying its involvement in tumorigenesis and apoptosis are largely unexplored. In the present study, by using specific oligonucleotide antisense against KRT7, in combination with KRT7-AS overexpression, we investigated the in vitro effects of the knockdown of KRT7 on tumorigenesis and apoptosis of breast cancer cell lines. According to the results, antisense targeting KRT7 in combination with KRT7-AS overexpression exerted a dose-dependent inhibitory effect on the viability of MDA-MB-468 and MCF-7 cell lines, whereas no cytotoxic effect was observed in normal cells. Our results suggest that KRT7 plays a significant role in directed migration, invasion, and proliferation during tumor growth, leading us to interpret that KRT7 is a metastasis-associated protein and has regulatory activity in EMT and subsequent cancer metastasis. In addition, our cellular studies showed that this combined approach resulted in a remarkable decrease in mammosphere formation (37% in mammosphere's number and 25% in size; in comparison to the control group of MDA-MB-468 and MCF-7 cells), as well as a decrease in cancer cells migration and an increase in cancer cell apoptosis (48% and 45%, respectively). Altogether, our findings have effectively established the involvement of KRT7 in the advancement of breast cancer through its regulation of the post-transcriptional sense mRNA.

Biography

Hamed Hosseinalizadeh is currently pursuing a Master's degree in Medical Biotechnology at Guilan University of Medical Sciences, Rasht, Iran. Prior to this, H. Hosseinalizadeh obtained a Bachelor's degree in Genetics from Tabriz University, Iran. H. Hosseinalizadeh published a number of papers in several preferred Journals. H. Hosseinalizadeh's research interests encompass drug delivery via cell-mediated mechanisms for the treatment of cancers, particularly glioblastoma multiforme, cancer-targeted therapy, and antisense therapy.

POTENTIAL ANTICANCER ACTIVITY OF ACETONE EXTRACTS OF *Toona ciliata*, *Seriphium plumosum* AND *Schkuhria pinnata* ON HELA CERVICAL CANCER CELLS

Mxolisi Justice Ndlovu, Victor Patrick Bagla, Matlou Phenius Mokgotho, Marema Ephraim Makgatho and Thabe Moss Matsebatlela

University of Limpopo, South Africa

Abstract:

Background: Cervical cancer is common in women in less developed regions of the world. The plant biomolecules can be employed for synergistic activity with chemo- and radiotherapy. This combination might result in reduced toxicity and increased efficacy of the treatment regimen.

Objectives: The anti-HeLa cells activity of the acetone extracts of *S. plumosum*, *T. cilliata* and *S. pinnata* was assessed using different parameters.

Methods: Secondary metabolite detection and antioxidant activity quantification were determined using the DPPH and ferric iron reducing assays. HeLa cell growth inhibition and mechanistics were assessed by employing MTT and Annexin-V flous assays.

Results: Observations revealed the presence of phenolic, flavonoids, tannins steroids and coumarins in all the plants extracts. High amount of total phenolic and flavonoid content were detected in *S. plumosum* and *T. cilliata. S. plumosum* extract had the best DPPH scavenging activity and ferric reducing powers.

Conclusion: Observable concentration dependent cell proliferation inhibition by test materials was exhibited. The leaf extracts from *T. cilliata*, *S. plumosum* and *S. pinnata* contain compounds of various polarities with free-radical, antioxidant and anti-cancerous activities that may play a beneficial role in treatment.

Biography

He is an originally from South Africa and he completed my MSc in Biochemistry at the University of Limpopo, South Africa, under the tutelage of Professor T.M Matsebatlela, Dr M.P Mokgotho, Dr V.P Bagla and Dr M.E Makgatho. My MSc work focused on the anticancer potential activities of selected medicinal plants on cervical cancer HeLa cell line and I also served as an assistant entomologist from 2017 to 2018 at a Malaria institute. What fascinates me a lot about research is the ability to contribute to the body of scientific knowledge in attempt to provide solutions for the ongoing problems related to cancers. Outside the lab, he enjoy playing hockey.

Some of the laboratory work has been published and presented during 35th International Papillomavirus Society conference which was held from the 17th till 21st of April 2023. Professionally,he is currently a registered Student Medical Scientist with the HPCSA since 2010, a member of African Society for Laboratory Medicine (ASLM), a member of the South African Society of Immunology (SAIS), a member of Wits Infectious Diseases Seminar, International Papillomavirus Society (IPVS) and Partners for Advancing Clinical Education (PACE).

LANDSCAPING OF MELALLOMACROCYCLES AS POTENTIAL ANTI-TUMOR AND ANTICANCER AGENTS – A JOURNEY OF ONE DECADE

Ashu Chaudhary
Kurukshetra University, India

Abstract:

The combined use of both molecular docking and *in vitro* studies has become a productive trend. Both methods provide valuable information for determining the structure and dynamics of the bio macromolecular complexes. Moreover, they have proved to be perfectly complementary techniques. In particular, their combination is widely used in drug discovery research. The rich diversity of macrocyclic compounds provides exciting prospects for the design of novel therapeutic agents with unique mechanisms of action. From such a viewpoint, a new class of bio activable tetradentate macrocycles of tin (II) have been derived from diamine and dicarboxylic acids. The newly synthesized scaffold displayed promising pharmacological property and cytotoxic activity. The compounds have been comprehensively characterized by elemental analysis, molecular weight determinations, infrared spectroscopy and multinuclear NMR spectroscopy and tested for antimicrobial, anti-inflammatory and anticancer activity. The various physico-chemical data indicate that the complexes have octahedral geometry. The coherence of the results obtained from the docking simulations and characterizations enables us to reliably distinguish the preferable structures. In studies of the cytotoxicity, the complex exhibited significant activity against a panel of cancer cell lines. The compounds have also exhibited noteworthy anti-inflammatory activity. The obtained results clearly indicate that the tin (II) complexes behave as very effective anti-inflammatory agents and could prove to be useful for the treatment of difficult to treat inflammatory diseases. The antimicrobial efficiency of the complexes was also examined by *in vitro* method against various pathogenic bacterial and fungal strains. The metal complexes were found to possess efficient antimicrobial properties compared to starting materials and most of these complexes could turn out to be excellent models for the design of effective antibiotic drug substances.

INVESTIGATING THE EXPRESSION OF UBE2C, LGR5, CXCL12, CCL5, CAV1 AND STAT3 GENES AT PROTEIN AND MRNA LEVELS IN METASTATIC AND NONMETASTATIC TISSUES OF GASTRIC ADENOCARCINOMA PATIENTS

Fatemeh Ghaemi[1], Hamed Yasavoli-Sharahi[2], Amirnader Emami Razavi[3], Mehdi Totonchi[1,4] and Marzie Ebrahimi[1,4]

[1]Royan Institute, Iran
[2]Department of Cellular and Molecular Medicine, University of Ottawa, Canada
[3]Iran National Tumor Bank, Cancer Institute, Tehran University of Medical Sciences
[4]Royan Institute for Stem Cell Biology and Technology, ACECR, Iran

Abstract:

Gastric cancer is one of the most common malignant cancers worldwide. Despite substantial developments in therapeutic strategies, the five-year survival rate remains low. Therefore, novel biomarkers and therapeutic targets involved in the progression of gastric tumors need to be identified. Recent studies revealed differentially expressed genes (DEGs) can cause metastasis in GC. Also, MicroRNAs (miRNAs) emerge as important players in regulating self-renewal and metastasis in CSCs. The former study in Royan Institute revealed the expression of miR-17-5p, miR-24-3p, miR-124-3p was upregulated and mir-145-5p was downregulated significantly in metastatic tumors compared to non-metastatic tumors. Based on the bioinformatics analysis performed in their regulatory networks, it appeared that UBE2C, LGR5, CXCL12, CCL5, CAV1 and STAT3 genes are expressing differently in metastatic GC versus non-metastatic GC. Real-time PCR (RT-PCR) was performed to determine the expression of candidate genes in mRNA level in 10 metastatic tumors compared to 10 non-metastatic gastric cancer samples, their adjacent normal tissues, 2D, 3D and spheroid culture of MKN-45 cell line. Immunofluorescence staining was used to assess the expression of STAT3 in protein level in 20 paraffin-embedded metastatic and non-metastatic gastric cancer tissues, 2D, 3D and spheroid culture of MKN-45 cell line.

The mRNA level of UBE2C in metastatic GC tissues was significantly greater (p-value<0.05) than non-metastatic GC tissues. And, the mRNA levels of STAT3, CXCL12, LGR5 and CAV1 in metastatic GC tissues were significantly lower (p-value<0.05) than non-metastatic GC tissues. The mRNA expression of CAV1 were found to be lower in early stage of GC and higher in advanced stages. Also, the protein expression of STAT3 in metastatic and non-metastatic GC tissues were observed both nucleic (as a TF) and cytoplasmic (as a Signal Transducer) and not significantly different.

Our results indicated overexpression of UBE2C contributes to the development of gastric cancer and as potential prognostic biomarkers to diagnose metastasis. Also, the expression of CAV1 is correlate with TNM (Malignant Tumors) staging (p-value<0.05).

IN VITRO CYTOTOXICITY AND ANTIMICROBIAL EVALUATION OF NOVEL TETRAAZA MACROCYCLIC BASED LIGANDS AND IT'S COMPLEXES OF COBALT(II): SYNTHESIS, CHARACTERIZATION, DFT AND MOLECULAR DOCKING STUDIES

Subhash and Ashu Chaudhary
University Kurukshetra, India

Abstract:

The most important area of research in the current scenario is the development of novel anticancer with unique bioactivities and capabilities to combat newly emerging diseases. In this regard, a series of novel macrocyclic complexes of Co(II) were synthesized using a 1:1 molar ratio of metal salt $CoCl_2$. $6H_2O$ and macrocyclic ligands ($MacL_1$-$MacL_3$) derived from dicarboxylic acid and diamines. The synthesized compounds were characterized by infra-red, ^1H NMR, ^{13}C NMR, mass, UV-visible, and powder X-ray diffraction spectral studies, together with elemental (CHN) analysis, molar conductance, and magnetic susceptibility measurements. Electronic spectra led to the assignment of an octahedral geometry to the synthesized macrocyclic complexes. The electronic properties of synthesized macrocyclic compounds were determined by DFT calculations. The synthesized macrocyclic ligands and their Co(II) complexes were tested for their antimicrobial potential against a number of bacterial and fungal strains. Moreover, the cytotoxicity of macrocyclic ligands and their Co(II) was also examined against three distinct cancerous cell lines, including A549, HT-29, and MCF7 cell lines. The observed IC_{50} values for the tested compounds against cancerous cell lines demonstrate a relatively good level of cytotoxicity. Docking studies were also executed to computationally reveal the anticancer potentialities of synthesized macrocyclic ligands. The macrocyclic complex $[Co(MacL_3)Cl_2]$ exhibited excellent antimicrobial activity and cytotoxicity, making it an attractive lead candidate for future metal-based anticancer and antimicrobial drugs.

Biography

Subhash Malik is a Ph.D. student in the Department of Chemistry Kurukshetra University, Kurukshetra, Haryana, India under the supervision of Ashu Chaudhary. He has his expertise in transition metals macrocyclic complexes. The synthesis of macrocyclic ligands and Transition metal complexes via various methods and biocidal evaluation. He has published more than 10 research/review articles in an international peer-reviewed journals. He has been awarded with young scientist award at Lords University Alwar Rajasthan (2022).

NATURAL KILLER CELL-DERIVED EXTRACELLULAR VESICLES (NK-EVS) EXHIBIT CYTOTOXICITY ON PANCREATIC CANCER SPHEROIDS

Alireza khosravani[1], Soroor Eslahi[2], Melika Sheykhan[2], Mehdi Tavallaei[3], Faezeh Shekari[2] and Marzieh Ebrahimi[2]

[1]*University of Science and Culture,Iran*
[2]*Royan Institute, Iran*
[3]*University of Shahid Beheshti Medical Sciences, Iran*

Abstract:

Background: Being a progressive malignancy, pancreatic cancer resists traditional treatments. Dendritic Cells, Natural Killer Cells, and T Cells can significantly enhance the efficacy of current therapeutic approaches. However, they are inhibited in cancer's microenvironment. NK cell-secreted nanoparticles, also known as Extracellular Vehicles (EVs), are currently being studied for potential use in cancer therapy due to their apparent stability against the tumor microenvironment. This study examines the cytotoxicity of NK-EV different fractions on pancreatic cancer spheroid models.

Methods: Supernatant of Cultured NK cells were collected and centrifuged at different speeds (2000 g (group A), 10000 g (group B), and 20000 g (group c)) to obtain EVs. The NK-EVs were characterized using SEM and DLS techniques. Specific markers of NK-EVs was identified using Western blot. Various concentrations of NK-EVs were delivered to spheroids generated in vitro from pancreatic tumor tissue, and the cytotoxicity of NK-EVs was determined using flow cytometry and MTS. Moreover, the cytotoxicity potential of NK-EVs delivery to spheroids was visualized by merged images of the live/dead experiment.

Results: According to DLS data, the sizes of the EVs in groups A, B, and C were 1020 nm, 548 nm, and 352 nm, respectively. Western blot analysis demonstrated that NK-EVs express CD63 and TSG101 specific markers. Also, the SEM revealed EV-like vesicles of approximately the same size and shape in group C EVs. These EV groups were delivered to Spheroids (300-500 nm diameters). According to MTS findings, group C EVs has shown the most cytotoxicity potential. The examination of the flow cytometry supported the MTS findings. The live/dead kit assay revealed that Group C NK-EVs delivery to Spheroids exhibited the highest levels of red fluorescence (indicating dead cell).

Conclusion: We demonstrated that NK-EVs especially in higher speeds (20000 g) have cytotoxic effects on pancreatic cancer cells. When used together with NK Cells, NK-EVs, which also display anticancer potential, may boost NK cell efficiency against pancreatic cancer cells.

Biography

Alireza khosravani a 29-year-old researcher with a degree in MLS (medical laboratory science) and an MSc in Clinical biochemistry. Working as a researcher specializing in Flow cytometry and cell culture at Royan Institute, Stem cell department, where he is a member of Professor Ebrahimi's research group investigating the effects of NK cells and NK-EV on Cancer.

PATHOLOGIC COMPLETE RESPONSE OBSERVED IN EARLY STAGE HER2 POSITIVE BREAST CANCER PATIENTS TREATED WITH NEOADJUVANT THERAPY OF TRASTUZUMAB AND CHEMOTHERAPY (C+T) VS TRASTUZUMAB, CHEMOTHERAPY, AND PERTUZUMAB (C+T+P); A COMPARATIVE META-ANALYSIS

Faizan Fazal and Usama Tanveer
Rawalpindi Medical University, Pakistan

Abstract:

Introduction: Breast cancer is the most common cancer occurring globally. 15-20% of breast cancers are HER2 positive. Early stage HER2 positive breast cancers require treatment with neoadjuvant chemotherapy and targeted therapy.

Methods: 3 Double arm clinical trials were included in this meta-analysis after searching for clinical trials using specific keywords on PubMed, Cochrane, and Embase. Only early stage, HER2 positive breast cancer patients were eligible for this study who were in the neoadjuvant treatment setting. Those studies were included that studied the pathological complete response (pCR) as their primary or secondary endpoint. pCR was defined as the proportion of patients without invasive cancer in the breast and axilla. pCR achieved after neoadjuvant treatment with C+T was compared against pCR achived after neoadjuvant treatment with C+T+P.

Results: pCR rates of both arms were available in all 3 trials included in this meta-analysis. The summary statistics showed that the incidence of pCR was more in the experimental group (C+T+P) as compared to the control group (C+T) with odds ratio of 2.10 (95% CI: 1.56-2.83) with I^2 =0%. In 3 double-arm trials, there were 840 participants in total, 445 in the experimental group (C+T+P) and 395 in the control group (C+T). 203(45%) patients out of 445 in the experimental group achieved pCR, whereas, 127(32%) patients out of 395 in the control group achieved pCR.

Conclusion: This meta-analysis has shown that adding Pertuzumab in the Neoadjuvant treatment with chemotherapy and trastuzumab provided improved pCR rates as compared to chemotherapy and Trastuzumab alone in early stage HER2 positive breast cancer patients.

Biography

Faizan Fazal is a researcher and medical student at Rawalpindi medical university, Pakistan. He has 11 research publications and is working on many projects including RCTs, meta-analysis and systematic reviews. He has also won the undergraduate fellowship award of world psychiatric association. But his main interest lies in the field of medical oncology.

IN VITRO GENERATION OF NK CELLS FROM UMBILICAL CORD-BLOOD MONONUCLEAR CELLS: A NOVEL AND SIMPLIFIED METHOD

Parisa Shams[1-3], Delbar Daneshjou[3], Yasaman Noori[3], Marzieh Ebrahimi[2]

[1]University of science and Culture, Iran
[2]Royan Institute for Stem Cell Biology and Technology, Iran
[3]Kian Immune Cell Co. (KIC), Iran

Abstract:

Background: To overcome the obstacle faced by NK cell manufacturers to reach the "off-the-shelf" NK cell products which can be cost-effective and avoid the requirement of the difficult purification process, the umbilical cord blood mononuclear cells (UCB-MNCs) represent a promising, suitable, feasible and available source. Cord blood stem cells are thought to be an efficient approach for clinical-grade manufacturing the NK cells which have great self-renewal, proliferative, and hematopoietic potential and can effectively be differentiated into many distinct cells of the erythroid, lymphoid, and myeloid lineages, including NK cells. Therefore, in the present study we aim to develop a novel and simplified method to generate NK cells from umbilical cord blood mononuclear cells without purification and feeder-free.

Methodology: Umbilical cord blood (UCB) units were collected in cord blood bags after written informed consent with regard to scientific use from the cord blood bank of the Royan Stem Cell Technology Company (RSCT Co., Iran). UCB-MNCs were harvested from healthy umbilical cord blood by Ficoll-Hypaque density gradient centrifugation and were cultured in cell culture plates with RPMI1640 medium, 5% autologous serum in the presence of the cytokine cocktail, small molecule inhibitors, and immunosuppressive drug for 21 days. This method allowed the effective differentiation of NK cells from hematopoietic stem cells/progenitor cells (HSC/HPCs) without purification and feeder-free. After 21 days NK cells' viability, fold increase, purity, and cytotoxicity against U-251 cells were analyzed.

Findings: Using flowcytometry-based assays, we showed expansion and differentiation of HSC/HPCs to CD56+CD3- cells with a mean 31-fold increase, about 40% purity, and >90% viability without purification and feeder-free. Moreover, our final product represents no T cell contamination, and about 40% cytotoxicity against U-251 cells.

Conclusion: This platform has advantages over existing procedures, as it allows easier, time-saving, and cost-effective manufacturing NK cells from umbilical cord blood mononuclear cells.

Biography

Parisa Shams has an M.Sc. in Cell and Developmental Biology at the University of Science and Culture in collaboration with Royan Institute. She has mainly worked on the differentiation and expansion of NK cells from various sources including cord blood and peripheral blood. Extensive research background using various cellular and flow cytometry techniques has helped her to be part of Kian Immune Cell Company, a knowledge-based company in the field of cancer immunotherapy, as an R&D expert.

CANCER CHEMOTHERAPY DOSAGE ESTIMATION USING OPTIMIZATION ASSISTED KALMAN FILTER

Mohite Utkarsha Laxman
MET's League of Colleges, India

Abstract:

Chemotherapy is a medication that is most often deployed for treating cancer, as cancer cells develop and proliferate faster than other cells in the body. Even though chemotherapy is an effectual method to diagnose various kinds of cancers, the treatment includes risk as it causes side effects due to improper drug usage. Thereby, this work develops a robust controller for controlling the dosage of drugs that are carried out under parameter estimation. In addition, a Modified Regularized Error Function-based Extended Kalman filter (MREF-EKF) is introduced for estimating the tumor cells and it can be exploited for diverse conditions. Moreover, the overfitting issue that occurs during drug dosage estimation is also solved using this approach. Further, to improve the performance of the developed approach, the initial state of EKF is fine-tuned via Mean fitness-based Particle Swarm Update (MF-PSU), which is the enhanced version of Particle Swarm Optimization (PSO). At last, the supremacy of the presented approach is proved concerning convergence analysis and error analysis.

Biography

Utkarsha L. Mohite is an Assistant Professor from MET's League of Colleges, Bhujbal Knowledge City. Completed Ph.D. from Sardar Vallabhbhai National Institute of Technology, in 2022. She received her B.E degree in Electrical Engineering from SPPU University, India, 2010, and her M.E degree in Electrical Control Systems from SPPU University, Pune, India, 2014. Her research interests are optimization techniques concerning control systems. Adaptive, robust, and optimal control, Hybrid Optimization techniques, Cancer Chemotherapy Dosage Estimation.

CANCER: A TYPE OF ASEXUAL REPRODUCTION

Delbar Daneshjou, Parisa Shams, Yasaman Noori, Marzieh Ebrahim, Soroor Eslahi and Alireza khosravani

Royan Institute, Iran

Abstract:

The usual definition of cancer is another type of cell growth in the body that is different from the one that is normal for our body. According to this definition, many attempts have been made to understand the general mechanism of cancer, which has not been prosperous. For the first time, we intend to offer a different definition of cancer. It seems that cancer can be considered as a type of asexual reproduction that occurs in primitive metazoan such as sponges. Porifera (sponges) are the lowest extant metazoan phylum. Reproduction in sponges may be asexual or sexual. Asexual propagation includes fragmentation, budding and gemmulation. As a whole, asexual reproduction seems to be part of the ground pattern of all metazoan. We intend to offer a different definition of cancer, which it seems lead to a different understanding of cancer. We think that the resulting cell mass, called cancer in humans and other animals, is a similar method of asexual reproduction and species survival in sponges. Therefore, in humans, where the survival of the individual is also important, this type of reproduction is considered a disease and has now become one of the biggest health challenges in societies. We hope that this new definition of cancer will help to better understand the mechanism of this global problem.

Biography

Delbar Daneshjou is a cell and developmental biologist with a PhD degree from Arak University in Iran. She works as a research and development manager at Kian immune cell company. she is interested in investigating signaling pathways and their alterations in cancer. She has authored several papers on Reproduction and cancer topics. She is curious about scientific gaps and likes to explore and evaluate different perspectives. Her interest in cancer research stems from the evolutionary significance of the immune system and the potential of immunotherapy for new cancer treatments.

AN EFFECTIVE WORK-FLOW TO PROPERLY INTERPRET INTRONIC VARIANTS IN CANCERS

Yuwei Cheng
Cleveland Clinic, USA

Abstract:

Background and Aims: It has been a clinical molecular diagnostic laboratory's challenge to properly interpret the intronic, non-canonical splicing site variants, especially for those identified in sporadic cancers in which treatment options may depend on the pathogenicity of these variants. We developed a work-flow that may facilitate the timely proper interpretation of such intronic sequence variants.

Materials and Methods: Two MET intron 14 variants were identified in Non-small cell lung cancer (NSCLCs) patients in a next-generation sequencing panel. The potential impact on MET exon 14 skipping (METex14) was predicted using in-silico tools. METex14 mutation was confirmed using reverse transcription (RT)-PCR and Sanger sequencing analysis on RNA extracted from stained cytology smears. The impact of gene splicing of two TET2 intronic variants derived from hematological malignancies were also tested using this work-flow.

Results: In-silico prediction analysis exhibited reduced splicing strength in MET (c.3028+3A>T and c.3012_3028del) and TET2 (c.3954+5_3954+8delGTTT and c.3954+5G>A) variants. RT-PCR and subsequent Sanger sequencing analyses confirmed these variants lead to METex14 skipping and TET2 frameshift mutation.

Conclusion: This study shows the usefulness of *in-silico* prediction in conjunction with RT-PCR and Sanger sequencing to properly interpret variants that may cause alternative splicing. This study also exemplifies the opportunity of routine cytology slides for RNA-based testing.

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WHAT DOES CLIMATE CHANGE HAVE TO DO WITH CANCER? A PILOT ASSESSMENT OF CAPACITY TO IDENTIFY AND RESPOND TO CLIMATIC DRIVERS OF CANCER OCCURRENCE IN KENYA

Loise Nyanjau Ndonga
National Cancer Institute of Kenya, Kenya

Abstract:

Background: Climate change impacts health, including non-communicable diseases (NCDs) such as cancer. Addressing determinants for NCDs in the Africa context, including those related to climate change, is critical. The objective of this study is to assess capacity to respond to climate change effects on NCDs among key stakeholders in Kenya. We present the results of a scoping review, the theory of change developed to guide this study, and the study protocol.

Methods: For this phase of the study, we used a "theory of change" (TOC) approach to map out determinants for successful capacity for climate change effect mitigation on NCDs in Kenya. This was conducted through a series of five meetings involving stakeholders from government, academia and the community with more than half of the team constituting Kenyans. A scoping review was used to inform core components of the TOC including: best practices for assessing these determinants in a resource limited setting, as well as mapping out key stakeholders to assess as part of the protocol. Consensus was reached to focus on cancer as the target NCD given burden of disease, predominant effects of climate change on the disease, inadequate prioritization, and stakeholder involvement in the team reflecting topic expertise.

Findings: Key outcomes were as follows: (1) The long-term outcome consisted of the: "ability for key stakeholders influencing political and public will in Kenya to respond in a timely and effective fashion to effects of climate change on NCDs". (2) Intermediate outcomes included: establishment of accountability, knowledge among policy-makers & front-line workers, and access to appropriate tools for situational assessments. (3) Short-term outcomes included: climate change being established as priority in the country, establishing authority among policy-makers to act on climate change, and having diverse stakeholders leveraged to address these effects. Key climate change factors, established from literature review, to prioritize included: (1) skin cancer (greenhouse gas emissions, ozone concentration, and ambient UV ray levels), (2) lung cancer (greenhouse gas emissions, wildfire risk index, air pollution & suspended particulate matter), (3) liver cancer (greenhouse gas emissions, ambient temperature, aflatoxin levels).

Conclusion: Capacity assessments in Africa on effects of climate change are necessary, particularly targeting NCDs. We plan to study the key stakeholders mapped in the scoping review and theory of change on the long-term outcomes, the determinants of the intermediate outcomes and the degree of attainment of the short-term outcomes.

ANTI-LIVER CANCER SYNERGISTIC EFFECT OF COMMON CHEMO-THERAPY AND SAFFRON-BASED BIOMOLECULE

Amr Amin
United Arab Emirates University, UAE

Abstract:

Objectives: To assess the synergistic effect of routine chemotherapy and novel biomolecule against liver cancer. Sorafenib has been shown to treat early and mild Hepatocellular carcinoma (HCC) lesions and it helped increase the survival rates at one year, but for only 44% of patients. HCC, however, has been proven to be chemo-resistant and the side effects of chemotherapies lower the quality of life for cancer patients due to their non-selective cytotoxicity.

Methods: A carcinogenesis model that mimics the human disease was developed here to test the effects of crocin, one of the major bioactive molecules found in saffron.

Results: In this study, effects of crocin were investigated on DEN induced HCC in male Wistar rats. Crocin induced apoptosis and inhibited tumor progression.

Conclusion: Sorafenib and crocin have a pronounced anti-liver cancer synergistic against liver cancer.

MOLECULAR ENGINES, THERAPEUTIC TARGETS AND CHALLENGES IN PEDIATRIC BRAIN TUMORS: A SPECIAL EMPHASIS ON HYDROGEN SULFIDE AND RNA-BASED NANO-DELIVERY

Rana A. Youness, Caroline Joseph Kiriacos, Alyaa Dawoud, Sherif Ashraf Fahmy, Yousra Ahmed Zeinelabdeen, Kerolos Ashraf Daniel, Omar Eltahtawy, Miriam Mokhtar Abdelhalim and Maria Braoudaki

German University in Cairo, Egypt

Abstract:

Central Nervous System (CNS) tumors in general are malignancies of all age groups and resembles one of the most fatal cancers. Apart from the psychosocial overburden and reduced quality of lives, these group of malignancies is still one of the most difficult to eradicate owing to their sophisticated pathophysiology. Among children, brain tumors are the most common solid malignancy and its incidence has increased in the last years. In spite of the advances in research and un-ended trials of developing more effective therapies, full understanding of involved molecular pathways in primary pediatric brain tumors is not yet achieved. Not only that, but also one of the obstacles that research face in these groups of tumors is the blood-brain barrier (BBB) which hinders the new therapeutic approaches. Hydrogen Sulfide (H_2S), one of the gasotransmitters, was found to have promising molecular targets in its synthesizing machinery in many cancers as breast and ovarian cancers. Yet, role of H_2S in primary brain tumors in general is not been fully investigated and in pediatric brain tumors in specific it is barely investigated. However, very few studies highlighted its regulatory role in brain tumors so this demands more investigation in its critical roles. In this work, the already available literature concerning H_2S in brain will be highlighted for extensive studying of its critical role and involvement in brain as well as the promising targets. Moreover, challenges that are facing molecular targeting approaches will be discussed and new strategies for brain delivery will be proposed aiming to realize better treatment results for those patients.

VALIDATION OF THE TAGALOG AND ILOKANO TRANSLATIONS OF THE FUNCTIONAL ASSESSMENT OF CANCER THERAPY - GENERAL (FACT-G) SCALE FOR ADULT CANCER CENTER PATIENTS IN A STATE-FUNDED

Earnest Caiser Q Dela Cruz
Baguio General Hospital and Medical Center, Philippines

Abstract:

Background: The utility of health related quality of life (HRQOL) in clinical decision making gave ground to the creation of multiple questionnaires for its measurement. The Functional Assessment of Cancer Therapy - General (FACT-G), one of the most widely used HRQOL questionnaires in cancer patients have Tagalog and Ilokano translations to bridge the language differences and make it more accessible globally. Prior to use validity and of these tools for the population it is intended to be used should be established. The study aimed to document validity and reliability of translated Tagalog and Ilokano versions of the FACT-G questionnaire for use in patients catered upon by the Baguio General Hospital and Medical Center (BGHMC).

Methodology: Psychometric evaluation of the above tools was done involving 384 adult cancer patients of BGHMC. Data management and analysis using SPSS software was used to evaluate reliability, face validity, content validity, and construct validity.

Results and Discussion: Both the Tagalog and Ilokano questionnaires had indices above the set value for reliability measured as Chronbach's alpha of 0.968 and 0.974, content validity indices of 0.95 and 0.95, and face validity indices of 0.98 and 0.98, respectively. Construct validity was established through an exploratory factor analysis comprised of a principal components analysis and Varimax factor rotation with Kaiser normalization.

Conclusion: The Tagalog and Ilokano questionnaires are reliable and valid tools for use of approximation of HRQOL of cancer patients catered by the BGHMC and is recommended to bed uses in the day-to-day practice in the hospital.

A STUDY OF VARIOUS APPLICATION OF ARTIFICIAL INTELLIGENCE AND MACHINE LEARNING FOR HEALTHCARE SERVICES ON ONCOLOGY

Georgios Zacharakis
Prince Sattam bin Abdulaziz University, Saudi Arabia

Abstract:

Scientists have been spurred by advances in computer innovation to build programs to aid physicians in making important decisions without contacting experts directly. Computer-programming makes use of human intellectual abilities, including thinking, decision-making, and learning, among others. Although AI is not a novel idea, it has recently gained acceptance as a new computer engineering technique. It has been used in a variety of fields, including academia, commerce, medicine such as oncology and industry. The promise of AI approaches, especially for web-based clinical uses, is explored in this research. Also offered is a paradigm for web-based clinical diagnosis as well as forecasting. The lack of medical specialists in most growing nations has increased the fatality of individuals suffering from numerous ailments. The presentation discusses the current trends in medicine oncology and how Artificial Intelligence is being used to give better outcomes to oncology patients and to make early diagnosis of cancer by artificial intelligence screening early cancer.

DPD MUTATION TESTING PRIOR TO ADMINISTRATION OF SYSTEMIC FLUOROPYRIMIDINE CHEMOTHERAPY FOR CANCER TREATMENT.

Holly West and Elisa Burke
University of Birmingham, United Kingdom

Abstract:

Background: Fluoropyrimidine based-drugs, such as capecitabine and 5-fluorouracil, are used to treat a variety of cancers.1 Deficiency of dihydropyrimidine dehydrogenase (DPD), an enzyme that catabolises fluoropyrimidines, significantly increases risk of drug toxicity1, therefore dose alteration is recommended.2 Prevalence of DPD deficiency is disputed, but initial estimates suggest 3-5%.3 Guidance from UK Chemotherapy Board (UKCB) recommends that all patients should have a DPD test prior to fluoropyrimidine treatment.4

Methods: All patients who receive a first dose of either capecitabine or 5-fluorouracil for systemic cancer treatment between 1st May and 31st August 2022 at Queen Elizabeth Hospital Birmingham (QEHB) have been retrospectively audited (n=163). Data collection and analysis includes: first dose date, DPD testing date and results, first dose alterations and delays awaiting results.

Results: Average time from patient sampling to result reporting was 7.0 days. 9.2% of patients did not have a result available prior to first dose, with 4.9% having no test at all. Despite test results being unavailable, 100% of these patients proceeded with treatment without delay. 6.7% of patients without timely testing subsequently had mutations detected after treatment had been initiated.

Conclusion: Compliance with the UKCB guideline appears poor, with many potential factors influencing this. Therefore, there is a risk of toxicity present which is easily preventable. Findings from this hospital are widely relevant to other oncology centres and emphasise the importance of improving DPD test rates in accordance with national guidance to improve patient care. Various techniques, such as automated reminders for testing when prescribing, may be advantageous for service improvement.

IMAGING OF MUTANT P53 IN PANCREATIC DUCTAL ADENOCARCINOMA XENOGRAFTS

Hudson Alakonya, Sofia Koustoulidou, Samantha L. Hopkins, Edward O'Neill, Mathew Veal, Gemma Dias, Michael Mosley, Julia Baguna Torres, Francesca Amoroso, Amanda Anderson, Alison Banham and Bart Cornelissen

University of Oxford, United Kingdom

Abstract:

More than 80% of Pancreatic Ductal Adenocarcinoma (PDAC) patients are diagnosed with late stage disseminated tumours that are refractory to standard-of-care therapies, resulting in low 5-year survival of <8%. p53 is mutated in over 75% of late-stage pancreatic intraepithelial neoplasia (PanIN-3) and invasive PDAC. Mutation of p53 plays an important role in tumorigenesis. Mutant p53 overexpression is associated with poor prognosis and therapy resistance among PDAC patients. P53 is mutated in over half of all cancers. Therefore, molecular imaging of p53 expression may aid in early diagnosis and prognosis.

Here, we confirmed that mutant p53 levels are significantly overexpressed in a panel of PDAC cell lines, compared to normal pancreas. An anti-p53 antibody (49A1/H10) was developed in-house, and validated in a panel of cell lines, showed it selectively bound to murine and human p53, with good affinity (KD =<1 nM). We developed an Indium-111 labelled anti-p53 (49A1/H10) monoclonal antibody, modified with the cell penetrating peptide, TAT, for imaging mutant p53 in PDAC xenografts using SPECT. There was a statistically significant higher tumour uptake of Indium-111 labelled anti-p53 (49A1/H10) monoclonal antibody (111In-DTPA-49A1/H10-TAT) in p53 expressing tumours, compared to an isotype control (111In-DTPA-Ms-IgG-TAT). This was corroborated in a genetically engineered mouse model of PDAC, KPC mice, That replicate the p53 and KRAS mutation found in many PDAC cancers. Our work has established the first imaging agent for *in vivo* SPECT imaging of mutant p53 in PDAC xenografts.

International Conference on
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THE ROLE OF SURGERY IN THE PALLIATIVE CARE OF CANCER. A RETROSPECTIVE ANALYSIS OF 22 YEARS

John Spiliotis
Interbalkan Medical Center, Greece

Abstract:

Aim: Surgical procedures in palliative care are common however the indications risks and outcomes are not well described. We present a retrospective review of management of cancer patients during a 22 years period.

Material and Methods: From 2000-2022, 11.700 cases of cancer from abdominal, gynecological, urological and breast are analyzed.

Group A: All patients divided in therapeutic intent in 6000 cases (51,3%) which include surgical procedures ± neoadjuvant and systemic chemotherapy and radiotherapy.

Group B: palliative approach in 2650 cases (22,6%) with surgery and medical management with systemic chemotherapy and radiotherapy. The essential roles of surgical palliation as defined by Ball et. al are initial evaluation of the disease local control of the disease control of discharge or hemorrhage control of pain and reconstruction and rehabilitation. Surgical procedures for palliation, in chide resections, reconstructions, ostomies, functional repairs, tube drainage and biopsies.

The intent of a surgical procedure may not be known until an exploration in the operating room occurs.

Group C: Best supportive care in 3050 cases (26,1%) which includes nutritional management with home parenteral or enteral nutrition, pain management physical and respiratory physiotherapy, fistulas or ulcers management.

Primary and points include survival advantages and quality of life QOL as secondary benefit. The risk of morbidity and treatment related mortality are also calculated between the different groups. Normally the MM'S risks are usually high owing to the nature of the advanced disease comorbid conditions and poor performance status especially in group B and C.

Results: A median follow up of 80 months were observed. The median O.S. for group A was 44,4 ± 16,3 months and for palliative care group (B) was 26,3 ± 11,7 m ($p<0,01$). On the other hand the median O.S. for the group C (Best supportive care) was 8,7 ± 5,2 m. More especially in our group of patients with peritoneal metastasis which include 5200 patients (44,5%) of the total cancer patients we analyzed in 4 subgroups. The role of palliative surgery with ± systemic or neoadjuvant chemotherapy offer a better O.S. when we compared with only systemic chemotherapy (13,4 ± 7,5 m *vs* 71 ± 4,3 m). With acceptable morbidity and mortality rates. Concerning the quality of life there are questionnaire which working from our team which demonstrates better quality of life in 70% of palliative procedures versus 88% in group A, and return to the social life events in 27% of group B versus 93% of group A.

Conclusion: In conclusion the need for holistic palliative care in cases of incurable malignancy, it is not entirely clear how best to integrate palliative surgical principles. The essential roles of surgical palliation are, initial evaluation of the disease, local control, control of discharge or hemorrhage, control of pain and reconstruction and rehabilitation.

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CENTRAL OBESITY AND ITS ASSOCIATED FACTORS AMONG CANCER PATIENTS AT THE UNIVERSITY OF GONDAR COMPREHENSIVE SPECIALIZED HOSPITAL, NORTHWEST ETHIOPIA

Meseret Derbew Molla, Haileab Fekadu Wolde, Ephrem Tafesse and Anteneh Ayelign Kibret

University of Gondar, Ethiopia

Abstract:

Purpose: Obesity, especially the hidden type of obesity (central obesity), has been believed to be the major risk factor for developing and progressing non-communicable diseases, including cancers. However, there are limited studies regarding the issue in Ethiopia and the study area. Therefore, this study aimed to evaluate the magnitude of central obesity and its associated factors among cancer patients visited the oncology unit of the University of Gondar Comprehensive Specialized Hospital.

Methods: an institutional-based cross-sectional study was conducted from January 10 to March 10, 2021. A total of 384 study participants were enrolled using a systematic sampling technique. The data were collected using a semi-structured interviewer-administered questionnaire and were pretested to address the quality of assurance. The weight of the participants was assessed using body mass index (BMI) and central obesity. Both bivariate and multivariate logistic regressions were conducted to identify the factors associated with central obesity, and p-values less than 0.05 with multivariate were considered statistically significant associations.

Result: Most respondents (60.16%) were stage I cancer patients. The study found that about 19.27% of the participants were prevalent central obesity, and none of them were obese by body mass index (BMI) categorization criteria. However, about 12.24% and 7.03% of the participants were found to be underweight and overweight, respectively. The variables associated with central obesity were sex (AOR=14.40; 95% CI: 5.26 - 39.50), occupation (AOR=4.32; 95%CI: 1.10 - 17.01), and residency (AOR=0.30; 95% CI: 0.13 - 0.70).

Conclusion: A significant number of the respondents (19.27%) were centrally obese. Being female, urban residency and having an occupation other than a farmer, merchant, and governmental were the factors associated with central obesity. Hence, cancer patients may be centrally obese with average body weight.

AN IMMUNO-BOOSTING PEPTIDE TO REPAIR ULTRAVIOLET RADIATION-INDUCED DNA DAMAGE

Michael Agrez, Mark Stephen Rybchyn, Warusavithana Gunawardena Manori De Silva, Rebecca Sara Mason, Christopher Chandler, Benjamin Blyth, Stephen Parker, Darryl Turner, Justyna Rzepecka, Gavin Knox, Anastasia Nika, Andrew Hall, Hayley Gooding and Laura Gallagher

University of Melbourne, Australia

Abstract:

Skin cancer is the commonest human malignancy. Approximately ten percent of skin cancers are melanomas that arise from melanocytes whilst the remainder are non-melanocyte-derived skin cancers arising from skin cells called keratinocytes. The global incidence of all types of skin cancer continues to rise and the cause is ultraviolet radiation (UVR) notwithstanding the increasing use of sunscreens. While most sunscreens block much of the ultraviolet radiation (UVR) from reaching the skin, they do not repair DNA damage which is necessary to prevent skin cancer.

In addition, the immune system is suppressed by UVR with the immunosuppressive and carcinogenic effects of UVR being related and linked to DNA damage. Exposure to UVR results in the formation of cyclobutane pyrimidine dimers (CPDs) and oxidative DNA damage in the form of 8-oxo-7,8-dihydro-2'-deoxyguanosine (8-OHdG) which are associated with suppression of the nucleotide excision repair process. This DNA repair process relies on the presence of an immune cell-derived cytokine, called interleukin-12 (IL-12), to prevent DNA damage and UVR-induced immunosuppression. Furthermore, upregulation of the interleukin-18 receptor (IL-18R) by IL-12 contributes to the DNA repair process. However, in UVR-exposed skin, IL-12 production by immune cells is kept at a low level which has implications for repair of damaged DNA.

InterK Peptide Therapeutics has developed a peptide that inhibits progression of melanoma metastases and induces expression of both IL-12 and IL-18R. Exposure of skin on hairless mice, human skin tissue explants and cultured keratinocytes to UVR leads to marked DNA damage that is significantly inhibited in the presence of peptide.

The peptide, designated IK14800, also prevents UVR-induced collagenase-1 (matrix metalloproteinase-1; MMP-1) production that is responsible for breakdown of fibrillar collagen leading to skin wrinkling. Moreover, when formulated in an aqueous cream-base, a single application on dry skin of human forearms results in significantly enhanced skin moisturisation twenty-four hours later when compared with application of the cream-base alone as measured by a corneometer. These observations raise the possibility that once daily topical application of formulated IK14800 prior to any level of UVR exposure may not only help maintain skin texture but also hinder development of skin cancers.

CHANGES AND CLINICAL SIGNIFICANCE OF TREG/TH17 IN ELDERLY PATIENTS WITH NON-SMALL CELL LUNG CANCER BEFORE AND AFTER RADIOTHERAPY

Pan-Fei Hou, Li-Jing Zhu, Yan Pan, Cheng-Shi Wang, Han-Xu Yu and Juan Pu
Kangda College of Nanjing Medical University, China

Abstract:

This study is to investigate the changes in regulatory T (Treg) cells and T helper 17 (Th17) cells and their balance (Treg/Th17) in elderly patients with non-small cell lung cancer before and after radiotherapy. A total of 20 patients with non-small cell lung cancer (NSCLC) were chosen as the carcinoma group, while 30 healthy people undergoing medical examination during the same period were chosen as the control group. The numbers of serum Th17 and Treg cells accounting for CD4+T cell proportions and the ratio of Th17/Treg cells were compared. The numbers of serum Treg cells accounting for CD4+T cell proportions and the Treg/Th17 ratio significantly increased in the carcinoma group compared with the control group ($P < 0.05$). After radiotherapy, the number of Treg cells accounting for CD4+T cell proportions gradually increased to the highest level for the 18th time, which was significantly different from that before radiotherapy ($P = 0.00$), Then, it gradually decreased for the 30th time, with no significant difference compared with that before radiotherapy ($P = 0.82$). The number of Th17 cells accounting for CD4+ T cell proportions decreased significantly after radiotherapy. The ratio of Treg/Th17 showed a significant upward trend since radiotherapy. Radiotherapy can aggravate the changes in the number of Treg and Th17 cells and the imbalance of Treg/Th17 ratio in NSCLC and affect the antitumor immune function of the body. Radiotherapy combined with immunotherapy is a novel choice for the precise treatment of tumors.

TUMOR BUDDING IN COLORECTAL CANCER: ASSOCIATION WITH CLINOPATHOLOGICAL PARAMETERS AND PROGNOSTIC IMPACT IN STAGES II AND III

Pietro Giovanni Giordano, Ana Gabriela Díaz Zelaya, Yari Yuritzi Aguilera Molina, Nestor Orlando Taboada Mostajo, Yelene Ajete Ramos, Ricardo Ortega García, Esteban Peralta De Michelis and Juan Carlos Meneu Díaz

Hospital Universitario Ruber Juan Bravo, Spain

Abstract:

Introduction: Tumor Budding (TB) is considered as an independent adverse prognostic marker in colorectal cancer (CRC). The prognostic impact of TB at the tumor invasive front in CCR remains unclear, hence institutional practices on the description of TB and methods for its assessment widely vary. This study was undertaken to clarify the clinicopathologic and pronostic implications of TB in patients with stage I to III CRC.

Methods: Between 01/2017 and 12/2022, patients undergoing colectomy or attempted rectal resection after neoadjuvant therapy for CCR were identified. Patients with diagnosis of colorrectal adenocarcinoma, stage M0 at the moment of surgery, and description of the TB status in pathological report were included in our study. The effect of TB on histological factors, clinical stage, local recurrance rate, disease-free (DFS) and overall survival (OS) was assessed.

Results: Of 78 cases of CRC, TB at the definitive pathological description was present in 56 patients (71,8%), including low grade in 22 (39,3%), intermediate grade 17 (30,4%) and high grade 17 (30,4%) patients. The proportion of patients showing regional lymph node metastasis, lymfovascular and perineural invasión was significantly higher in patients with TB (26,8% vs 0 %, p=0,008; 41,1% vs 4,5%, p=0,002; 16,1% vs 0% p=0,054; respectively). Moreover, pathological T1 stage group showed a significantly higher proportion in TB negative group than the TB positive group (31,8% vs 8,9, p=0,031). DFS was 86,3% in TB low, 75,3% in TB intermediate, and 70,3% in TB high grade, respectively. Intermediate and high grade TB were associated with shorter OS compared to low TB (93,7% and 75,4% vs 100%, respectively p=0,0021).

Conclusion: These results suggest that the TB expression may be a useful risk factor for lymph node metastasis, local recurrence and distant mestastasis. TB at the tumor invasive front is associated with shorter overall survival after curative surgery for CRC.

IN VITRO AND *IN VIVO* ANALYSIS OF A NOVEL THERAPEUTIC AGENT FOR BREAST CANCER TARGETING LOX-12

Sharmistha Dey, Abhinay Kumar Singh, Renu KP and Atul Batra
All India Institute of Medical Sciences, India

Abstract:

Human breast cancer cell proliferation involves a complex interaction between growth factors, steroid hormones and peptide hormones. The interaction of growth factors, such as epidermal growth factor (EGF), with their receptors on breast cancer cells can lead to the hydrolysis of phospholipids and release of fatty acid such as arachidonic acid, which can be further metabolized by cyclooxygenase (COX) and lipoxygenase (LOX) pathways to produce prostaglandins. The high concentration of prostaglandins has been associated with chronic inflammatory diseases and several types of human cancers. This is due to the over expression COX, LOX and other inflammatory enzymes. Ten peptides were designed and synthesized by solid phase peptide synthesis and analyzed *in vitro* for enzyme inhibition. Out of these peptides, YWCS had shown significant inhibitory effects. The dissociation constant (KD) was determined by surface plasmon resonance (SPR) analysis and was found to be 3.3961028 M and 8.661028 M for YWCS and baicalein (positive control), respectively. The kinetic constant Ki was 72.4561027 M as determined by kinetic assay. The peptide significantly reduced the cell viability of estrogen positive MCF-7 and estrogen negative MDA-MB-231 cell line with the half maximal concentration (IC50) of 75 mM and 400 mM, respectively. The peptide also induced 49.8% and 20.8% apoptosis in breast cancer cells MCF-7 and MDA-MB-231, respectively. The YWCS was also found to be least hemolytic at a concentration of 358 mM. *In vivo* studies had shown that the peptide significantly inhibits tumor growth in mice (p,0.017). This peptide can be used as a lead compound and complement for ongoing efforts to develop differentiation therapies for breast cancer.

CHALLENGES AND OPPORTUNITIES IN DATA SCIENCE FOR CANCER BIOMARKERS RESEARCH

Yu Shyr
Vanderbilt University Medical Center, USA

Abstract:

The key concepts of precision medicine are prevention and treatment strategies that take individual molecular profile and clinical information into account. Single-cell next-generation sequencing technologies (scNGS), liquid biopsy for circulating tumor DNA (ctDNA) analysis, microbiomics, radiomics, spatial omics, and other types of high-throughput assays have exploded in popularity in recent years, thanks to their ability to produce an enormous volume of data quickly and at relatively low cost. The emergence of these big data has advanced the goals of precision medicine; however, across the entire continuum of big data capture and utilization, many more mathematical and statistical challenges lie ahead-from analysis of high-throughput biomarkers to maximum exploitation of the electronic health record (EHR), to the ultimate goal of clinical guidance based on a patient's genome.

In this presentation, I will offer some perspectives on the changing landscape for applied mathematical and statistical data science, including the concept of merging different Omics data; the need for biologists and oncologists to adjust their mindset around the explosive growth in information technology; machine learning; and the AI revolution. These areas present great opportunities for our profession to strengthen our role in the cancer research arena. I will finish up with my recent research about single cell RNA-seq data analysis which we developed a new method to identify dysregulated ligand-receptor interactions from single cell transcriptomics.

IDENTIFICATION OF ACTIONABLE TARGETS IN METASTATIC TRIPLE NEGATIVE BREAST CANCER

Eldad Zacksenhaus
University Health Network, Canada

Abstract:

Triple negative breast cancer (TNBC) is an aggressive subtype affecting young women worldwide, with particularly high incidence in women of African descent. Metastatic TNBC is virtually incurable with median overall survival of ~1-1.5 year. Current treatments including resection, chemotherapy, radiation and immune-therapy only modestly improve outcome, hence more effective approaches are urgently needed. One approach to tackle this issue is to identify oncogenic alterations or pathways that drive metastatic TNBC. The tumor suppressor RB1 and PTEN are often lost together with TP53 in TNBCs, driving both primary and metastatic disease. We demonstrated that Rb pr Pten loss alone or combined mutations in Rb plus p53 or Pten plus p53 in the mouse mammary gland induces diverse BC subtypes or TNBC-like lesions and identified therapeutic vulnerabilities in each case. In many breast tumors, RB is intact but the protein, pRB, is inactivated by phosphorylation through cyclin-dependent kinases (CDK4/6 and CDK2). Interestingly, while pRb loss induces cancer, systemic inhibition of pRb phosphorylation in knock-in mice accelerates aging and diabetes. To identify oncogenic networks that cooperate with Rb loss, we conducted mammary-specific Sleeping Beauty (SB) transposon-mutagenesis screens on a background of murine Rb deletion and identified gene-centric common insertion sites (gCIS) that drive primary mammary tumors and metastatic lung lesions. Clonal relationships between primary tumors and lung metastases were established, and genes and oncogenic networks induced by these gCISs, representing actionable targets, have been identified (manuscript, in revision).

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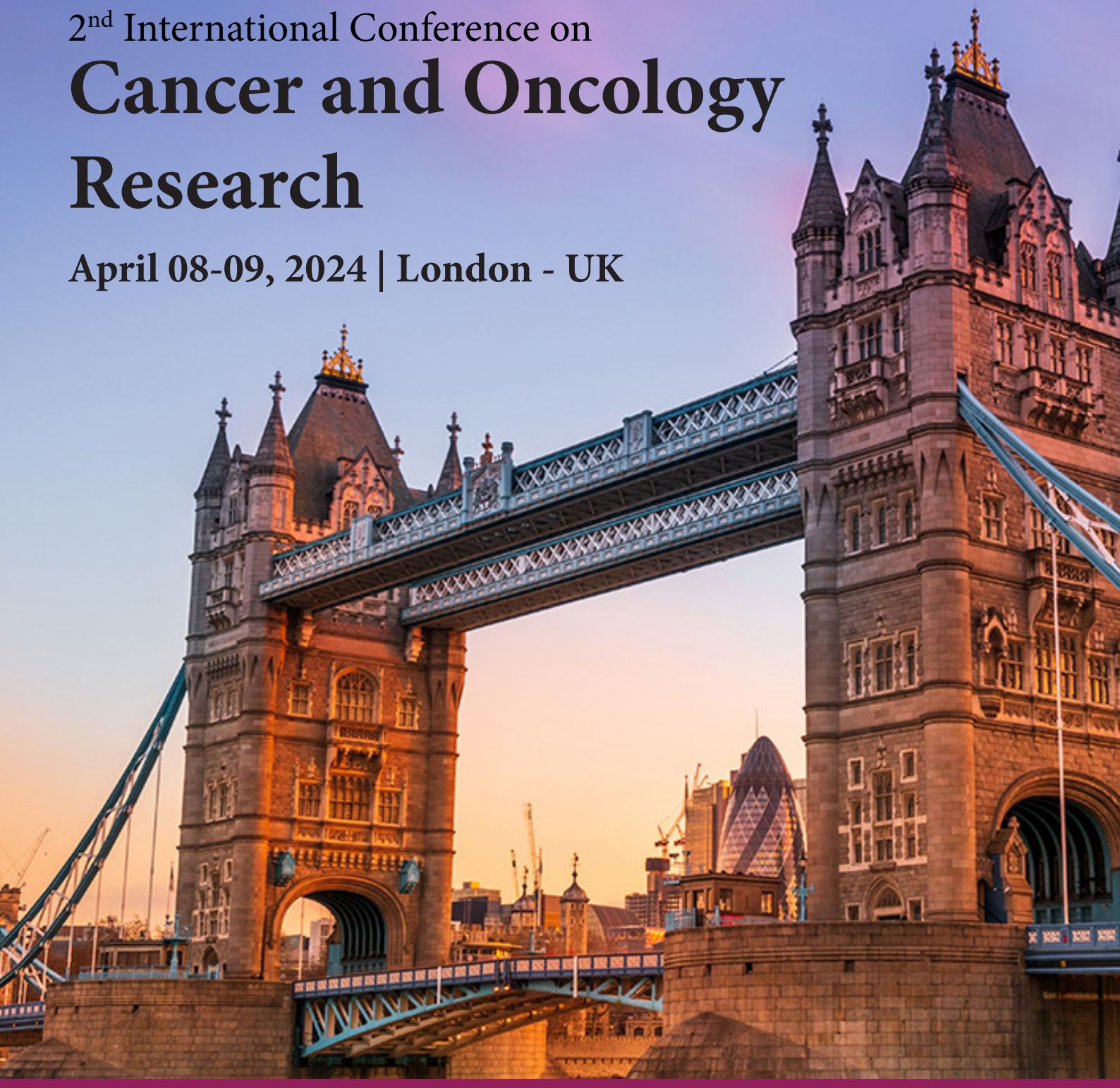

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