

# 25<sup>th</sup> Global Meet on Cancer Research & Oncology & World Congress on Primary Healthcare and Medicare Summit

May 20-21, 2019 | Rome, Italy

Poster





### World Congress on PRIMARY HEALTHCARE AND MEDICARE SUMMIT

May 20-21, 2019 | Rome, Italy

# The Notch ligand DLL1 exerts pro-carcinogenic effects in human breast cancer luminal A MCF-7 cells

#### Gabriela Silva

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**Background:** Breast cancer (BC) is the most common cancer in women and has a high rate of relapse and death. The Notch signaling pathway plays an important role in normal breast development and homeostasis. Dysregulation of Notch receptors and its ligands Jagged1, Jagged2, and DLL4 has been detected in BC and implicated in tumor development, progression, drug resistance, and recurrence. The Notch ligand DLL1 has emerged as a player in BC as its expression is undetectable in normal breast tissues, but moderate to high in BC. In this study, we examined the role of DLL1 in BC luminal A MCF-7 cells. Methodology: DLL1 siRNA and recombinant DLL1 protein were used to evaluate the effects of DLL1 in MCF-7 cells. Gene expression was analyzed by qRT-PCR and immunobloting. Cell growth and proliferation were assessed by trypan blue exclusion and the MTT methods. Microscopy and scratch wound-healing assays were used to evaluate colony formation efficiency, and migration. On the other hand, treatment with recombinant DLL1, which activates the Notch signaling pathway, increased MCF-7 cell proliferation and migration, confirming that DLL1 contributes to these processes in these luminal A BC cells. Conclusion: These findings provide evidence that DLL1 contributes to the pro-carcinogenic effects of luminal A MCF-7 cells by promoting clonogenic growth, cell proliferation, and migration.

#### **Biography**

Gabriela Silva holds a PhD in Biology from the Instituto de Biologia Experimental e Tecnológica, Portugal. From 2002 to 2008 she worked as Post-Doctoral fellow in the Instituto Gulbenkian de Ciência, Portugal, on projects that contributed to the understanding how HO1-1 protein affords cytoprotective and anti-inflammatory effects in various diseases. After that, she developed research in cancer. First on the role of HDAC inhibitors on hematologic malignancies and then on the mechanisms by which p16 protein exerts anti-oncogenic effects in osteosarcoma and on the mechanisms underlying the stromal fibroblast transformation in breast cancer. Since 2014, she has been a scientist at Instituto de Biologia Experimental e Tecnológica, Portugal, where she works on projects in the fields of biopharmaceutical process development and oncology. Her main scientific interests relate to the mechanisms underlying cancer development and therapy.

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# Plasma filtration (PF) effectively removes circulating pegylated liposomal doxorubicin (pld) and modifies chemotherapy-related toxicity in metastatic ovarian cancer

#### Ondřej Kubeček

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**Statement of the Problem:** Pegylated liposomal doxorubicin (PLD), a formulation of doxorubicin hydrochloride encapsulated in polyethyleneglycol-coated liposomes, has proved its efficacy in the treatment of ovarian cancer and other solid tumors. The major dose-limiting toxicities include hand-foot syndrome (HFS) and mucositis. Thanks to the unique pharmacokinetic properties of PLD and the defective vasculature of the tumor tissue, the peak PLD concentration in the tumor is attained considerably faster than in other tissues in which toxic reactions occur. Interestingly, less than 5% of the administered dose is delivered to the target tissue; hence, it is believed that the majority of the administered PLD has a limited therapeutic value and is merely responsible for organ toxicity. Therefore, the extracorporeal removal of circulating PLD could be a promising method to increase PLD tolerability while preserving its antitumor activity. This study seeks to evaluate the safety and efficacy of PF and the related changes in chemotherapy-related toxicity.

**Methodology & Theoretical Orientation:** Patients with platinum-resistant ovarian cancer were treated with PLD 50 mg/m2 in one-hour IV infusion q4w, followed by plasma filtration (PF) performed at hours 44(46)-47(49) post dose. Plasma PLD concentration was measured to assess the pharmacokinetic parameters and PF efficacy. Treatment-related toxicity and the patients' outcome were also evaluated.

**Findings:** Fifteen patients were enrolled in this study and received a median of 3 (2-6) chemotherapy cycles. In all, 53 PF cycles were evaluated. PF eliminated a median of 30.1% (12.7-64.6%) of the administered PLD dose. Only one case of grade 3 HFS and grade 1 mucositis were documented.

**Conclusion & Significance:** Plasma filtration represents a potent method in the removal of circulating PLD. It is well tolerated and it seemingly reduces the incidence of hand-foot syndrome and mucositis.

#### **Biography**

Ondřej Kubeček is a graduate of Charles University, Faculty of Medicine in Hradec Králové, Czech Republic. He has been practicing since 2012 as the medical oncologist at the Department of Oncology and Radiotherapy at the Hradec Králové University Hospital. He focuses on the treatment of GI cancers, malignant melanoma, and ovarian cancer. In 2016, Kubeček worked as a research scholar at the Department of Experimental Medicine and Pathology at Mayo Clinic, Rochester, USA. As a PhD student, he is currently working on a research project dedicated to the use of extracorporeal elimination of pegylated liposomal doxorubicin to improve the treatment tolerability in patients with ovarian cancer

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# Reactive carbonyl compounds of protein in patients' blood after surgical treatment of breast cancer

#### Sabina Zhumakayeva

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**Introduction.** The problem of breast cancer (BC) is one of the important and complicated in oncology. In this aspect, there is a significant amount of interest in the study of oxidative processes, since their disorders can act as one of the pathogenetic factors of carcinogenesis.

**Aim of the study:** To study the Reactive carbonyl compounds of proteins (RCCs) in plasma and in erythrocytes of blood of the BC patients after surgical treatment.

**Materials and methods:** The blood of 20 women with BC was examined, which have I-IIIa stages after surgical treatment in the volume of radical resection or radical mastectomy performed at the first stage of treatment. The control group consisted of practically healthy women (n = 15). The level RCCs in erythrocytes and in blood plasma was determined by the method of Levine R.L et al. (1990).

**Resultsof the study:** In erythrocytes of BC patients with I stage, there was a slight decrease in the percentage of RCCs. At the same time, an increase of RCCs was observed in II stage BC patients (by 50% compared to control, p <0.05). The level of RCCs in erythrocytes of BC patient's blood with III stage was 2 times lower than the control. In blood plasma of BC patients with I stage the significant increase in RCCs was observed (3 times compared with the control). In BC patients with II stage, this indicator exceeded control by 70-75% (p <0.05), whereas in patients with III stage of BC, the content of RCCs did not differ significantly from control.

**Conclusions:** These data suggest the development of carbonyl stress in the body of BC patients. Surgical removal of the tumor in breast cancer does not eliminate the conditions for the oxidative modification of proteins.

#### **Biography**

Sabina Zhumakayeva works at Medical University of Karaganda as 1-year doctoral student of the Oncology Department. Education (university and graduation year): Karaganda State Medical University, 2015. Faculty: General Medicine. Specialization, postgraduate education: oncologist, radiodiagnosis, including ultrasound, CT, MRI, X-ray. Work experience in the speciality: over 3 years. Academic degree and title: Master of Medical Sciences. Scientific works, copyright certificates: 9 publications, 1 certificate of state registration of the object of intellectual property.

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#### Anesthetic management of a patient with cancer and hyperhomocysteinemia

#### Cindy Yeoh

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**Case:** A 57-year-old female with a history of uterine and breast cancer s/p chemoradiation presented for cervical LEEP/cone biopsy/D&C. Her medical history was complicated by elevated LFTs with recent hyperhomocysteinemia (> 50micromol/l, normal 4-15). She was seen by a hematologist prior to surgery, and it was concluded that elevated homocysteine levels were due to cancer therapy and alcohol consumption. The procedure was performed under monitored sedation, with 2mg of Midazolam, 50mcg of Fentanyl, and a bolus of 70mg of Propofol followed by a steady infusion of 150mcg/kg/min.

**Discussion:** Causes of hyperhomocysteinemia include genetic predisposition, acquired deficiencies (folate, B6, B12), malignancies, and renal disease. Elevated homocysteine levels result in thromboembolic complications by causing endothelial dysfunction, increasing procoagulant activity, and decreasing antithrombotic effect. Challenges of patients with hyperhomocysteinemia undergoing anesthesia are related mainly to the procoagulant state and efforts should be focused on thromboprophylaxis and maintenance of hemodynamics and euvolemia. Nitrous oxide should be avoided as it inhibits methionine synthase and can further increase homocysteine levels. Patients with co-morbidities that include coronary artery disease, peripheral vascular disease, and cerebrovascular disease are at increased risk for peri-operative thrombotic events. This risk is amplified for high-risk procedures under general anesthesia.

**Conclusion:** In this case, the patient presented for a low-risk procedure. She did not have a history of coronary or cerebrovascular disease, but had risk factors (surgery, age>50yrs, malignancy, cancer therapy) in addition to a hypercoagulable state (due to elevated homocysteine levels) that posed increased peri-operative risk for thrombotic events such as deep venous thrombosis and pulmonary embolus. The decision was made to proceed with monitored sedation over general anesthesia so as to avoid fluctuations in hemodynamics and decrease the risk of venous stasis. The procedure took approximately 45 minutes and the patient recovered uneventfully and was discharged home the same day.

#### **Biography**

Cindy Yeoh is an associate attending in the Department of Anesthesiology and Critical Care Medicine at Memorial Sloan Kettering Cancer Center in New York. She is a member of the department's Quality Assurance Committee and her research interests include patient safety, outcomes and performance, and technology in the field of anesthesiology. Her recent publications have focused on real-time locating systems and its effects on the efficiency of anesthesiologists in the perioperative setting.

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# Identify and characterize the cancer stemness role of maelstrom in hepatocellular carcinoma

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**T**epatocellular carcinoma (HCC) is the fourth most common type of cancer in Hong Kong SAR and ranks Has third leading mortality rate of cancer type worldwide. A wise strategy for better understanding the enrolled molecular mechanisms in HCC progression, which is needed to discover novel diagnostic markers and therapeutic targets. According to analysis our RNA sequence data of three paired HCC and non-tumor tissue samples, human maelstrom (MAEL) gene was chosen to study. Our preliminary data suggested that MAEL frequently upregulated in HCC patients, associated with tumor size, adjacent organ invasion, tumor recurrence and worse overall survival rate. Previous study demonstrated that MAEL promoted HCC cells proliferation and metastasis as well as upregulating several stemness related genes expression in mRNA level through AKT/GSK3β/Snail signaling pathways. However, the cancer stemness regulating ability and downstream targets of MAEL are still not well studied. Therefore, this project would focus on revealing novel targets of MAEL and further investigate the unique role in regulating cancer stemness. We analyzed MAEL expression and survival data in TCGA LIHC cohort, the results were consistent with our previous findings. We found that overexpress MAEL could not only promote the ability of HCC cell proliferation and mobility in vitro, but also increase the proportion of CD133+ cells, self-renew and sorafenib resistant ability. Moreover, knockout MAEL showed reverse results in PLC8024 cell line inhibited these functions. We applied next generation sequencing (NGS) technology to compare with vector group and MAEL transfected group cells which revealed that MAEL enrolled in extracellular matrix (ECM) receptor interaction pathways mediated cancer stem cell marker CD44 expression. This finding confirmed by Q-PCR, western blots and flow cytometry. Taken together, these data suggest MAEL could promote HCC cells proliferation, metastasis as well as increasing stem cell features

#### Biography

Shi Chaoran was graduated from Capital Medical University in 2015 as the major of Medical Laboratory Tests (MLT). After finished the internship in Beijing Anzhen Hospital, he joined in Department of Clinical Oncology, HKU as research in October 2015. In September 2017, he began his postgraduate study in the same laboratory with supervision of Prof. Dora Kwong and Prof. XY Guan. Their laboratory focuses on discovering novel cancer related genes and mir-RNAs in gastric cancer (GC), hepatocellular carcinomas (HCC), esophageal carcinomas (ESCC) and nasopharyngeal carcinoma (NPC). His current study is supported by Health and Medical Research Fund (No.04150826).

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# Prognostic value of CD8 Immunogradient indicators in tumour-stroma interface zone of colorectal cancer

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**Statement of the Problem:** The immune response within the tumour microenvironment assessment methods were proposed to predict patient survival and therapy outcomes in colorectal (CRC) and other cancers; nevertheless, automated operator-independent approaches are lacking. We present a new image analysis method to automatically extract Immunogradient indicators and their prognostic value in CRC patients.

**Methodology & Theoretical Orientation:** Surgically excised CRC samples from 101 patients were stained for CD8, scanned, and analyzed by Indica labs HALOTM software. The image analysis data was then subsampled by a hexagonal grid which was used to extract and rank the tumour interface zone (IZ) according to distance to the tumour edge. Lastly, a set of novel Immunogradient indicators representing CD8 cell density profiles across the IZ were computed. The prognostic value of the indicators was tested by univariate and multiple survival statistics. Findings: The Immunogradient indicators ImmunoDrop (ID) and Centre of Mass (CM) for the CD8 cells, as well as CD8 cell densities within tumour and stroma aspects of the IZ and their factor scores provided significant stratifications of CRC patients into prognostic groups (p<0.05). Multiple Cox regression analyses of extracted indicators along with conventional clinicopathologic characteristics revealed ID and the Aggregated IZ CD8 cell response factor as strong independent predictors of worse (HR: 2.41, p=0.0126) and better (HR: 0.41, p=0.0196) 5-year overall survival, respectively.

**Conclusion & Significance:** The proposed automated, data-driven digital image analysis method for the IZ immune infiltrate assessment provides strong independent prognostic biomarkers is operator-independent and is based on single CD8 immunohistochemistry slides.

#### **Biography**

Ausrine Nestarenkaite works as a medical geneticist at the National Center of Pathology and is a doctoral student at Vilnius University, Institute of Biosciences, in Lithuania. She focuses on the multiparametric and spatial analysis of tumour microenvironment components in digital microscopy slides. Main scientific interests: Molecular genetics of colorectal cancer, cancer immunology, and digital pathology applications.

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# The Immunogradient of CD8+ cell density in the tumour-stroma interface zone predicts overall survival of patients with hormone receptor-positive invasive ductal breast carcinoma

#### **Dovile Zilenaite** Vilnius University Hospital Santaros Clinics, Lithuania

**Statement of the Problem:** Tumour infiltrating lymphocytes (TIL) are associated with better prognosis in triple-negative and HER2-positive breast cancer (1, 2), and TIL assessment by digital image analysis (DIA) has been successfully implemented in colorectal and other cancers (3). However, results in hormone receptor-positive breast cancer (HRBC) based on manual scoring remain contradictory (2). Here we used an automated DIA method to extract prognostic value of novel Immunogradient indicators in CD8+ cell density profiles in HRBC.

**Methodology & Theoretical Orientation:** Surgically excised HRBC samples from 102 patients were immunohistochemically stained for CD8, digitized and analysed by the HALO<sup>¬¬</sup> platform. The DIA data was subsampled by a hexagonal grid and explicit rules were then used to extract the tumour-stroma interface zone (IZ) and compute novel Immunogradient indicators from TIL density profiles across the IZ. The prognostic value was evaluated by survival analysis. Findings: The IZ Immunogradient indicators (mean CD8+ density in the tumour aspect of the IZ, Immunodrop, Centre of Mass) allowed prognostic stratification of patients in univariate analyses (hazard ratios: 0.21 (p=0.0002), 2.79 (p=0.0140), and 0.28 (p=0.0044), respectively). The best and independent indicator of better OS by multiple Cox regression model (hazard ratio: 0.23 (p=0.0007)) was an aggregated Immunogradient factor (Agg. Factor), obtained by the sum of two factor scores (CD8+ density and "gradient towards the tumour"). Remarkably, the aggregated Immunogradient factor revealed a striking drop of patients' survival probability 5 years after surgery.

**Conclusion & Significance:** The Immunogradient indicator for CD8+ cell density is an independent predictor of better OS in HRBC patients with the particular diversion of OS 5 years after the surgery.

#### Biography

Dovile Zilenaite is a medical geneticist at the National Center of Pathology, Affiliate of VULSK and a doctoral student at Vilnius University Faculty of Medicine. Her research focuses on the development and standardization of multiple IHC procedures for multiparametric and spatial analysis, digital image analysis and prognostic modelling in the breast cancer patients. Main scientific interests: genetics, cancer biology, immunology, digital analysis and analytics of whole slide pathology images to describe heterogeneity of tumor cell population and microenvironment.

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# Influence of NECC (Nutrition and Exercise Center for Cancer Patients) on survival and body composition in gastrointestinal cancer patients

#### Nina G. Sautter

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**BACKGROUND:** Gastrointestinal cancer patients are particularly predisposed to develop cancer cachexia. Cachectic patients are characterized by loss of adipose tissue as well as skeletal muscle wasting which has a tremendous impact on quality of life and survival (1, 4). In terms of improvement for this multifactorial syndrome, Klinikum rechts der Isar (MRI) in Munich, Germany has founded NECC, a treatment concept including nutrition intervention and an individual training program.

**METHODS:** In this study we focused on patients with pancreatic (n = 15) and upper gastrointestinal cancer (n = 21). Body composition using CT images was analyzed initially, 4 weeks, 3 months and 6 months after initial visit of NECC (Image 1). To underline the outcome, NECC patients were matched to adequate partners who correspond in age, gender, diagnosis with TNM classification and type of surgery. The control group does not receive any further support concerning nutrition and physical exercise.

RESULTS: Our study demonstrates that NECC has impact on overall survival (Image 2). Skeletal muscle mass index (SMAI) was higher 4 weeks and 3 months after initial visit in NECC patients compared to control group. Intramuscular adipose tissue index (IMATI) was higher after 6 months in NECC patients compared to controls.

**CONCLUSION:** The NECC program influences overall survival in patients with gastrointestinal cancer. This effect was significant in patients with pancreatic cancer but not in patients with upper GI cancer. Additionally, we observed effects of NECC on SMAI 4 weeks and 3 months after initial visit and on IMATI 6 months after initial visit. The promising results should be further investigated in randomized studies.

#### **Biography**

Nina Giulia Sautter graduated from Ludwig-Maximilians Universität in Summer 2018 in the field of Dentistry. She is passionately interested in improvement of life quality of cancer patients. In 2016 she started her thesis about the importance of physical exercise and nutrition as a part of treatment in gastrointestinal cancer patients. The results of her research show a significant impact on the patient's survival.

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# Accecpted Abstracts





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# The process of oncology nurse practitioner patient navigation: A grounded theory approach

### Frances Johnson

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**Introduction:** Nurse practitioner (NP) navigation, in general, has been shown to achieve cost effective quality care, while saving millions of dollars. Research though scant has shown that oncology nurse practitioner navigators' improve clinical outcomes. For purposes of this study, oncology NP (ONP) navigators are nurse practitioners with a certification in oncology who utilize navigation processes to care for cancer patients along any aspect of the cancer care continuum. Navigation process is defined as a series of actions or steps taken in order to achieve a particular end.

**Method:** Twenty ONP navigators were interviewed though the use of a semi-structured interview utilizing grounded theory methodology.

**Results:** This resulted in a well-defined set of concepts and theoretical framework for the process of ONP navigation which lays the groundwork for program evaluation and role delineation.

**Conclusions:** A navigation process has been identified for ONP navigators. Researchers have concluded that an understanding of the structure and process requirements for planning a care innovation is the basis for safe and effective patient care. Implications for further research would center upon further defining the categories of this navigation process for program. Oncology related triage tools are of crucial importance as the best of care plans can be thwarted by an inept triage process. Additionally, research has indicated a need to define the value of the NP role in terms of delivering patient outcomes (Grainne, Plummer, O'Brien, & Boyd, 2011). Identification of standardized outcome measures will serve to promote interprofessional collaboration on a global basis. The findings indicate that not all of the participants guided the patient entirely through the cancer. This definition of navigation processes can serve to promote clarification of the navigation role, and serve as the basis for nurse practitioner training and development. Finally the basic social process that centered on the core category was staying connected to the patient and to the system.

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# How routine is follow-up monitoring of atrial fibrillation patients prescribed direct oral anticoagulants? A Case study of Irish GPs using a count model

Ann Kirby, Aileen Murphy, Colin Bradley University College Cork, Ireland

**Background:** Direct Oral Anticoagulants (DOACs) are widely marketed as medicines that don't require routine laboratory monitoring. However, owing to their complex pharmacological properties and side effects prescribing and monitoring guidelines have emerged. These advocate monitoring for renal and hepatic impairment; bleeding episodes; liver function; co-medication; circulation and occurrence of side effects. Though advocated, follow-up is currently not routine and its implementation creates an externality for general practitioners (GP)s managing Atrial Fibrillation (AF) patients in the community.

**Objectives:** This study investigates the frequency, the type of follow-up, and the factors that influence follow-up amongst Irish GPs, who prescribe DOACs to patients with AF, to prevent strokes.

**Methods:** The frequency and type of follow-up care is estimated and a count model is applied to determine the GP and practice characteristics that influence the implementation of follow-up.

**Results:** The most frequently observed guidelines are those pertaining to renal function (82%), bleeding episodes (71%), liver function (69%), circulation (54%) and side-effects (55%). The regression analysis revealed that female GPs (P=0.05) and GPs who observe all seven guidelines (P=0.06), practice more frequent follow-up while those in training practices (P=0.09) provide less frequent follow-up.

**Conclusions:** Results show that there is a lack of adherence to prescribing guidelines with only 24% adhering to all seven guidelines and infrequent patient follow-up. Results indicate that existing education and decision support tools are not being incorporated into routine workflows for GPs managing AF patients prescribed DOACs.

**Conclusions:** Metformin succeeded to limit weight gain the obese with pregnancy.

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# Transient resistance to DNA damaging agents is associated with expression of microRNAs-135b and -196b in human leukemia cell lines

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The acquisition of resistance to anticancer drugs is widely viewed as a key obstacle to successful cancer therapy. However, detailed knowledge of the initial molecular events in the response of cancer cells to these chemotherapeutic and stress responses, and how these lead to the development of chemoresistance, remains incompletely understood. Using microRNA array and washout and rechallenge experiments, we found that short term treatment of leukemia cells with etoposide led a few days later to transient resistance that was associated with a corresponding transient increase in expression of ABCB1 mRNA, as well as miR-135b and miR-196b. This phenomenon was associated with short-term exposure to genotoxic agents, such as etoposide, topotecan, doxorubicin and ionizing radiation, but not agents that do not directly damage DNA. Further, this appeared to be histiotype-specific, and was seen in leukemic cells, but not in cell lines derived from solid tumors. Treatment of leukemic cells with either 5-aza-deoxycytidine or tricostatin A produced similar increased expression of ABCB1, miR-135b, and miR-196b, suggesting a role for epigenetic regulation of this phenomenon. Bioinformatics analyses revealed that CACNA1E, ARHGEF2, PTK2, SIAH1, ARHGAP6, and NME4 may be involved in the initial events in the development of drug resistance following the upregulation of ABCB1, miR-135b and miR-196b. In summary, we report herein that shortterm exposure of cells to DNA damaging agents leads to transient drug resistance, which is associated with elevations in ABCB1, miR-135b and miR-196b, and suggests novel components that may be involved in the development of anticancer drug resistance.

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# Breast cancer induces tolerogenic state of healthy activated CD4+ lymphocytes, characterized by reduced PI3K, NFκB, JAK-STAT, Notch, and increased TGFβpathway activity

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Cancer cells can induce a state of immunotolerance, which may be reversed by checkpoint blocker immunotherapy. Prediction of immunotherapy response remains a challenge. CD4+ lymphocytes are important for activating the adaptive immune-response, while conversion to immune-suppressed state impairs the anti-cancer immune-response. Lymphocyte function is controlled by a number of signaling pathways. We developed tests to quantitatively measure activity of signaling pathways (e.g. Hedgehog, Wnt, TGF $\beta$ , Notch, NF $\kappa$ B, PI3K, JAK-STAT 1/2 and 3, and MAPK) based on Bayesian model inference of activity from measurements (microarray, qPCR) of mRNA levels of target genes of the transcription factor associated with the respective signalling pathway[1],[2],[3],[4],[5],[6]. Tests were biologically validated on individual cell/tissue samples, including immune cells and can be used to characterize functional activity status of immune cell types. The cellular mechanism underlying breast cancer-induced immunosuppression of CD4+ lymphocytes was investigated.

**Method:** Generation of Affymetrix expression microarray data has been described [7]. In brief, dissected breast cancer tissue fragments from fresh surgical specimens were mechanically dissociated in X-VIVO-20 (SN). Following standard activation, healthy donor CD4+ lymphocytes were incubated with SN. Signaling pathway activities were measured on Affymetrix data from the CD4+ lymphocyte samples.

**Results:** CD4+ lymphocyte activation resulted in induction of PI3K, NFkB, JAK-STAT1/2, JAK-STAT3, and decrease of TGF $\beta$  pathway activities. Incubation with cancer SN only reduced activity of PI3K, NFkB, JAK-STAT1/2, JAK-STAT3 pathways, while increasing TGF $\beta$  pathway activity, in activated lymphocytes, but. Conclusion: A soluble factor from breast cancer tissue induces immunotolerance in CD4+ lymphocytes, by increasing TGF $\beta$  pathway activity, and reducing activity of effector immune pathways. Investigation as to the nature of the soluble factor is in progress. Signaling pathway assays can quantitatively measure the functional immune activity state of CD4+ lymphocytes. Envisioned application is in prediction and monitoring of immunotherapy response and identification of novel drug targets to reverse cancer-induced immunosuppression.

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#### Development of an attitude scale towards sexuality during pregnancy

Neslihan Yilmaz Sezer Ankara University, Turkey

**Statement of the Problem:** This research was methodologically conducted to develop an attitude scale during pregnancy, which will help to assess the sexual attitudes of pregnant women and partner of pregnant women during pregnancy. The practice was carried out in a university hospital pregnancy outpatient unit.

**Methodology & Theoretical Orientation** The required institutional consent and ethics committee approval were obtained. The sample was consisted of 1035 persons. Data were collected via Attitudes Towards Sexuality in Pregnancy Qualitative Interview Form, Descriptive Information Forms, Attitude Scale Toward Sexuality in Pregnancy Trial Form and Attitude Scale Toward Sexuality in Pregnancy. Data analyzes were performed with SPSS v.22 and LISREL (v.8.80) programs. In the evaluation of the data, confirmatory and exploratory factor analysis, t-test, one-way ANOVA, Cronbach Alpha internal consistency coefficient and test retest reliability tests were used.

**Findings:** As a result of the statistical analyzes, 34 items and 3 factor scale describing the 41,24% of the variance was obtained. Cronbach Alpha coefficients were 0.850 for Anxiety about Sexual Intercourse in Pregnancy; 0,860 for Beliefs and Values for Sexuality in Pregnancy; for 0.815 Recognition Sexuality in Pregnancy and 0.902 for all of the scale. The test–retest reliability coefficient was found 0.869. It was found statistically significant that gender, age, education level, education level of the partner, getting information about sexuality in pregnancy, the amount of information in this subject, regarding sexuality as risky in pregnancy, the sexuality prohibition by the doctor effected the attitude towards sexuality in pregnancy (p< 0.05).

**Conclusion & Significance:** In the direction of these results Attitude Scale Towards Sexuality During Pregnancy was accepted as a valid and reliable tool for assess the sexual attitudes of pregnant women and partner of pregnant women during pregnancy. It is suggested that this scale should be used by nurses and other health professionals who provide services to the pregnant women and that they should be used in different groups to determine their attitudes towards sexuality in pregnancy.

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# Results of enhance VHVs to promote health behaviors to decrease stroke risk by applied SSRT focus on specific risk factors among the people who live in Nonglak Chumpong district Nakhon Ratchasima, Thailand

#### Patama Vajamun

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Stroke is the leading cause of death and handicap in Thailand even though the national chronic disease control program was implemented for many years in contrast the problems continuously increasing according to changing to elderly society. Thai VHVs are provided basic health care and health promotion is one of the key success of health care improvement in Thailand. Methodology: 10 VHVs were trained for changing health behaviors of villagers and how to use SUT Stroke Risk Tool (SSRT) to assessed and classified risk factors of target group to guided individuals for changed their significant modifiable health behaviors. 50% of VHVs could encouraged 96% (48) of the risk group changed to healthy behaviors; increase regular exercises, decrease BP, BS, weight, waist, cholesterols, salt, sweet, and alcohol consumption including gave up smoking. Only 4% (2) of them were uncontrolled and referred to the hospital for health check up. It revealed that specific training of VHVs by employed SSRT as a tool could increased healthy behaviors among people who were at risk of stroke in Nonglak village and none of them developed stroke within a year follow up. So that further study may be benefit in general population.

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### Prevalence and associated factors of the incorrect administration of Metered Dose Inhaler (MDI), dispensing a short-acting bronchodilator by COPD patients in primary care setting

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**Background:** Chronic Obstructive Pulmonary Disease (COPD) is a common lung disease characterized by airflow limitation. The Global Initiative for Chronic Obstructive Lung Disease (GOLD) guideline suggests a short-acting inhaled bronchodilators and anticholinergic inhaled agents as a first line COPD treatment. In spite of its popularity, many COPD patients use inhalers incorrectly.

**Material and Method:** This is a cross-sectional study. The sample includes patients diagnosed with COPD who visit Muangsongkhla hospital (N=92) during 1-31 July 2016. The inhaler technique was directly observed during their visits. Data were analyzed by Program R version 2.13.0.

**Results:** 92 patients diagnosed with COPD were enrolled in this study. Prevalence of the incorrect administration of MDI dispensing a short-acting bronchodilator by COPD patients in primary care setting was 72.8%. Breath-holding for at least 10 seconds after inhalation was found to be the most critical step that was mistaken. Education was found to be significantly associated with the incorrect administration of MDI dispensing a short-acting bronchodilator.

**Conclusion:** Almost three quarters of COPD patients in primary care setting administer short-acting bronchodilator incorrectly. The most important factors associated with incorrect inhaler usage of the MDI are education and income. Therefore, healthcare provider team should carefully provide the instruction for the methods of using MDI administration to COPD patients and reinforce them periodically asking the patients to demonstrate how they administer MDI.

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# 25<sup>th</sup> Global Meet on CANCER RESEARCH & ONCOLOGY

### World Congress on Primary Healthcare and Medicare Summit

May 20-21, 2019 | Rome, Italy

### Ultra-low dose DPI is a cheap and effective potential therapeutic agent to prevent colitisassociated colorectal cancer

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**Background:** There are about 15-20% colorectal cancer developed from colitis. The most common forms of inflammatory bowel disease are Crohn's disease (CD) and ulcerative colitis (UC). The pathogenesis of UC and CD is various and including immunologic, environmental and genetic factors. Excessive reactive oxygen species (ROS) production has been observed in the inflamed mucosa of IBD patients. ROS is widely known as a negative factor on cancer initiation, progression and survival stage. NADPH oxidases (NOXs) are the main resource of ROS. Although diphenyleneiodonium (DPI) were assessed as inhibitors of both mitochondrial respiration and ROS synthesis and used in research for decades, few research using it as an potential drug in mice model.

**Methods:** We used male C57BL/6 mice were treated with 3.5% DSS and 2% DSS respectively for five days and seven days to make fatal enteritis and early stage colitis. After the DSS period, ultra-low dose DPI or control solvent was intraperitoneal injection everyday. Then, the survival rate and inflammatory level of intestinal tract in different groups were observed. Quantitative PCR and enzyme-linked immuno sorbent assay (ELISA) were applied to evaluate the inflammatory factors between experimental and control groups. Intracellular ROS were meatured by fuorescence microscopy using 2'7'-dichlorofluorescein diacetate(DCFH-DA). Htoxylineosin (H&E) staining assessed histological patterns of several organs in DPI group and control group. Disease activity index and histological activity index were assessed. Certain signal pathways were verified on protein level.

**Results:** In the fatal enteritis model, compared with control group, ultra-low dose DPI group has a better survival rate. In early stage colitis model, mice's weight and colon length are better than those in control group. The level of inflammatory factors--COX2, IL6, TNF-a and IL12 are lower than the control group. In RAW246.7 cell line, compared with other concentrations, ultra-low dose DPI group had a lower level of inflammatory factor, such as COX2, IL6, CCL5, IP10, TNF-a and MCP1.Utral-low dose DPI could inhibited NF- $\kappa$ B and MAPK pathway. Histological patterns of DPI and control groups had no significant differences.

**Conclusion:** Ultra-low dose DPI could prevent the progress of inflammatory bowl diseases and have no negative effect on other organs. This study will provide a new pharmacological evidence that ultra-low dose DPI has a positive significance for prevention of colitis-associated colorectal cancer.

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#### Lung cancer mimicking community acquired pneumonia

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**Introduction:** Lung cancer sometimes can mimic or present as non-resolving pneumonia. Patients usually present with pneumonia like symptoms not resolving over course of 1-2 weeks despite being treated with antibiotics.

**Case:** 43-year-old female with an active smoking history of 20 years presented to us with complaints of fever, cough, fatigue, headache, and shortness of breath. One month prior to presentation, he traveled by car for 2 days after spending 2 months in Louisiana. She was recently seen at an outside hospital with similar complaints, where she was treated with a 10-day course of amoxicillin-clavulanate for presumed community acquired pneumonia. On presentation, patient's vitals were BP 127/87, Pulse 117, Temp 38C, and Oxygen saturation 88%. On examination, she was noted to have decreased breath sounds on the right lower lung and swelling of the left leg. Pertinent labs included an elevated white blood cell count (13.4), eosinophils (790), and D-dimer (27,529). Due to concerns for PE, CT thorax was done, which showed extensive multifocal consolidation of the right and left lungs, mediastinal lymphadenopathy, bilateral pleural effusions more pronounced on the right side, and pericardial effusion. A small PE was also noted on left side. Leg Duplex showed an acute DVT of the left leg. The patient was started on IV Heparin for the acute DVT and PE. Per pulmonology recommendation, she was started on antibiotics for suspected severe multi-focal community- acquired pneumonia. She proved refractory to antibiotic treatment. Subsequent work-up for atypical pneumonia included cold agglutinin titer/ Mycoplasma titers, Q fever, Chlamydia titers 1:64, Strongyloides, Histoplasma, Fungitell, Cryptococcus, and HIV. All were negative. Cardiac surgery and pulmonary team were consulted. Patient had pericardial window drained and pleural pig-tail placed. Bronchoscopy was also done. Fluid cytology was positive for adenocarcinoma of lung. Further imaging studies revealed metastases to the brain , left adrenal gland and sacral spine.

Discussion: Patients presenting with pneumonia like symptoms and not improving despite treatment with antibiotics should undergo further work up to rule out other causes including lung cancer. High clinical suspicion is required for the early diagnosis as delayed diagnosis can lead to poor prognosis.

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#### World Congress on PRIMARY HEALTHCARE AND MEDICARE SUMMIT

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### Comparative Study of Rural and Urban Primary Health Centers of Ajmer Rajasthan India

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A jmer is located in the center of Rajasthan (INDIA) between 250 38 "and 260 58 "north Latitude and 73 0 54 "and 75 0 22" east longitude covering a geographical area of about 8481sq km hemmed in all sides by Aravalli hills. Famous Pushkar lake is also there near Ajmer. The Dargah of khawaja Moinuddin Chisti is Acclaimed and venerated shrine next to Mecca in the world. Ajmer has hot dry summer and cold bracing winter. temperature varies from 20 C in winter and 49 0 C in summer. The normal annual rainfall is 527.3mm. The primary health is ubiquitous health care available to all individuals of the world. WHO elaborates the role of PHC in 3 categories empowering people, multisector policies, and public health functions? Total Primary Health care centers of Ajmer are 47. Out of which 7 are in Arai, 8 in Bhinai, 4 in Jawaja, 7 in Kekri, 6 in Kishangarh, 7 in Masuda and 8 in Srinagar. 600 more PHC will be converted into Model Primary Health centers in the state. More health care centers are required in Ajmer, according to population and area of Ajmer. At least one PHC should be there in every village. There are 41,352 villages in Rajasthan out of which 39,752 are inhabited and 1600 are uninhabited. The national health policy 2017 was formulated to achieve the highest possible level of good health and wellbeing, and universal access to good quality health care without having financial hardship. A step to fulfil the vision is national health policy 2017. Ayushman Bharat 2017. It is a pioneering initiative to adopt continuum of holistic approach to healthcare. It has two pillars: 1. 1.5 lakh health and wellness centers for healthcare. It will bring about paradigm shift in healthcare. 2. PMJAY (Pradhan Mantri Jan Arogya Yojana) which will provide health protection to poor and vulnerable families. In the present paper health care centers of Ajmer Rajasthan and facilities were studied. Urban Ajmer has more Private and Government Health care centers than Rural areas. More than 90 % visits to PHC's are from rural background they travel for treatment more than 50 kms and they also have no money for treatment. Quality and quantity of PHC and CHC should be for betterment in Ajmer and Rajasthan.

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## 25<sup>th</sup> Global Meet on CANCER RESEARCH & ONCOLOGY

### World Congress on PRIMARY HEALTHCARE AND MEDICARE SUMMIT

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# Overexpression of MAGE-A1 in lung cancer: a novel biomarker for prognosis, and a possible target for immunotherapy

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Recently, broad advances have been made in diagnostic and therapeutic modalities against lung cancer. However, little improvement in patient outcome has been achieved, especially for advanced, recurrent, and metastatic lung cancers that have a significantly poor prognosis. We investigated melanoma-associated antigen A1 (MAGE-A1) expression in lung cancer tissues and its correlation with prognostic factors. In this cross-sectional study, samples from 101 patients with lung cancer [including 80 NSCLCs (frequency of NSCLC subtypes, SCC = 43, AC = 23, undifferentiated carcinoma = 9, and LCC = 5) and 21 SCLCs] were obtained between 2007 and 2014 and stained for MAGE-A1 by immunohistochemistry. Correlation with prognostic factors was assessed by t-test and  $\chi^2$  and Pearson tests. MAGE-1 IHC staining was positive in 56 (55.44%) patients with different degrees of staining; PN1 in 13 (12.9%), PN2 in 24 (23.8%), and PN3 in 20 (19.8%) patients. Eighty nonsmall cell and 21 small cell lung cancer specimens were stained for MAGE-A1. MAGE-A1 was detected more commonly in adenocarcinomas and was expressed more frequently in male (P = 0.0001) and patients >60 years (P = 0.005). MAGE-A1 expression was more frequent in the elderly, male patients, and those with advanced stage and adenocarcinoma subtypes of lung cancer. Further investigations are needed to assess MAGE-A1 expression as a potential cancer biomarker. This retrospective study had all of the limitations associated with this type of longitudinal cohort study. However, our study included a considerable number of patients, which was done for the first time in our region. Also, we assessed the expression of MAGE-A1 as the products of CT-X genes (instead of its presence, such as in studies that were conducted by PCR). This feature of our study provided preliminary information for future investigation in term of new immune checkpoint therapy drugs.

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