


**2nd International
Congress on**

ADVANCES IN CLINICAL RESEARCH & TRIALS

June 22–23, 2022

Peers Alley Media

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PROGRAM-AT-A-GLANCE

CLINICAL R&T
2022

BST- British Summer Time

08:45-09:00 Opening Ceremony

Distinguished Speaker Talks

Sessions: Clinical Research and Clinical Trials | Clinical Study Designs | Patient-Centric Clinical Trials | Innovations In Clinical Trials | Clinical Data Management and Statistics | Clinical and Medical Case Reports | Pharmacovigilance and Drug Safety | Drug Discovery and Development | Bioethics and Quality Regulation | AI In Clinical Trials | Digital Technology in Clinical Trials | Evidence-Based Medicine | Diagnosis of COVID 19

09:00-09:25

Title: Utilising a hybrid blood collection regime of remote dried blood spot sampling and in-clinic venipuncture to maximise data output in clinical trials

Elisabeth Karsten, Sangui Bio, Australia

09:25-09:50

Title: Use of a walking stick to aid mobility, decrease freezing of gait and enhance postural stability in Parkinson's disease

Roy G. Beran, University of New South Wales, Australia

09:50-10:15

Title: Medicinal cannabis in integrative cancer management

Kylie O'Brien, Torrens University, Australia

10:15-10:40

Title: Effects of neoadjuvant chemotherapy in ovarian cancer patients with different germline BRCA1/2 mutational status

Hualei Bu, Shandong University, China

10:40-11:05

Title: Acupuncture for Parkinson's disease: From theory to practice

Jing-Qi Fan, Guangzhou University of Chinese Medicine, China

11:05-11:30

Title: A pragmatic approach to treat lung cancer through loading theaflavin -3,3'-digallate and epigallocatechin gallate in spanlastic

Syed Saif Imam, HIMT College of pharmacy, India

11:30-11:55	<p>Title: Biological studies with phytochemical analysis of <i>Cornus mas</i> unripe fruits</p> <p>Christina Vasiliki Karakousi, Aristotle University of Thessaloniki, Greece</p>
11:55-12:20	<p>Title: A proprietary fermented wheat germ extract in cancer and autoimmune clinical studies – A new paradigm</p> <p>Mate Hidvegi, University of Jewish Studies, Hungary</p>
12:20-12:45	<p>Title: Genome sequence analysis of SARS-COV-2 isolated from a COVID-19 patient in Erbil, Iraq</p> <p>Hazha Jamal Hidayat, Salahaddin University, Iraq</p>
12:45-13:10	<p>Title: Prospects of photodynamic inactivation of tracheobronchial tree pathogenic microbiota using methylene blue</p> <p>Irina Tiganova, Gamaleya National Research Center of Epidemiology and Microbiology, Russia</p>
Lunch Break 13:10-13:40	
13:40-14:05	<p>Title: Anti-PEG IgE in anaphylaxis associated with polyethylene glycol</p> <p>Zhao-Hua Zhou, Food and Drug Administration, USA</p>
14:05-14:30	<p>Title: A novel, safe, effective treatment for opioid use disorder</p> <p>Fredric Schiffer, McLean Hospital and the Harvard Medical School, USA</p>
14:30-14:55	<p>Title: Computational modelling of chromatin accessibility identified important epigenomic regulators</p> <p>Yanding Zhao, Baylor college of Medicine, USA</p>
14:55-15:20	<p>Title: Soluble Guanylate Cyclase (sGC) as a therapeutic target for diabetic nephropathy</p> <p>Gayathri Swaminath, Greenfire Bio, USA</p>
15:20-15:45	<p>Title: One platform endless pipelines: CAR-NK cells from engineered pluripotent stem cells using 3-D platform technology</p> <p>Shi-Jiang (John) Lu, HebeCell Corporation, USA</p>

15:45-16:10

Title: Impact of teleconsultation on patients with type 2 diabetes in the Brazilian public health system: Protocol for a randomized controlled trial
Daniela Laranja Gomes Rodrigues, *Hospital Alemão Oswaldo Cruz, Brazil*

Refreshment Break 16:10-16:25

16:25-16:50

Title: Effect of blue and red led on inflammatory acne: Controlled and randomized clinical trial
F. Mara Lúcia Gonçalves Diogo, *Universidade Nove de Julho, Brazil*

16:50-17:15

Title: Bobath in Brazil: What is the best study design for intervention for children with cerebral palsy?
Claudia R M Alcântara de Torre, *Centro de Apoio Terapeutico – Physiotherapy, Brazil*

17:15-17:40

Title: Device and non-device-guided slow breathing to reduce blood pressure in hypertensive patients: A systematic review and meta-analysis
Kamila Shelry de Freitas Gonçalves, *University of São Paulo, Brazil*

Panel Discussion

End of Day 1



BST- British Summer Time

Workshop

10:00-10:40

Title: DUCG-aided general clinical diagnosis enabling primary clinicians to diagnose diseases like experts and know why: Real applications

Qin Zhang, *Tsinghua University, China*

10:40-11:20

Title: Breastfeeding in prevention of postpartum acute pancreatitis (AP). A Sicilian population-based case-control study

Alberto Maringhini, *ARNAS Civico, Italy*

Refreshment Break 11:20-11:35

Distinguished Speaker Talks

Sessions: AI in Clinical Trials | Digital Technology in Clinical Trials | Medical writing in Clinical Research | Evidence-based medicine | Clinical Trials in Ophthalmology | Clinical Research in Gastroenterology | Clinical Trials in Microbiology | Clinical Trials in Obstetrics Gynaecology | Clinical Trials in Sports Medicine | Clinical Development of Vaccines | Clinical Trials in Diabetes | Clinical Research in Neuroscience

11:35-12:00

Title: Band-engineered laterally-oriented quasi-AlGaIn barrier /GaIn well, High-Electron-Mobility-Avalanche-Transit-Time (HEMATT) oscillator: Medical applications

Sulagna Chatterjee, *Adamas University, India*

12:00-12:25

Title: Comparative study of response surface methodology and adaptive neuro-fuzzy inference system for removal of 6-APA in aqueous media

N. Soleimanpour Moghadam, *Amirkabir University of Technology, Iran*

12:25-12:50

Title: CNS tumors: New techniques in radiation oncology

Marilena Theodorou, *Bank of Cyprus Oncology Center, Cyprus*

12:50-13:15

Title: SARS-CoV-2 spike T cell responses induced upon vaccination or infection remain robust against Omicron

Roanne Keeton, *University of Cape Town, South Africa*

Lunch Break 13:15-13:45

13:45-14:10

Title: Effect of sleeve gastrectomy on metabolic status in type 2 obese diabetics

Ibrahim El-Bayoumy, *University of South Wales, UK*

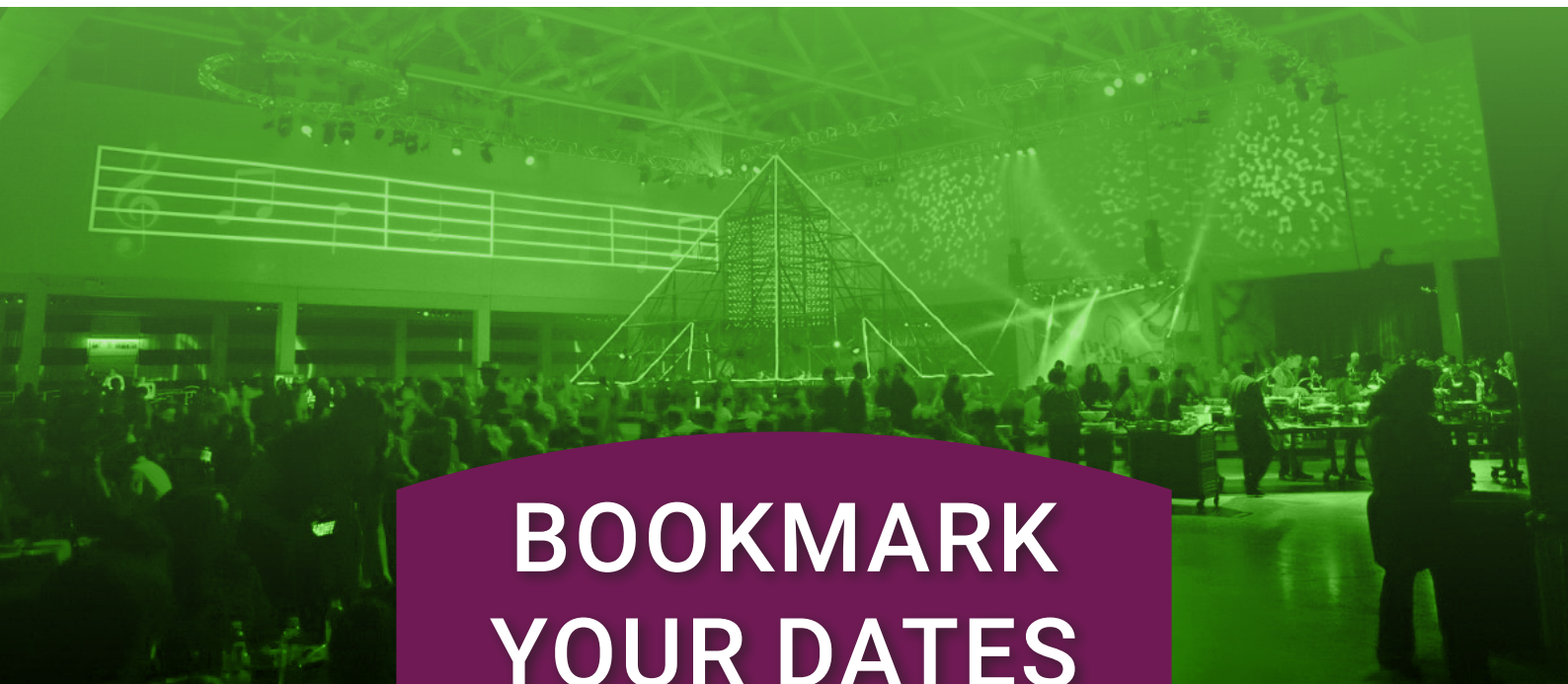
14:10-14:35

Title: Selection, expansion, and unique pretreatment of allogeneic human natural killer cells with anti-CD38 monoclonal antibody for efficient multiple myeloma treatment

Benjamin Motais, *University of Ostrava, Czech Republic*

End of Day 2

Closing Remarks



**BOOKMARK
YOUR DATES**

3RD INTERNATIONAL CONGRESS ON ADVANCES IN CLINICAL RESEARCH & TRIALS

MARCH 2023 | LONDON, UK

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SCIENTIFIC ABSTRACTS

DAY 1



Virtual Event

2nd International Congress on Advances in Clinical Research and Trails

June 22-23, 2022

CLINICAL R&T 2022

2nd International Congress on Advances in Clinical Research and Trails

Utilising a hybrid blood collection regime of remote dried blood spot sampling and in-clinic venipuncture to maximize data output in clinical trials

E. Karsten^{1,2,3}, C. Hill^{1,2} and B. Herbert^{1,2}

¹Sangui Bio, Australia

²Kolling Institute, Australia

³University of Sydney, Australia

Whilst liquid blood sampling enables the most comprehensive analysis of biomarkers and their source in different blood components, this approach is logistically more challenging in the context of clinical trials and can become difficult and expensive to manage in large studies.

Alternatively, dried blood spot (DBS) sampling can be performed by the participants themselves and can be done remotely. This enables both increased numbers of participants and more frequent sampling, which, for longitudinal studies, should increase the chance of detecting biomarker changes as they are occurring. Studies requiring large sample quantities, such as proteomics, has traditionally been limited by the small volumes of blood captured. However, modern advances in the sensitivity of multiplexed analytical techniques have made DBS a compelling sampling platform. This makes DBS a hugely valuable addition to traditional biospecimen collection in trials.

Our laboratory is employing a hybrid blood

collection regime for longitudinal studies that includes both liquid blood collected in clinic and DBS collected at home between clinic visits. To maximise the data points collected from a single sample, we have also developed a series of methods to sequentially extract and fractionate proteins from DBS. Using these methods, we have demonstrated the detection and robust quantitation of up to 1,600 proteins from mass spectrometry analysis of dried whole blood, a significant increase compared with analysis of undepleted plasma. In fact, some proteins not previously reported in blood have been detected with this approach. In a pilot study of lung cancer, liquid blood analysis revealed 12 significantly different proteins compared to the control group and DBS analysis revealed an additional 19 differentially expressed markers.

This sampling regime is an excellent research tool that, in our trials, has reduced the logistical burden of frequent venepuncture sampling and has increased the quality and breadth of data that can easily be collected from a single participant.

Biography

Elisabeth is a Co-founder and Principal Scientist of Sangui Bio. She has 8 years of research and technology experience with a focus on biomarker research. This work has covered hands-on laboratory work to clinical trial management. She completed her PhD with the University of Sydney in 2017 and is an author on 12 peer-reviewed papers with a total of 381 citations. She is an inventor on three of Sangui Bio's patent applications and has developed numerous novel blood cell analysis techniques.



Use of a walking stick to aid mobility, decrease freezing of gait and enhance postural stability in Parkinson's disease

Roy G Beran

*University of New South Wales, Australia
 Griffith University, Australia
 Moscow First State University, Russia*

Aim: Parkinson's disease (PD) is associated with stiffness/rigidity, tremor, bradykinesia and postural instability. This presentation provides a simple explanation and means to overcome these difficulties.

Methods: There has been an appreciation of the problems accompanying gait disturbance, in PD, which result from stiffness/rigidity which impedes righting reflexes, superimposed on the bradykinesia, gait instability and tremor, the diagnostic hallmarks of PD. This has evolved into a method of using a walking stick, to overcome many of these issues, which counteracts them once the technique has been adopted and perfected.

Results: This presentation demonstrates and explains the appropriate use of a walking stick in PD, via a pre-recorded, professionally produced video, to allow others to adopt the technique and use it in the management of patients who are experiencing gait problems, as a consequence of their PD.

Discussion: The appropriate use of a walking stick in PD depends on an understanding that the main problem with gait relates to moving around the centre of gravity which, when stable, standing in one position with the feet somewhat apart, rests between the feet thereby providing stability in that position. With stiffness and rigidity, it is difficult to correct for balance disturbance following a shifting of the centre of gravity and the patient has often learnt to recognise this difficulty with subsequent falls. Using a walking stick, as an additional leg substitute, allows the patient to maintain stability which shifting the centre of gravity forwards following which the patient can then move around that newly created centre of gravity with a feeling of safety and comfort. This has the capacity to enhance mobility, improve quality of life and is a simple approach to facilitate the ability to avoid falls and subsequent injuries that are so common in this population due to their gait instability.

Biography

Prof. Beran is a neurologist and sleep physician. He is Conjoint Professor of Medicine, University of NSW; Professor, School of Medicine, Griffith University, Queensland; and Professor Sechenov Moscow 1st State University, Russia. He is a Fellow of the Australasian College of Legal Medicine, the Australian Governor and Vice President of the World Association for Medical Law and Honorary Fellow of the Faculty of Forensic & Legal Medicine [Royal College of Physicians (London)]. He is a: Fellow of the Royal Australasian College of Physicians; Fellow of the Royal College of Physicians, Edinburgh; Corresponding Fellow of the American Academy of Neurologists; and Member of the Australian and New Zealand Association of Neurologists and Australasian Sleep Association. He published >360 papers, book chapters and letters to the editor, presented >400 papers at national and international meetings and written/edited 17 books, including being the editor in chief of the international journal, Medicine and Law.

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Medicinal cannabis in integrative cancer management

Kylie O'Brien

Torrens University, Australia


International College of Cannabinoid Medicine, UK

Surveys indicate that those with cancer often use medicinal cannabis. There is much preclinical research to indicate that key constituents of cannabis including cannabidiol (CBD) and tetra hydrocannabinol (THC) have anti-cancer activity, targeting many of the hallmarks of cancer and associated signaling pathways involved in the pathogenesis of cancer. However, research in humans is less strong in terms of altering hard endpoints such as mortality. Not with standing this, there is preclinical research evidence and in many cases, also human research that

suggests medicinal cannabis may have an important role to play in the management of signs and symptoms associated with cancer and its orthodox treatment. Such signs and symptoms include anxiety, depression, sleep disorders, chemotherapy-induced nausea and vomiting, cancer-related pain, cachexia, and oral mucositis. Medicinal cannabis may also have an important role to play in palliative care. In this presentation, we will explore some of the scientific evidence that medicinal cannabis may have a role to play in the integrative management of cancer.

Biography

Kylie has had a strong academic career in Chinese medicine, integrative medicine and since 2018, medicinal cannabis after career changing from optometry. She has held senior leadership positions in the Australian university and private education sector and is one of the leaders in cannabis education in Australia. She works as the Chief Scientific Officer at Releaf Group Ltd and Academic Director of the International College of Cannabinoid Medicine. She is currently conducting a two-year observational study in medicinal cannabis users. Her first book O'Brien and Sali, *A Clinician's Guide to Integrative Oncology: What You Should Be Talking About With Cancer Patients and Why*, was published in 2017 (Cham: Springer) and her latest book, *O'Brien & Blair, Medicinal Cannabis and CBD in Mental Healthcare* (Cham: Springer) was released in 2021.



Effects of neoadjuvant chemotherapy in ovarian cancer patients with different germline BRCA1/2 mutational status

Hualei Bu, Mengdi Fu and Beihua Kong
Shandong University, China

Background: Whether neoadjuvant chemotherapy (NAC) followed by interval debulking surgery (IDS) against primary debulking surgery (PDS) has a differential effect on prognosis due to Breast Cancer Susceptibility Genes (BRCA)1/2 mutations has not been confirmed by current studies.

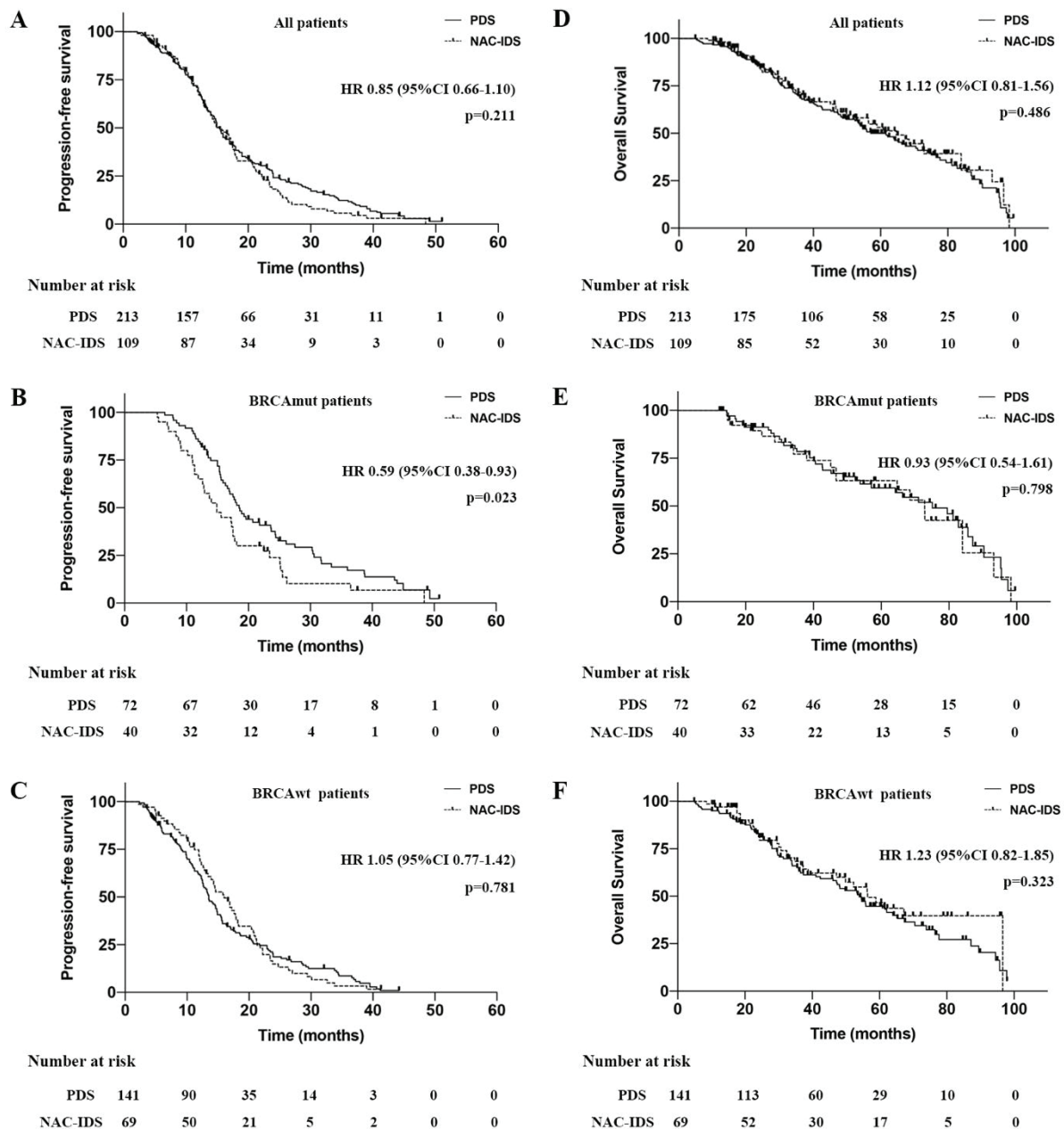
Methods: All patients included in this retrospective study were admitted to Qilu Hospital of Shandong University between January 2009 and June 2020, and germline BRCA1/2 mutation was tested. Patients in stage IIIB, IIIC, and IV, re-staged by International Federation of Gynecology and Obstetrics (FIGO) 2014, were selected for the analysis. All patients with NAC received 1-5 cycles of platinum-containing (carboplatin, cisplatin, or nedaplatin) chemotherapy. Patients who received maintenance therapy after chemotherapy were not eligible for this study. All relevant medical records were collected.

Results: A total of 322 patients were enrolled, including 112 patients with BRCA1/2 mutations (BRCAmut), and 210 patients with BRCA1/2

wild-type (BRCAwt). In the two groups, 40 BRCAmut patients (35.7%) and 69 BRCAwt patients (32.9%) received NAC. Regardless of the BRCA1/2 mutational status, there were no statistical differences in NAC-IDS and PDS groups for progression-free survival (PFS) (Figure A; median: 15.4 vs. 15.6 months, HR=0.85; p=0.211) or overall survival (OS) (Figure D; median: 57.1 vs. 64.7 months, HR=1.12; p=0.486). Further analysis found that PFS of BRCAmut patients was significantly reduced after NAC (Figure B; median: 14.9 vs. 18.5 months; p=0.023); however, there was no difference in OS (Figure E, median: 75.1 vs. 72.8 months; p=0.798). Whether BRCAwt patients received NAC had no significant effect on PFS (Figure C; median: 13.5 vs. 16.0 months; p=0.781) or OS (Figure F, median: 54.0 vs. 56.4 months; p=0.323).

Conclusions: For ovarian cancer patients with FIGO IIIB, IIIC, and IV, NAC-IDS did not adversely affect survival outcomes due to different BRCA1/2 germline mutational status.

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Biography

Dr. Hualei Bu, MD; Attending physician of Qilu Hospital, Shandong University, China; Member of Chemotherapy and Clinical Trial Research Committee, Gynecological Oncology Branch, Shandong Anti-cancer Association, China.

Dr. Bu has participated in more than ten international and domestic clinical trials of gynecological malignant tumors as a key Sub-I, including FZOCUS-1/2/3 studies of Fluzoparib for recurrent ovarian cancer and maintenance therapy, SOLO-1/SOLO-2/L-MOCA studies of Olaparib, NORA/PRIMA studies of Niraparib, and studies on the treatment of recurrent endometrial carcinoma and cervical cancer of PD-1/PD-L1 antibodies. As a clinician, Dr. Bu has rich clinical experience in surgical treatment, chemotherapy and targeted therapy of gynecological malignant tumors.



Acupuncture for Parkinson's disease: From theory to practice

Jing-Qi Fan and Li-Xing Zhuang

Guangzhou University of Chinese Medicine, China

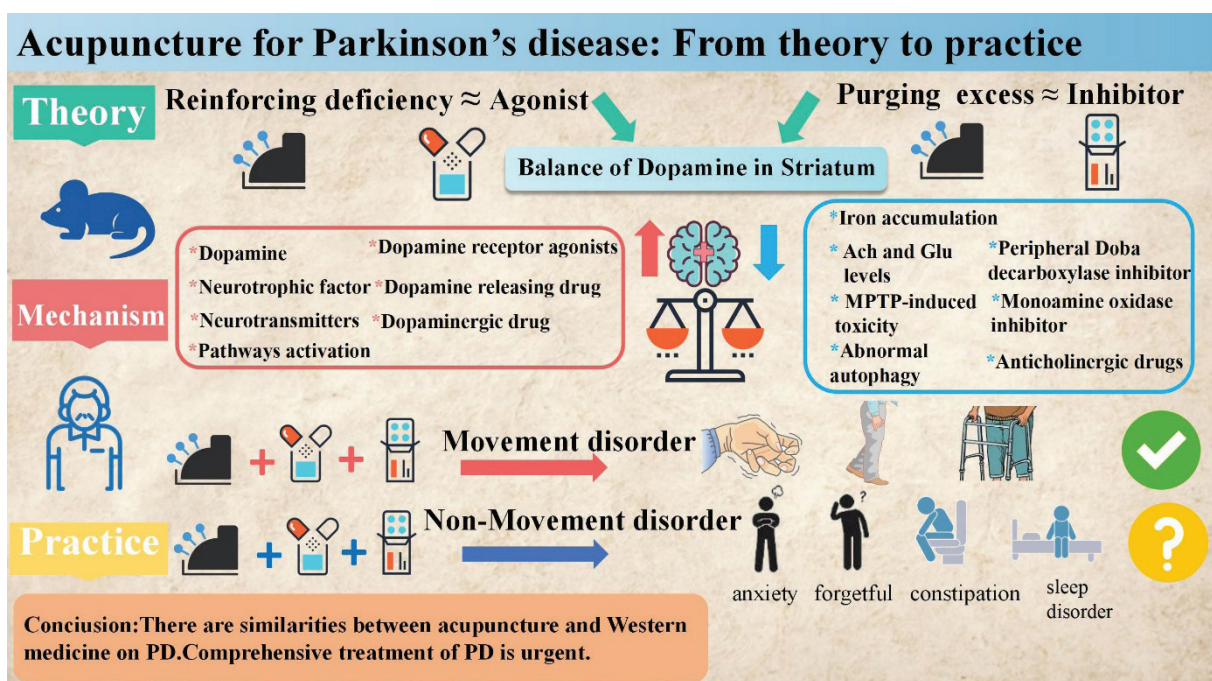
Advances in molecular biology and biochemistry have improved the treatment of Parkinson's disease (PD). There has been extensive evidence on the benefit of standard treatment (e.g., deep brain stimulation, levodopa, and dopamine agonists) and acupuncture for PD.

Objectives: This presentation aims to distill the similarities and differences in the treatment concepts between Chinese and

Western medicine from the perspective of reinforcing the deficiency and purging the excess, summarize the latest evidence on the benefits of acupuncture for PD from theory to practice, and propose prospective treatment options for PD.

Scope: Application of alternative medicine in Parkinson's disease

Conclusion: Although the methods of Western medicine treatment and acupuncture



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treatment differ, the main treatment ideas overlap. DA receptor agonists and supplements are consistent with the reinforcing effect of acupuncture, and relevant inhibitors are consistent with the purging effect of acupuncture. However, the theory of deficiency and excess is not completely equivalent to the pathological study of PD. The pathogenesis of PD is heterogeneous, involving many pathways and pathological products, and the cross

talk between them is not clear. Therefore, summarizing the pathogenesis of PD from deficiency and excess and the mechanism of acupuncture from reinforcing deficiency and purging excess will help to understand the heterogeneous pathogenesis and treatment principles of PD more vividly. It will also provide more ideas for the study of the mechanism of acupuncture in the treatment of PD.

Biography

Jingqi Fan is a doctoral student of Guangzhou University of traditional Chinese medicine. Main research direction is the pathogenesis of neurodegenerative diseases and the clinical efficacy of acupuncture.

A pragmatic approach to treat lung cancer through loading theaflavin-3,3'-digallate and epigallocatechin gallate in spanlastic

Syed Saif Imam and Smriti Agarwal

HIMT College of Pharmacy, India

When compared to other cancers, lung cancer has the highest fatality rate. If given effectively, the anti-proliferative and antioxidant properties of epigallocatechin gallate (EGCG) and Theaflavin-3,3'-digallate (TF3) can play a crucial role in treatment. To improve the chemical stability and therapeutic potential of EGCG and TF3 in the respiratory tract, a spanlastic made up of Tween-80, Span-60, and cholesterol was produced. It encapsulates EGCG and TF3 inside its vesicular structure and delivers it to cancer cells precisely. The cholesterol layer will allow for more efficient penetration, while tween-80 and span-60 will aid in deformability and lower interfacial tension, resulting in a small Z-average diameter, allowing for effective penetration between cell layers. The APIs'

stability at alkaline pH (7.6) is ensured by the nano-vesicular structure, which also boosts cellular antioxidant activity and APIs' Ferric lowering antioxidant capabilities. Spanlastic has several advantages, including improved encapsulation efficiency and safe consideration by MTT testing. The lung cancer cell loses the ability of apoptosis, which can be restored using a nano-vesicular system containing EGCG and TF3, as well as the activation of several other properties such as cell arrest, activation of miR-210, suppression of cyclin D1, and inhibition of MAPK, ERK, and JAK-STAT at their maximum potential. In addition, a new type of spacer and pMDI canister has been designed to improve drug stability and delivery efficiency.



Biological studies with phytochemical analysis of *Cornus mas* unripe fruits

C.V. Karakousi, S. Moussouni, P. Tsatalas, D. Lazari and E. Kokkalou

Aristotle University of Thessaloniki, Greece

C*ornus* fruits are widely known for possessing anticancer, anti-inflammatory, antioxidant, anti-microbial and hypoglycemic effects.

The aim of the study was the detection and isolation of biosynthetic precursors of compounds found in the unripe fruits and the assessment of the antioxidant activity and the ALR2/ALR1 inhibitory activity of their extracts.

The LC-DAD-MS (ESI+) analysis revealed the presence of 3-ferulic-3'-ellagic-difuranoside, scandoside methyl ester, and swertiamarin in the Et₂O fraction, and *cornuside* II in the EtOAc fraction. All compounds were found for the first

time in *C. mas* L. Our investigation of the Et₂O and EtOAc fractions resulted in the isolation of *trans*-ferulic acid, gallic acid, methyl gallate, protocatechuic acid, methyl caffeate, *trans*-p-coumaric acid, caffeic acid, quercetin 3-O-β-D-glucuronide-6''-methyl ester, 1,2,3,6-tetra-O-galloyl-β-D-glucose, dimethylmalate, quercetin 3-O-β-D-glucuronide, 1,2,3-tri-O-galloyl-β-D-glucose, 1,2,6-tri-O-galloyl-β-D-glucose, 1,2,3,4,6-penta-O-galloyl-β-D-glucose, and 1,2,4,6-tetra-O-galloyl-β-D-glucose.

EtOAc extract exhibited the highest scavenging activity determined as EC₅₀ = 0.35 ± 0.01 with the DPPH• assay due to presence

Antioxidant Activities of *Cornus mas* L. unripe fruits

Fraction	DPPH ^{a1} (EC ₅₀ ± SD, µg/mL) ^{a1*}	DPPH ^{a2} (AE ± SD) ^b	Co(II)/EDTA-LCL (IC ₅₀ ± SD, µg/mL) ^{a2*}	Co(II)/EDTA-LCL (AE ± SD) ^b
MeOH	0.43 ± 0.05	2.32 ± 0.26	1.05 ± 0.05	0.95 ± 0.03
Et ₂ O	0.38 ± 0.01	2.60 ± 0.12	0.13 ± 0.01	7.60 ± 0.32
EtOAc	0.35 ± 0.01	2.89 ± 0.06	0.36 ± 0.01	2.75 ± 0.10
BuOH	1.78 ± 0.37	0.59 ± 0.15	1.93 ± 0.37	0.52 ± 0.05
H ₂ O	20.06 ± 7.82	0.05 ± 0.03	10.52 ± 7.82	0.09 ± 0.002

^{a1} Efficient concentration (mg antioxidant/mg DPPH): amount of antioxidant required for the decrease in the initial concentration of DPPH• by 50%; ^b (AE) antiradical efficiency: 1/EC₅₀ standards: Trolox_{AE} = 1.24, quercetin_{AE} = 14.5, and ascorbic acid_{AE} = 8.0;

^{a2} inhibitory concentration: amount of antioxidant needed to reduce 50% of the initial CL emission during the catalyzed oxidation of luminol. *Values represent means of triplicate determination (n = 3) ±SD standards trolox_{AE} = 0.1, quercetin_{AE} = 1.12, and ascorbic acid_{AE} = 0.04.

Table 1: Antioxidant Activities of *Cornus mas* L. unripe fruits

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of gallotannins while the Et₂O had strong antioxidant activity with an IC₅₀ = 0.13 ± 0.01 with the chemiluminescence assay.

Et₂O fraction is a potent ALR1 inhibitor with 90 ± 0.53, whereas EtOAc fraction is a potent ALR2 inhibitor with 91.81 ± 1.78 90% .Ellagic acid is known for its exceptionally high ALR2 inhibitory activity, gallotannins and quercetin are potent ARIs inhibitors as well.

The fruits were exhaustively extracted with solvents of increasing polarity from PE to MeOH. Isolation of compounds was achieved

by means of CC and HPLC. All fractions/ extracts were tested for their antioxidant activity (DPPH, chemiluminescence), ALR2/ ALR1 inhibitory activity. LC-DAD-MS (ESI+) analysis, 1H-NMR and 13C-NMR spectroscopy were utilized for the structural elucidation.

The present work demonstrates the nutritional value of the *Cornus mas* unripe fruits as an antioxidant but also as a deterrent to the onset of secondary complications of diabetes II that could lead to the exploitation for nutritional pharmaceutical purposes.

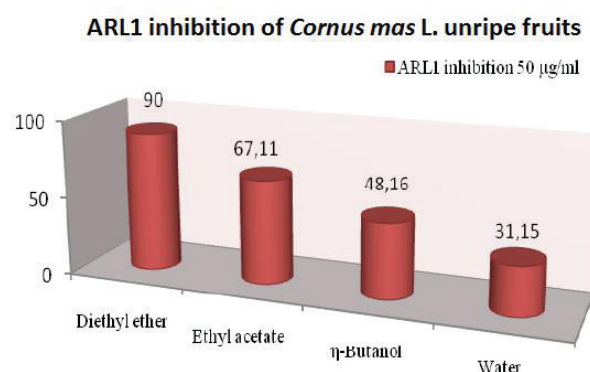
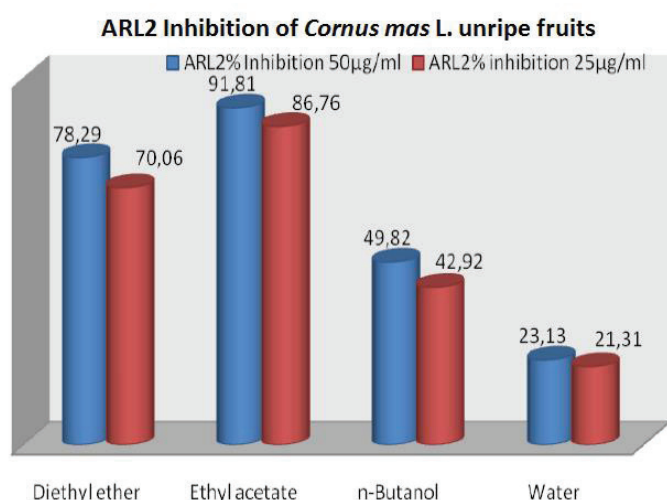


Figure 1: ALR2/ALR1 inhibitory Activity

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A proprietary fermented wheat germ extract in cancer and autoimmune clinical studies-A new paradigm

M. Hidvegi

Jewish Theological Seminary – University of Jewish Studies, Hungary

Avemar is a proprietary fermented wheat germ extract with anticancer properties — a complex mixture of thousands of molecules. Most of them are chemically unidentified, yet present in constant ratios and quantities from batch to batch; standardized to methoxy-substituted benzoquinone markers, i.e. 2,6-Dimethoxy-p-benzoquinone and 2-Methoxy-benzoquinone, which are the oxidation products of the corresponding hydroquinones.

The benzoquinones are locked in raw wheat germ as glycosides and, during fermentation, the fermenting organism, *Saccharomyces cerevisiae* unlocks them as aglycones by the action of glycosidases.

In animal experiments and *in vitro* cell lines, Avemar has shown significant anticancer, immunomodulatory, and anti-inflammatory properties. In addition, its active compounds impair the functional manifestation of the malignant metabolic phenotype, such as the Warburg effect, the pentose-phosphate-pathway, ribonucleotide reductase, and poly-(ADP)-ribose-polymerase, and repair the operation of the transformed mitochondria in neoplastic tissues.

The proprietary wheat germ extract has a firmly established safety profile and has gained a self-affirmed Generally Recognized As Safe (GRAS) status. Manufactured in a GMP pharmaceutical plant in Kunfeherto, Hungary, and distributed as a nonprescription dietary supplement worldwide; in some countries of the European Union, Avemar is a dietary FSMP—Food for Special Medical Purposes—for cancer patients.

Eleven open-label clinical studies have verified Avemar's benefits on cancer, mostly in combination with standard oncology treatments. The clinical oncology studies include colorectal, lung, breast cancers, cancers of the oral cavity, hematology-oncological cancers, advanced melanoma, head-and-neck cancer, refractory prostate cancer, and a matched-pair study in children with solid tumors.

Two clinical studies verified Avemar's benefits in treating autoimmune diseases, a non-randomized study in refractory rheumatoid arthritis and a double-blind, randomized study in lupus (SLE) patients.

This lecture presents the results of the clinical trials with Avemar.

Biography

Prof (Hon). Mate Hidvegi, PhD (b. 1955) is a visionary Hungarian biochemist, and food scientist. Inventor of over twenty herbal supplements and patented compounds, he is best known as the originator of Avemar, the original fermented wheat germ extract. Awarded the President's Gold Medal in Hungary, his mission is to help the lives of those touched by cancer. He lives in Budapest.



Genome sequence analysis of SARS-COV-2 isolated from a covid 19 patient in Erbil, Iraq

**Hazha Jamal Hidayat⁵, Bashdar Mahmud Hussen¹,
 Dana Khdr Sabir², Yasin Karim³ and
 Karzan Khawaraham Karim⁴**

¹Hawler Medical University, Iraq

²University Charmo, Iraq

³Hawler Medical University, Iraq

⁴The American University of Kurdistan, Iraq

⁵Salahaddin University, Iraq

In the city of Wuhan, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first recognized among humans at the end of December 2019, and has since spread to every country around the world. The emergence of this new coronavirus has attracted global attention to work towards finding a treatment and developing an effective vaccine against the virus. In this study, we sequence a full genome of SARS-CoV-2 isolated from a male patient in the city of Erbil, Iraq. The virus was sequenced using Sanger sequencer and 21 distinct mutations were found in our isolate compared to the full genome sequence of the SARS-CoV-2 isolated

from the city of Wuhan/China (Accession number: NC_045512.2). Sequence analysis showed that four of the mutations were located at the spike glycoprotein (S), and ten of them were in non-structural proteins (nsp1, nsp3, nsp12, and orf3a), which had been shown to be related to structural changes at various sites. Moreover, phylogenetic analysis and transmission supported the conclusion that the cases in Iraq were of independent origins of infections and had a close relation to the isolates from Iran. This is the first report on the DNA sequence of the SARS-CoV-2 genome isolated from the Kurdistan region of Iraq.

Prospects of photodynamic inactivation of tracheobronchial tree pathogenic microbiota using methylene blue

I. Tiganova

Gamaleya National Research Center of Epidemiology and Microbiology, Russia

The treatment of patients after mechanical ventilation of lungs, suffering from a multi-species infection of the tracheobronchial tree became complicated rapidly in recent years. The situation is aggravated in patients with post intubation tracheal stenosis, where infection plays a leading pathogenetic role in damage to the tracheal wall resulting in infected tracheal stenosis (ITS). The aim of this work was to study *in vitro* the possibility of photodynamic inactivation of pathogenic microbiota, typical for patients with ITS, using methylene blue (MB) as a photosensitizer (PS). Gram-positive (*Staphylococcus aureus*, *Corynebacterium propinquum*, *Corynebacterium striatum*, *Enterococcus faecalis*) and Gram-negative (*Pseudomonas aeruginosa*, *Proteus mirabilis*, *Klebsiella pneumoniae*, *Stenotrophomonas maltophilia*) bacteria, multi- and pan-resistant to antibacterial drugs, in combinations of up to 4 microorganisms in one patient, were found. Minimal bactericidal concentration of

MB was evaluated for 13 isolates of 8 species of bacteria from 9 patients. Incubation of bacteria with 30 μ M MB for 15 min and irradiation with LED at a dose of 25 J/cm² allow to completely inactivate bacteria found in the tracheobronchial secretions of patients with ITS, including *Pseudomonas aeruginosa*, the most resistant to photodynamic inactivation. Analysis of absorption and fluorescence spectra revealed, that in these ranges, aggregation and photo-bleaching of methylene blue is negligible and PS retains its optic-physical properties and provides effective inactivation of isolated Gram-positive and Gram-negative bacteria, including multi- and pan-resistant to antibacterial drugs. MB can be delivered via nebulizing and medical lasers with fiber-optic means for delivering light radiation, with specially shaped diffusers, can provide the irradiation, required for photodynamic therapy inside the tracheobronchial area for treatment and disinfection.

Biography

I.G. Tiganova was graduated from Biology, she is faculty, M.V. Lomonosov Moscow State University and till now works at Gamaleya National Research Center of Epidemiology and Microbiology, Moscow, Russia. The field of interests was repair, mutagenesis and SOS- response. PhD from 1992, from 2018 leading researcher. From 2012 the subject of the studies is antimicrobial photodynamics.



Anti-PEG IgE in anaphylaxis associated with polyethylene glycol

Zhao-Hua Zhou¹, Cosby A. Stone², Baruch Jakubovic³, Elizabeth J. Phillips², Gordon Sussman⁴, JuMe Park¹, Uyen Hoang¹, Susan L Kirshner¹, Robert Levin⁵ and Steven Kozlowski¹

¹Food and Drug Administration, USA

²Vanderbilt University Medical Center, USA

³Sunnybrook Health Sciences Centre, Canada

⁴University of Toronto, Canada

⁵Food and Drug Administration, USA

Polyethylene glycol (PEG) with its unique properties, including solubility in water and non-polar solvents, has been used in many medical and pharmaceutical products including LNP/mRNA COVID vaccines as an active ingredient or excipient.

Despite the success of these products, acute drug allergic reactions associated with PEG have been observed in both clinical trials and practice, with many cases occurring without a known prior PEG exposure. Many cases of PEG associated anaphylaxis may not be recognized, especially for products where PEG is not identified as an active ingredient.

Although skin testing suggested a potential IgE-mediated type 1 hypersensitivity reaction in some cases, a reliable lab assay to sensitively detect specific anti-PEG IgE was not available to evaluate these events. Studies with ELISA-based anti-PEG assays have reported high background and lack of specificity and thus,

could only detect higher levels of IgG and IgM.

To fill this important gap in assessing the increasing risks associated with the use of PEG and PEGylated drugs, we developed a dual cytometric beads assay (DCBA, with built-in specificity control) for the detection of anti-PEG antibodies, with a 100-fold greater sensitivity than conventional assays. This increased assay sensitivity allows for reliable detection of anti-PEG IgE. This assay was used to test samples from patients who had developed clinical anaphylaxis upon PEG exposure (cases) and those who did not (controls). The DCBA method and results enabled us to first confirm the long-considered hypothesis that PEG-associated acute allergy can be due to IgE-mediated type 1 hypersensitivity. We also demonstrated pre-existing antibodies to PEG in normal sera that can explain allergic responses on apparently initial exposures.



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Biography

Zhaohua (Joe) Zhou, Ph.D., is a Research/Reviewer Scientist at the Office of Biotechnology Products, CDER, US Food & Drug Administration. Dr. Zhou's research interest is in the development of lab models to pinpoint and predict drug-induced acute allergic reactions. These methods are based upon and covering current understanding to the mechanisms of a clinical anaphylaxis, including: 1) Drug-specific IgE screening and *in vitro* Type 1 sensitization model (drug-binding antibodies and mast cell degranulation); 2) Drug-specific IgG/IgM screening followed by complement- activation through classical and non-classical pathway-generated anaphylatoxins assay (C3a, C4a and C5a); 3) mast cell directly degranulation; 4) cytokine storm assay (activated T cells and macrophages using PBMC or whole blood culture); and 5) contact system (kinin/kallikrein) activation assay. These models, when using comprehensively, can quickly rule in and rule out drug quality related causes as well as predict patient sensitivity to particular therapeutics.



A novel, safe, effective treatment for opioid use disorder

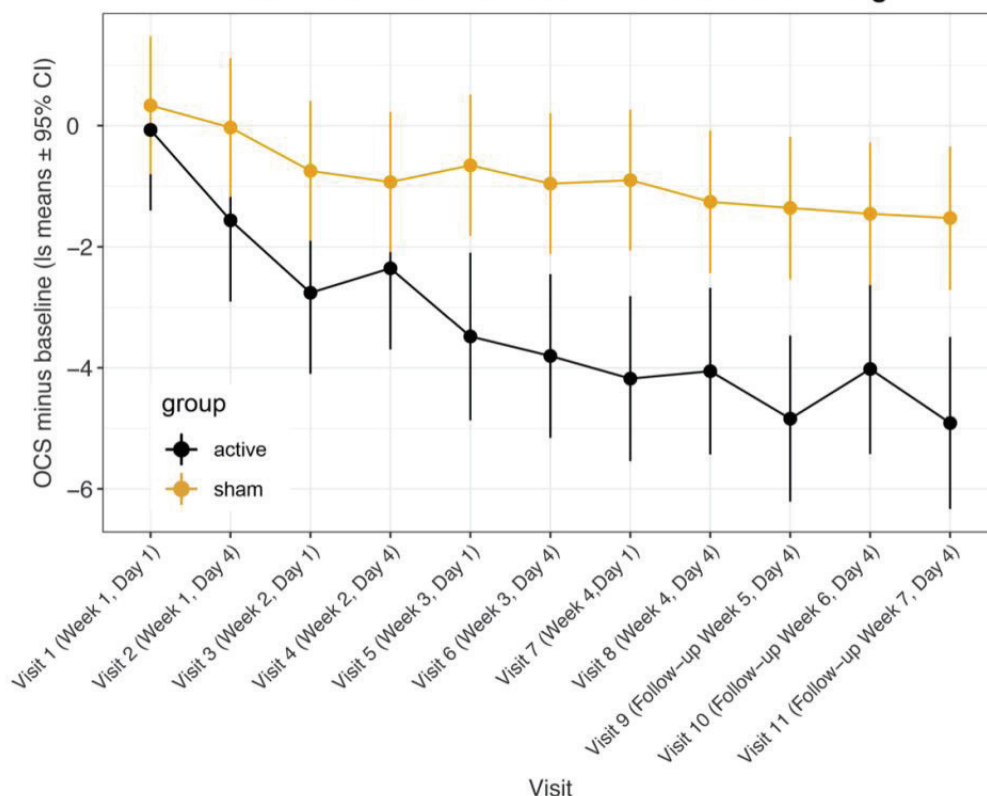
F. Schiffer

McLean Hospital and the Harvard Medical School, USA

Schiffer has proposed and tested and published his novel hypothesis about the relation between the cerebral hemispheres and psychopathology. His ideas come out of his clinical observations and the split-brain studies and are combined in what he has termed dual-brain psychology (DBP), which posits that one brain hemisphere, left or right, as a trait in an individual is more

affected by early complex traumas and he has found in his clinical practice and in two published randomized control trials that activating the healthier hemisphere with unilateral transcranial photobiomodulation (UtPBM), near infrared mode has been highly successful in treating a range of psychiatric disorders including opioid use disorder. Here we will focus on the latest NIH funded trial

Effects of Active versus Sham Treatment on Craving





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in which we sought to treat 39 participants mostly from CraigsList.com who reported significant opioid cravings. 19 participants were treated with an active LED and 20 with a sham, which used the identical device with foil over the LED. The study was conducted and 2 sites, both of which reported similar results. The participants were treated twice a week for 4 weeks with 3 weekly follow-ups. The results as shown in Figure 1. showed that from baseline to the 3rd follow up there was a highly significant better improvement in the active group versus the sham and at the end of treatment and at the 3rd follow-up with an effect size was 1.5. At the McLean site

there was also a very significant decrease in opioid use in the active group but not sham. In Schiffer's private practice he combines this UtPBM treatment with psychotherapy based on DBP, but in this control study, participants received only a twice weekly UtPBM treatment or sham. We feel the study show that UtPBM can be used as a stand-alone treatment or in combination with buprenorphine. From private practice, we feel it is greatly augmented when combined with dual-brain psychotherapy and we feel that this randomized control trial supports the novel hypotheses of DBP from which the UtPBM evolved. There were no adverse reactions observed or reported.

Biography

Fredric Schiffer, MD, is a research associate at McLean and an assistant professor of psychiatry, part-time, at Harvard Medical School. He has been studying the relationship between past traumas, cerebral laterality, and depression, anxiety, and addiction and has developed a hypothesis on the physical nature of conscious experience and its relation to the brain and to psychological function. Dr. Schiffer also studies the role that near infrared light directed through the forehead to the brain may play as a treatment for psychological problems, including opioid use disorders. He maintains a private practice of adult psychiatry in Newton, Massachusetts and is the Founder and CEO of MindLight, LLC and the Dual-Brain Psychology Institute.



Computational modelling of chromatin accessibility identified important epigenomic regulators

Yanding Zhao and Chao Cheng

Baylor College of Medicine, USA

Chromatin accessibility is essential for transcriptional activation of genomic regions. It is well established that transcription factors (TFs) and histone modifications (HMs) play critical roles in chromatin accessibility regulation. However, there is a lack of studies that quantify these relationships. Here we constructed a two-layer model to predict chromatin accessibility by integrating DNA sequence, TF binding, and HM signals. By applying the model to two human cell lines (GM12878 and HepG2), we found that DNA sequences had limited power for accessibility prediction, while both TF binding and HM signals predicted chromatin accessibility with high accuracy. According

to the HM model, HM features determined chromatin accessibility in a cell line shared manner, with the prediction power attributing to five core HM types. Results from the TF model indicated that chromatin accessibility was determined by a subset of informative TFs including both cell line-specific and generic TFs. The combined model of both TF and HM signals did not further improve the prediction accuracy, indicating that they provide redundant information in terms of chromatin accessibility prediction. The TFs and HM models can also distinguish the chromatin accessibility of proximal versus distal transcription start sites with high accuracy.

Biography

Yanding Zhao is a computational biologist with a focus on cancer genomics and epigenomics. He is currently a post doctoral fellow studying cancer epigenomics in Dr.Howard Y.Chang's and Dr.Christina Curtis' labs at Stanford University. His research includes four main areas: (1)developing computational frame works to characterize the function of tumor driving genemutants; (2)decomposition of tumor micro environment using machine-learning based algorithm; (3)computational modelling of epigenomic changes to illustrate the regulatory mechanism of chromatin remodeler; (4) single cell omics for understanding cell type specific regulatory program.



Soluble Guanylate Cyclase (sGC) as a therapeutic target for diabetic nephropathy

**Gayathri Swaminath, Lufei Hu, Yinhong Chen,
Xiaoyan Zhou, Maarten Hoek, Jason Cox, Ken Lin,
Yang Liu, Wendy Blumenschein and Jeff Grein**
Greenfire Bio, USA

Diabetic nephropathy (DN) is the most common cause of end-stage renal disease (ESRD) and is characterized by a progressive decline in renal function accompanied by mesangial expansion, glomerular basement membrane thickening, and tubulointerstitial damage. Current treatments include glycemic and blood pressure control to delay the progression. Novel drugs including SGLT2i inhibitors, GLP-agonists, and mineralocorticoid receptor antagonists are reported to be effective in treating the disease. Furthermore, endothelial dysfunction is the leading cause for the progression of DN. The nitric oxide-soluble guanylate cyclase-cyclic guanosinemonophosphate (NO-sGC-cGMP) signaling cascade pathway plays a critical role in regulating renal function. Cyclic guanosine monophosphate (cGMP) vasodilates renal vasculature and directly influences renal blood flow, renin secretion, glomerular function, and tubular exchange. We hypothesized that the sGC

stimulator Compound 1 is protective against DN at stages in which NO bioavailability is low or diminished. The effects of renal function were investigated with an sGC stimulator under acute & chronic treatment in a preclinical DN model. The chronic treatment of sGC stimulator alone reduced kidney hypertrophy, significantly slowed the progression of proteinuria, and reduced urinary albumin and creatinine ratio. In combination with Enalapril, the sGC stimulator significantly decreased the incidence of glomerulosclerosis lesions, as observed by the reduction in interstitial fibrosis and in the tubules, interstitial, and glomeruli nephropathy score. Our data strongly suggests that sGC stimulator improves renal function as a monotherapy & exhibits greater benefit in attenuating the progression of the disease with standard of care drug Enalapril, underpinning the importance of the NO-sGC-cGMP pathway in the pathogenesis of DN.

Biography

Gayathri has over 17 years of drug discovery and drug development experience from early hit to late stage in areas of diabetes, oncology, cardiovascular, fibrosis, inflammation, pulmonary hypertension, and renal diseases. Progressed molecules to FIH including Verquvo for chronic heart failure. Gayathri has held several leadership roles in discovery, preclinical, and clinical development programs at Amgen & Merck. Currently she is working as a Vice President for research and business development at Greenfire Bio. She has co-authored over 30 publications in peer-reviewed journals and holds several patents. Gayathri completed her Ph.D. in Biochemistry from the University of Hyderabad, India, postdoctoral training with Dr. Brian Kobilka (Nobel Laureate) at Stanford University and has an MBA from Cornell University.

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One platform endless pipelines: CAR-NK cells from engineered pluripotent stem cells using 3-D platform technology

Shi-Jiang (John) Lu

HebeCell Corporation, USA

Clinical success of adoptive cell therapy with chimeric antigen receptor (CAR) T cells for treating hematological malignancies has revolutionized the field of cellular immunotherapy. However, critical to the success of CAR-engineered immune effector cell therapies will be the industrialization---converting the technologies into universal and cost-effective therapies for a large number of patients. Autologous CAR-T cell therapy faces two major obstacles: cell availability and high manufacturing cost, which makes it difficult for most patients. Donor-based CAR-T cells circumvent some of the above challenges, but still face the problem of graft versus host disease caused by allogeneic T cells. Natural killer (NK) cell is a specialized immune effector cell type that recognizes and kills targets without human leukocyte antigen (HLA) restriction and prior sensitization. CAR-NK cells do not cause graft versus host

disease (GvHD) and can be obtained from unrelated donors as well as pluripotent stem cells (PSC), representing an ideal off-the-shelf therapeutics for all patients. HebeCell has developed a robust proprietary scalable 3D-platform technology for PSC expansion and feeder-free NK cell differentiation with superior scalability and consistency compared to traditional approaches. As gene editing and CAR-engineering can be performed in PSCs, the establishment of master PSC-CAR cell bank targeting indication-specific antigens will provide inexhaustible cell sources for the manufacture of truly off-the-shelf and cost-effective CAR-NK cells for all patients of cancer, infectious and autoimmune diseases. The establishment of our proprietary 3D PSC-CAR-NK platform allows scalable, reproducible and efficient production of homogenous functional CAR-NK cells, which can be rapidly deployed worldwide for all patients.

Biography

Shi-Jiang (John) Lu, PhD, MPH, is currently the President and CEO of HebeCell Corporation, focusing on the development and clinical translation of regenerative medicine and cell therapy technologies, especially iPS-CAR-NK cells for the treatment of cancer, autoimmune and viral infectious diseases. Before establishing HebeCell, he was the Senior Director of Research at Advanced Cell Technology/Ocata Therapeutics, which was acquired by Astellas Pharma in 2016. John is an expert in stem cell biology and regenerative medicine with 20 years of experiences. He has been conducting translational research and discovery of novel therapeutic strategies utilizing human pluripotent stem cells (PSC) and their derivatives. The goal of his research is to generate human PSC-derived products for the treatment of human diseases. He also has extensive experience in process development and large-scale production of human PSC derivatives under defined conditions for clinical trials. John is the inventor of more than 20 patents in stem cell field: in an analysis of global stem cell patent landscape by Nature Biotechnology in 2014, John's patent application and citation ranked No. 7 and No. 5, respectively. In addition to stem cell research, Dr. Lu also has more than 10 years of experiences in cancer research. John received his BS degree in Biochemistry from Wuhan University, MSc degree in Oncology/Pathophysiology from Peking Union Medical College, MPH degree in Molecular Toxicology/Environmental Sciences from Columbia University and PhD degree in Molecular Cancer Biology from University of Toronto.



Impact of teleconsultation on patients with type 2 diabetes in the Brazilian public health system: Protocol for a randomized controlled trial

Daniela Laranja Gomes Rodrigues¹, Gisele Silvestre Belber¹,
 Frederica Valle De Queiroz Padilha¹, Ligia Fonseca Spinel²,
 Frederico Rafael Moreira³, Marcos Aurélio Maeyama⁴,
 Ana Paula Neves Marques Pinho² and Álvaro Avezum Júnior³

¹Hospital Alemão Oswaldo Cruz, Brazil

²Social Responsibility Centre, Hospital Alemão Oswaldo Cruz, Brazil.

³Innovation, Research and Education Institute, Hospital Alemão Oswaldo Cruz, Brazil

⁴Telehealth Center, Brazil

Background: Although the Brazilian Unified Health System (SUS) offers universal health coverage, access to quality care is often limited by social inequality and location. Although telemedicine has been shown to be an important tool in the efforts to overcome this problem, because it can provide access to specialist care and break the geographical barriers to health care, there are no national studies demonstrating its use in public health.

Objective: This study aims to test the hypothesis that remote consultation can be as effective as standard face-to-face consultation for type 2 diabetes mellitus in the Brazilian public health system and to assess the associated costs related to teleconsultation in public health scenarios, for patients referred from Primary Health Care units of the SUS for specialist care.

Methods: This is a pragmatic, phase 2, unicentric, open-label, noninferiority, blinded allocation, data-blinded, centrally randomized clinical trial. The inclusion criteria will be adults, both sexes, ≥ 18 years old, glycated hemoglobin (HbA1c) $\geq 8\%$. Outcomes will be

evaluated by assessing symptoms, laboratory exams, anthropometric measurements, blood pressure, adverse events, and satisfaction level for 6 months. The costs of the teleconsultation will be assessed using the time-driven activity-based costing (TDABC) method to compare the costs with the face-to-face consultations. The noninferiority margin was set at 0.5%. Assuming an SD of 1.3% for both groups, true difference between the means of zero, and a type I error level of 5% (one-sided), it was estimated that 117 individuals per group would be necessary to achieve 90% power. Statistical analysis of the efficacy will be done using intention-to-treat and per-protocol approaches.

Results: The results from this trial will be reported according to the CONSORT guidelines. The trial was approved by the institutional review board on October 5, 2019. Data collection started in January 2019 and is expected to finish in 2022. At the time of manuscript submission, 18 participants were recruited.

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Conclusions: Our expectations are that providing remote access to health care will result in improvements in the health and quality of life of patients with type 2 diabetes and reduce costs and that both patients and clinicians will benefit from and be satisfied with this technology.

Biography

Daniela Laranja Gomes Rodrigues, graduated in Medicine at the Federal University of Espírito Santo (2000), residency in Neurology at the State University Júlio de Mesquita Filho - UNESP (2005) and post-graduated in Vascular Neurology and Neurosonology at the Federal University of São Paulo (2007). as preceptor of the Neurology Residency at Hospital Santa Marcelina - Itaquera and as on duty at the HAOC Telemedicine Project until 2015, when the project ended. She is currently a volunteer doctor in the Vascular Neurology and Neurosonology sector at the Federal University of São Paulo and works in Social Responsibility at Hospital Alemão Oswaldo Cruz, as neurologist, research coordinator and involved in projects aimed at the SUS and telehealth. Has experience in Neurology, acting on the following subjects: cerebrovascular diseases, telemedicine and Transcranial Doppler.

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Effect of blue and red led on inflammatory acne: Controlled and randomized clinical trial

F. Mara Lúcia Gonçalves Diogo and Lara Jansiski Motta
Universidade Nove de Julho (UNINOVE), Brazil

Inflammatory acne is the leading cause of visits to dermatologists offices. Topical products such as retinoids are used to treat acne, but they have cutaneous side effects. Acne usually improves after exposure to sunlight or artificially produced sunlight. The purpose of this research is to compare the effect of combined blue/violet, red and blue and red LED lights on grade II and III inflammatory acne. We will recruit 144 participants, aged between 12 and 25 years, with a Fitzpatrick rating scale from I to IV, with mild to moderate inflammatory acne and will be randomized into 4 groups: G1: mask with blue LED 415 nm

(± 20); G2 : mask with red LED 660 nm (± 20); G3: mask with combined red and blue LEDs (415 nm and 660 nm) and G4 - Control - Peeling with 20% salicylic acid once every 15 days. The evaluations will be carried out on the first, fifteenth and thirtieth day of treatment, verifying the reduction of erythema and skin appearance and the degree of oiliness through clinical evaluation. Descriptive analysis will be performed for all variables and data, presented as absolute number, mean and standard deviation (SD). The p-values after the Wilcoxon classification test will also be calculated for statistical significance.

Biography

Mara Lúcia Gonçalves Diogo is Graduated in Nursing from the Nursing School Wenceslau Braz (1986). Postgraduate in Occupational Nursing from the Catholic University of Santos (1989), title of Specialist in Dermatology by the Brazilian Association of Nursing in Dermatology - SOBENDE (2007). He is currently a freelance professional, working in a private practice. Experience in Nursing, with emphasis on Nursing in Dermatology and aesthetics. Invited professor in specialization courses in Dermatology throughout Brazil, done in person or through online classes. Master's and PhD student in Biophotonics at Universidade Nove de Julho, São Paulo.

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Bobath in Brazil: What is the best study design for intervention for children with cerebral palsy?

Claudia R M Alcantara De Torre

Centro de Apoio Terapeutico – Physiotherapy, Brazil

Brazil is a very heterogeneous country in terms of health services, not only in its remote regions but also in the larger cities. We have physiotherapy centres throughout Brazil that offer specialized assistance for individuals with cerebral palsy (CP), but there are not nearly enough. Particularly in rural areas, there are good quality services staffed with professionals dedicated to improving their skills but perhaps with not as much up-to-date equipment. Of course there are universities throughout Brazil offering courses in physiotherapy. As a physiotherapist and Bobath instructor teaching in several of these institutions, I always emphasize the importance of evidence and good research practice (e.g., using measurable functional tasks before and after intervention, including videos recording and standardized tests), not only for publishing papers but also to ensure that such specialized treatment works. It is important that studies published in English are also published in the native language from where they take place. This enables greater dissemination of crucial knowledge within these particular communities. A good example is the paper by Furtado et al. (and this commentary) also written in Portuguese.¹ This review made us aware of the current state of research in

Brazil and also points the way for new studies. According to the International Classification of Functioning, Disability and Health (ICF), participation is as important as body functions and structure. The ICF clearly shows the reciprocal nature of all these components. Most of the good therapeutic work done in Brazil is by Bobath trained therapists, but such practice has also been criticized based on published research, in part due to problems with definitions and study designs.² Conducting a clinical randomized controlled trial for children and adolescents with CP can be very difficult. This is because of the many differences in locality and time of lesion, motor disorders, associated impairments, previous treatment, and family-related issues. These and other factors can make a homogeneous group almost impossible. So, which is the best study design for CP? Each child with CP is unique, with different desires and environments. How is best to respect the goals of the child and the family?³ Even though the studies in Furtado et al.'s scoping review did not include the goal-directed practice of real-life tasks, child self-active movements, participation, and family engagement in therapeutic planning are all used today in neurodevelopmental therapy (NDT) in Brazil.⁴ But it is difficult to affirm that

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all physiotherapists trained in Bobath/ NDT have incorporated these changes into their practice. An update of the NDT/Bobath includes individualized therapeutic handling based on movement analysis and the therapist uses the ICF model in a problem-solving approach to assess activity and participation. The principles of the Contemporary Bobath Concept⁵ have also recently been updated and clarified. They highlight the practice and transference of daily life skills and include measurable goals. Online therapies (tele rehabilitation) may provide many benefits, but the presence of the child

or individual with CP and the physiotherapist is still necessary for proper assessment and intervention. This interaction can never be replaced by a remote procedure, while we also must remember that parents cannot be called on to act as therapists. It is not only experimental evidence which should be considered, but also the scientific knowledge that forms the basis for any intervention. We hope in the future physiotherapists in Brazil and all over the world will produce such evidence with study designs that truly move CP research forward.

Device and non-device-guided slow breathing to reduce blood pressure in hypertensive patients: A systematic review and meta-analysis

Kamila Shelry de Freitas Gonçalves^{1,2,3} and Eugenia Velludo Veiga¹

¹University of São Paulo, Brazil

²University of Campinas, Brazil

³Universidade Paulista, Brazil

Objectives: What is the impact of prolonged use of device or non-device guided slow breathing compared to usual care, on the BP values of hypertensive patients?

Design: Systematic review and meta-analysis of randomized clinical trials.

Participants: Hypertensive patients, with or without comorbidity, over 18 years old, of both sexes, with or without hypertensive medication.

Intervention: The selected studies showed comparisons between groups that performed device-guided and/or non-device-guided slow breathing with control conditions.

Outcome measures: The primary outcome was the value of systolic blood pressure (SBP) and diastolic blood pressure (DBP) after the interventions. The secondary outcome was the reduction in the quantity/dosage of drugs administered to control hypertension.

Results: Twenty-two studies involving 17,214 participants were included in the quantitative analysis. Considerable heterogeneity was revealed between studies. Using random effect model, it was found that device-guided slow breathing did not significantly reduce SBP and DBP compared to usual care, both in terms BP values and in relation to their variations (SBP, MD -2.13 mmHg, [95% CI -12.71 to 8.44], 288 individuals; I² = 93%, high heterogeneity : DBP, MD -0.90, 95% CI -3.97 to 2.11, 288 individuals; I² = 63%, substantial heterogeneity . SBP variations MD - 2.42, 95% CI -7.24 to 2.40, 443 individuals; I² = 85% high heterogeneity / DBP variations MD -1.67, 95% CI -4.57 to 1.24, 443 individuals; I² = 80%, high heterogeneity).

Conclusion: Based on these results it appears that device-guided slow breathing did not reduce blood pressure in hypertensive patients. Registration: PROSPERO CRD42020147554.

Biography

Kamila Shelry de Freitas Gonçalves, Postdoctoral fellow at the University of São Paulo (USP- Ribeirão Preto). PhD in Health Sciences from UNICAMP (2015), she carries out her research activity at UNICAMP in the Blood Pressure Study and Research Group (GEPPA) and at USP in the Interdisciplinary Research Group on Hypertension (GIPHA). Master in Health Sciences from UNICAMP (2009) she is specialist in Physiotherapy applied to Orthopedics and Traumatology by UNICAMP (2005). She was graduated in Physiotherapy from Universidade Paulista (2004) and has experience in Hospital Physiotherapy (Cardiology, Pulmonology, Neurology, Orthopedics, Traumatology, Pediatrics, Neonatal ICU and Adult ICU). Professor of the Physiotherapy course at Universidade Paulista (since 2015) and Coordinator of the Lato Sensu Postgraduate course in Neurofunctional Rehabilitation at Universidade Paulista (since 2017).

WORKSHOP

DAY 2



Virtual Event

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CLINICAL R&T 2022

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BIOGRAPHY

Qin Zhang graduated from Tsinghua University, Beijing, China, with BS., MS. and Ph.D. Degrees in nuclear engineering in 1982, 1984 and 1989 respectively. He was a visiting scholar with University of Tennessee, Knoxville, TN, USA, and University of California, Los Angeles, CA, USA, from 1987 to 1989, working on system reliability engineering and intelligent fault diagnoses. He is now a professor of Institute of Nuclear and New Energy Technology and Department of Computer Science and Technology, Tsinghua

University, emeritus member of China Association for Science and Technology, member of International Nuclear Energy Academy, fellow of China Association for Artificial Intelligence (CAAI) and director of the specialized committee for uncertainty in AI of CAAI, consultant of the specialized committee for wise medical care of CAAI. He originally developed a new AI model called Dynamic Uncertain Causality Graph for fault diagnoses and disease diagnoses.

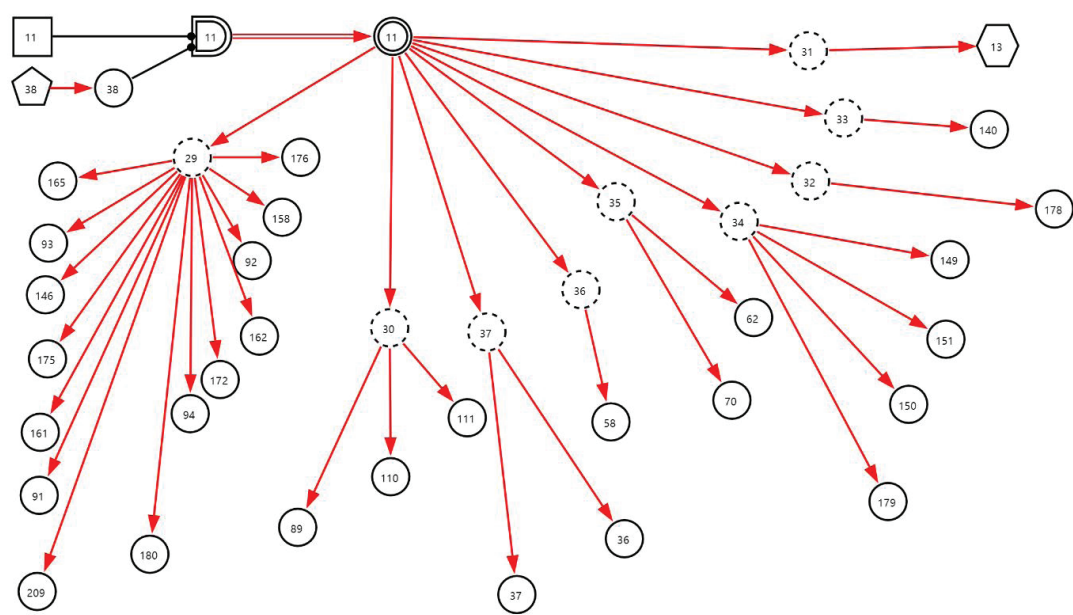
Q. Zhang

Tsinghua University, China

DUCG-aided general clinical diagnosis enabling primary clinicians to diagnose diseases like experts and know why: Real applications

DUCG(Dynamic Uncertain Causality Graph) is a new AI model to graphically represent domain uncertain causal knowledge and make probabilistic reasoning with natural interpretabilities. This presentation will show online how DUCG works to guide primary clinicians to make clinical diagnoses under 43 chief complaints covering more than 1000 diseases, including how to collect clinical information and make what medical checks, step by step according to the condition of a primary hospital or clinics. The 43 chief complaints include: dizzy, headache, nasal congestion, epistaxis, sore throat, jaundice, dysphagia, cyanosis, cough and expectoration, dyspnea, neck waist and back pain, hemoptysis, lymphadenopathy, chest pain, palpitation, hematemesis, arthralgia, abdominal pain, nausea and vomiting, numbness of limbs, edema, bloody stool, constipation, rash, fever, anemia, obesity, emaciation, child fever,

diarrhea, syncope, abdominal distention, related disease of department of gynecology (four chief complaints), lower urinary tract symptoms(including frequent urination, urgency, pain, dysuria, polyuria, gross hematuria and urinary leakage).In total, the differential diagnostic precision verified by third-parties for every chief complaint is more than 95%, in which the precision for every disease is no less than 80%. More than 200,000 real application cases were performed in Jiaozhou city and Zhongxian county, China. In which, only 8 diagnoses were incorrect due to the imperfectness in DUCG knowledge bases. After correcting DUCG knowledge bases, incorrect diagnoses were no long found. Statistics in the real world shows that DUCG can increase the ability of primary clinicians to diagnose diseases several times overthat without DUCG.





A subgraph within a DUCG for the chief complaint arthralgia

Symbol	Variable	<i>n</i>	Description
\boxed{n} and $\odot n$	B_n and BX_n	3	Lyme disease
		11	Polymyositis
$\odot n$	X_n	7	Erythema migrans
		12	ECG shows cardiac block
		16	Radiculopathy
		17	Experience of field travelling
		36	ESR
		37	CRP
		38	Sex
		40	Conjunctivitis
		58	ANA
		60	RF
		62	WBC
		70	HGB
		85	Skin rash
		89	Splenomegaly
		91	Arthralgia (acute or chronic)
		92	Arthralgia (large or small joint)
		93	Arthralgia (axis or peripheral)
		94	Arthralgia (self-limited or aggravating)
		95	CSF-WBC
		96	CSF-P
		99	CSF-PRO
		100	Abnormal ultrasonocardiography
		101	Headache
		102	Nausca

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*Descriptions of the
symbols in the figure*

		103	Vomit
		104	Mental disorders
		105	Facial palsy
		106	Meningeal irritation sign
		110	Lymphadenectasis
		111	Hepatomegaly
		140	Chest CT shows interstitial pneumonia
		144	Testis swelling
		145	Borrelia burgdorferi-IgG
		146	Fever
		147	Cerebellar ataxia
		149	AST or ALT
		150	TBIL
		151	DBIL
		158	Myalgia
		161	Dysphagia
		162	Myasthenia
		165	Facet joint of hand pathological change
		172	Arthralgia (quantity)
		175	Limbs proximal myasthenia
		176	Weight loss
		178	Electromyogram shows myogenic muscular atrophy
		179	CK
		180	Dyspnea
		209	Anorexia
	C_n	29	Symptom
		30	Sign
		31	Brucella culture
		32	Other imaging tests
		33	CT
		34	Blood biochemical test
		35	Anti-MCV antibody
		71	PLT
		72	CT shows sacroiliac joint injury
		73	ECG
		74	Ultrasonocardiography
		75	Rheumatic test
		76	Blood RT
		77	CSF RT
		78	CSF biochemical test
		79	Virus and infection related test
		80	Autoimmune antibody test
	SX_n	13	Muscle biopsy shows myositis

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BIOGRAPHY

The long-standing research Interest of Alberto Maringhini, M.D. is in biliary and pancreatic diseases. He started with a peculiar interest on portal hypertension and bleeding in cirrhotics and then in diagnosis of portal hypertension and hepatocellular carcinoma. Then he started his interest on gallbladder and pregnancy, acute pancreatitis diagnosis and prognosis, pancreatic cancer clinics and epidemiology. Chronic pancreatitis laboratory

diagnosis and clinical presentation. Finally, acute pancreatitis and pregnancy and breast feeding in prevention of post partum acute pancreatitis.

His clinical work in internal medicine and mainly in gastroenterology started in 1977 and nowadays he is direttore of internal medicine in the largest hospital in Sicily and in southern Italy after "Cidarelli Hospital" in Naples.

Alberto Maringhini

ARNAS Civico, Italy

Breastfeeding in prevention of postpartum acute pancreatitis (AP). A Sicilian population-based case-control study

Background: Gallstones acute pancreatitis has increased incidence in young women in the 2 years postpartum. Middle aged women with longer period of breastfeeding have less hospitalization for gallbladder disease.

Methods: We identified all sicilian women who delivered (2013-2016) and had acute pancreatitis within 2 years postpartum, reviewed their medical records and for each case we matched 4 women of the same age (+ 5 years), date (+ 30 days) and hospital of delivery without acute pancreatitis. Univariate and multivariate logistic regression was used to estimate the Odds Ratio (OR) to assess associations between acute pancreatitis and clinical variables.

Results: In the 74 women with AP and 298

controls at univariate analysis: > 6 months oral contraception history ($p < 0.01$ - OR 3.30 - 95% CI 1.33-8.16); previous biliary disease ($p < 0.001$ - OR 5.90 - 95% CI 1.98-17.57) and smoking ($p = 0.035$ - OR 2.04 - 95% CI 1.04-4.0) were predictors of acute pancreatitis; amenorrhea > 3 months ($p < 0.001$ - OR 0.34 - 95% CI 0.19-0.59) and breastfeeding > 3 months ($p < 0.001$ - OR 0.07 - 95% CI 0.03-0.14) were protective. At multivariate previous biliary disease ($p = 0.011$ - OR 5.49 - 95% CI 1.48-20.38) was predictor and breastfeeding > 3 months ($p < 0.001$ - OR 0.06 - 95% CI 0.03-0.14) was protective for acute pancreatitis.

Conclusions: Women without a history of biliary disorders and who breastfeed for at least 3 months have reduced risk to develop AP in the 2 years after delivery.

SCIENTIFIC ABSTRACTS

DAY 2



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Band-engineered laterally-oriented quasi-AlGaN barrier / GaN well, High-Electron-Mobility-Avalanche-Transit-Time (HEMATT) oscillator: Medical applications

Sulagna Chatterjee

Adamas University, India



An Avalanche-Transit-Time (ATT) diode with lateral orientation has been designed. The proposed diode has a High-Electron-Mobility (HEM) active region that constitutes of 2-Dimensional-Electron-Gas (2DEG). For the first time ever, quasi-AlGaN barrier has been deployed to induce desired degree of band-engineering in the device. Such barrier consists of successive AlN/GaN thin epitaxial layers. So that the entire barrier behaves like a sustained quasi-AlGaN material. Within such quasi-material, polarization electric field and band mismatch create periodic perturbation. Again, band offset for such perturbed quasi-material barrier and the GaN active region results in the formation of high electron mobility 2DEG. Such 2DEG formation is further supported by the positively charged Cathode-Field-Plate (CFP) under reverse biased ATT operation condition. At the same time, the laterally oriented device results in such 2DEG to exist precisely along the active region. Subsequently, the first ever two-terminal high-electron mobility ATT diode having 2DEG based active region comes into play. This design has rendered a third terminal or gate, as is

necessary for high-electron-mobility-transistors, i.e. HEMTs, to be redundant. Electron mobility in such 2DEG transport region $\sim (1600-2000)\text{cm}^2/\text{V}\cdot\text{sec}$. Such mobility is twice that of standard alloy AlGaN material barrier and GaN well, where the mobility $\sim 800\text{cm}^2/\text{V}\cdot\text{sec}$. This in turn leads to high RF output power and exceptionally high DC to RF conversion efficiency. Optoelectronic performance of such device has been studied by an ingenious, experimentally-supported Strain-corrected-Mixed-Quantum-Tunneling-Drift-Diffusion (Sc-MQTDD) simulation model. Both single and array configurations of these ATT diodes have greatest documented efficiency of DC to RF conversion, i.e. 23% & 27%, and also RF output power, i.e. $980 \times 10^9 \text{W}/\text{m}^2$ & $1163 \times 10^9 \text{W}/\text{m}^2$, respectively. Also, the interaction between photons in the UV region and carrier electrons has been studied. Responsivity in UV domain and quantum efficiency have been respectively predicted to be 0.7A/W and 80%, for 3×3 array. Subsequently, the scope of application of such cutting-edge device in bio-medical domain has been explored.

Biography

Dr. Chatterjee did her Ph.D. in Nano Science and Nano Technology, from University of Calcutta. She won many prestigious fellowships from Government Of India: CSIR-SRF, DST-INSPIRE, Indian Institute of Technology Fellowship ECE (I.I.T. Kharagpur). She did her M.Tech. in Radio Physics and Electronics from University of Calcutta, where she stood FIRST CLASS FIRST and was AWARDED THE GOLD MEDAL. She was awarded OUTSTANDING ACADEMIC EXCELLENCE AWARD. She did her M.Sc. with excellence in Electronic Science from University of Calcutta. She received NATIONAL MERIT scholarship from Government of India for her B.Sc. from University of Calcutta. She is Reviewer for many esteemed international SCI journals. She has bagged various prestigious awards, Young-Achiever, Research-Excellence, Academic-Excellence, Global-Teaching-Excellence, Excellence-in-Review, etc. She has been invited and visited several times to UK, Italy, USA, Japan, Belgium etc. as an EXPERT and INVITED SPEAKER, both offline and online. She has 12 international SCI Journal papers: among them 10 high impact SCI Journals as First author, including several IEEE Transactions. She has received several BEST PAPER AWARDS including Science-Congress (Govt.). She has 3 international book chapters.



Comparative study of response surface methodology and adaptive neuro-fuzzy inference system for removal of 6-APA in aqueous media

N. Soleimanpour Moghadam, A. Azadmehr and A. Hezarkhani

Amirkabir University of Technology, Iran

Antibiotic contaminated waters treatment is an important step for pollutant reduction and the promotion of water environment quality. Uncertainty in wastewater treatment technology, fluctuations in effluent water quality and operation costs cause an emerging issue to develop materials effective for removal of antibiotics. The environment-friendly clay such as vermiculite, could be potentially promising candidates for removing 6-APA (6-Aminopenicillanic) from pharmaceutical effluent. Antibiotic removal was achieved by using eco-friendly, time-saving, powerful and easy-

applying synthesis method via tetraethoxysilane (Si). Expert systems are widely powerful tools for minimizing the complexities and complications in wastewater treatment. Response surface methodology (RSM) and adaptive neuro-fuzzy inference system (ANFIS) models were used to develop systematically predicting interactions of synthesis conditions on 6-APA adsorption capacity and optimize the best amount of compound. The effect of process variables investigated by RSM through central composite design (CCD) matrix and the results compared with ANFIS model.

Biography

N. Soleimanpour Moghadam Ph.D. graduated from the Amirkabir University of Technology, Medicinal Mineral Chemistry branch as First-class with the highest distinction. She was awarded the 'Top student' in Ph.D. degree. She is also patented the invention of drug formulation in her own name in Iran. A major focus of her work was the study and development of polymers to deliver drugs, particularly antibiotics at controlled rates and for prolonged periods of time. Her research has been focused on the experimental design, synthesis, polymers, hydrogels, controlled release, characterization, XRD, XRF, SEM, FTIR, TEM, UV, BET analysis evaluation of novel biomaterials compounds, in Vitro assays, and in Vivo testing, and developing target-specific drug candidates as antibiotics. She also investigated the mechanism of release by using RSM, ANFIS techniques. She has published several authored articles and attended several conferences.

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CNS tumors: New techniques in radiation oncology

**Marilena Theodorou^{1,2}, Andriana Peratikou¹,
 Nektarios Poullos³ and Demetrios Andreopoulos¹**

¹Bank of Cyprus Oncology Center, Cyprus

²European University, Cyprus

³General Hospital, Cyprus

New techniques in radiation oncology such as VMAT (volumetric modulated arc therapy) occur high dose to target and more safety for the organs at risk. Most of the brain tumors need high dose radiation therapy but due to the anatomical location of the tumor the delivery of the dose is limited in order to avoid radiation to the organs at risk. Most of the pediatric tumor are brain tumor that need

also high dose therapy. Using VMAT technique we can deliver high dose radiation with safety for the organs at risk. Every healthy organ has a tolerance dose that means a dose that can tolerate but any dose above the tolerance dose can cause damage for the future. The risk of radio necrosis can be decreased using modern technique in radiation oncology.

SARS-CoV-2 spike T cell responses induced upon vaccination or infection remain robust against Omicron

Roanne Keeton^{1,2}, Marius B. Tincho^{1,2}, Amkele Ngomti^{1,2}, Richard Baguma^{1,2}, Ntombi Benede^{1,2}, Akiko Suzuki^{1,2}, Khadija Khan^{3,4}, Sandile Cele^{3,4}, Mallory Bernstein^{3,4}, Farina Karim^{3,4}, Sharon V. Madzorera^{5,6}, Thandeka Moyo-Gwete^{5,6}, Mathilda Mennen⁷, Sango Skelem⁷, Marguerite Adriaanse⁷, Daniel Mutithu⁷, Olukayode Aremu⁷, Cari Stek^{1,7}, Elsa du Bruyn^{1,7}, Mieke A. Van Der Mescht⁸, Zelda de Beer⁹, Talita R. de Villiers⁹, Annie Bodenstein⁹, Gretha van den Berg⁹, Adriano Mendes¹⁰, Amy Strydom¹⁰, Marietjie Venter¹⁰, Jennifer Giandhari¹¹, Yeshnee Naidoo¹¹, Sureshnee Pillay¹¹, Houriiyah Tegally¹¹, Alba Grifoni¹², Daniela Weiskopf¹², Alessandro Sette^{12,13}, Robert J. Wilkinson^{1,7,14,15,16}, Tulio de Oliveira^{11,17}, Linda-Gail Bekker^{1,7,18}, Glenda Gray¹⁹, Veronica Ueckermann²⁰, Theresa Rossouw⁸, Michael T. Boswell²⁰, Jinal Bihman^{5,6}, Penny L. Moore^{1,5,6,21}, Alex Sigal^{3,4,22}, Ntobeko A. B. Ntusi^{1,7,14,23}, Wendy A. Burgers^{1,2,14} and Catherine Riou^{1,2,14}

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⁴School of Laboratory Medicine and Medical Sciences, University of KwaZulu-Natal, South Africa

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⁶SA MRC Antibody Immunity Research Unit, School of Pathology, Faculty of Health Sciences, University of the Witwatersrand, South Africa

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The SARS-CoV-2 Omicron variant has multiple Spike (S) protein mutations that contribute to escape from antibody neutralization and reduce vaccine protection from infection. The extent to which other components of the adaptive response such as T cells may still target Omicron and contribute to protection from severe outcomes is unknown. We assessed the ability of T cells to react with Omicron spike in participants who were vaccinated with Ad26.CoV2.S, BNT162b2, or unvaccinated convalescent COVID-19 patients (n=70). We found that 70-80% of the CD4 and CD8 T cell response to spike was maintained across study groups. Moreover, the magnitude of Omicron cross-reactive T cells was similar to Beta and Delta variants,

despite Omicron harbouring considerably more mutations. In Omicron-infected hospitalized patients (n=19), there were comparable T cell responses to ancestral spike, nucleocapsid and membrane proteins to those patients hospitalized in previous waves dominated by the ancestral, Beta or Delta variants (n=49). Thus, despite Omicron's extensive mutations and reduced susceptibility to neutralizing antibodies, the majority of T cell responses, induced by vaccination or infection, cross-recognise the variant. Well-preserved T cell immunity to Omicron is likely to contribute to protection from severe COVID-19, supporting early clinical observations from South Africa and elsewhere.



Effect of sleeve gastrectomy on metabolic status in type 2 obese diabetics

Ibrahim El Bayoumy

University of South Wales, UK

Background: Limited data are available about evaluation of the effects of sleeve gastrectomy on the glycaemic control on diabetes mellitus. The objective of this study is to evaluate the effectiveness of sleeve gastrectomy in improving the control of glycemic status in obese diabetic patients.

Patients and Methods: This is retrospective cross sectional study to review the maintained data base collected between May 2018 to April 2021 in department of laparoscopic surgery in Farwaniyah hospital-Kuwait.

A total 120 patients with diabetes mellitus who had undergone laparoscopic sleeve gastrectomy were studied at 3 months and 6 months of follow up visits, collected data about variation in Body Mass Index (BMI). And glycosylated hemoglobin (HbA1c), and fasting blood glucose were analyzed.

Results: Of the 120 diabetic patients with ≥ 6 months post-operative follow up 72 diabetic patients (60%) are still taking medications

for diabetes mellitus and 48 diabetic patients (40%) are resolved at 3 months and 6 months of follow up. HbA1c has decreased from 9.22 ± 1.36 ($n=18$) preoperatively to 6.02 ± 0.22 after 3 months of surgery and 30 diabetic patients, HbA1c become 5.88 ± 0.22 after 6 months.

Body Mass Index (BMI) has decreased from 47.43 ± 11.33 in the sample of the study (120 diabetic patients) preoperatively to 37.82 ± 6.80 at 3 months and to 33.25 ± 3.12 Kg/m after 6 months of surgery.

Patients with short duration of diabetes less than 5 years have had better weight loss after surgery and achieved greater resolution rates (euglycemic state).

Conclusion: Sleeve gastrectomy has improved the glycemic control in obese diabetic patients in the form of improvement and resolution and also succeeded in reduction of the body weight in the sample of the study.

Biography

Ibrahim El- Bayoumy holds bachelor of medicine and surgery (Tanta faculty of medicine-Egypt, 1989), then he earned his master degree in public health, preventive and social medicine (Tanta faculty of medicine-Egypt 1996), and MD, PhD in public health, preventive and social medicine 2003 from Tanta faculty of medicine-Egypt and McGill faculty of medicine -Montreal -Canada in division of clinical epidemiology in Royal Victoria hospital through double channel system as scholarship from ministry of education-Egypt. He is Full professor of public health and community medicine in Tanta faculty of medicine-Egypt since November 2016. Now he is working in ministry of health in Kuwait as consultant of public health and preventive medicine.

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Selection, expansion, and unique pretreatment of allogeneic human natural killer cells with anti-CD38 monoclonal antibody for efficient multiple myeloma treatment

Motais Benjamin and Charvátová Sandra

University of Ostrava, Czech Republic

Following promising results in various clinical trials with chimeric antigen receptor T cells, cellular immunotherapy is emerging as a new pillar in cancer treatment. However, there are some drawbacks to this novel therapy, including off-tumor toxicity, cost, and tumor recurrence in heterogeneous tumors. To overcome these constraints, we take advantage of the unique anti-tumor properties of natural killer (NK) cells. Our study's goal was to obtain a clinically relevant number of allogeneic NK cells derived from peripheral blood (median of 14,050 million cells from a single donor) to target a wide range of solid and liquid tumor types. Allogeneic NK cells were combined with the approved anti-cluster of differentiation 38 (CD-38) monoclonal antibody Daratumumab to achieve a synergistic

therapeutic effect against incurable multiple myeloma. To avoid unwanted fratricide, the combination treatment was refined with CD16 polymorphism donor selection and uncomplicated novel *in vitro* pretreatment, increasing the *in vitro* specific lysis by more than 20% against the CD-38 positive multiple myeloma cell line. After time-lapse imaging of mice with subcutaneous human multiple myeloma xenografts, we discovered that combining selected and pretreated NK cells with Daratumumab resulted in tumor volumes that were 43-fold smaller than controls. With an allogeneic source of fully functional NK cells, combined treatment may be helpful in future clinical settings to avoid the low therapeutic efficacy of monoclonal antibodies in MM patients due to NK cell dysfunctionality.

Biography

Benjamin Motais is a third-year Ph.D. student at the University of Ostrava. He graduated a Master's degree in Biology from the University of Orléans, France. He is currently working in the field of NK cell therapy in the Blood Cancer Research Group at the University Hospital of Ostrava.

ACCEPTED ABSTRACTS



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June 22-23, 2022

CLINICAL R&T 2022

“ **Leveraging auxiliary
covariates to improve
efficiency of inferences:
A general framework
and practical
considerations** ”

Min Zhang¹ and Baqun Zhang²

¹*University of Michigan, USA*

²*Shanghai University of Finance and Economics, P.R.China*

Auxiliary covariates are routinely collected in randomized clinical trials. Although it has been long recognized in statistical literature that incorporating covariates can improve the efficiency of inferences and reduce chance imbalance, covariates adjustment has not been used as often as it should be in the primary analysis of clinical trials in practice. This is partly due to that many practitioners remain skeptical of its usefulness or have other concerns regarding model misspecifications. We try to address these concerns and discuss a general framework that allows one to adjust

covariates robustly. That is, this framework can guarantee improvement in efficiency, if covariates are predictive of outcomes, and valid inferences regardless of whether the specified models for covariates are correct or not. Therefore, it can eliminate the concern over model misspecification. We further discuss practical considerations in terms of covariate adjustment, focusing on finite sample effects, stratified randomization, and what variables to adjust. We attempt to address the question of how and when to use covariate adjustment for randomized clinical trials in practice.

“Using AI and machine learning as a substitute to CT scan in the diagnosis of appendicitis”

J. Muñoz

US Navy, Walter Reed National Military Medical Center, USA

Background: Appendicitis is one of the most common surgically treated diseases in the world. CT scans are often over-utilized and ordered before a surgeon has evaluated the patient. Our aim was to develop a tool using machine learning (ML) algorithms that could substitute, or obviate the need for, a CT scan.

Methods: Retrospective chart review of 100 randomly selected cases who underwent appendectomy and 100 randomly selected controls was completed. Variables included components of the patient's history, laboratory values, CT readings, and pathology. Pathology was used as the gold standard for appendicitis diagnosis. All variables were then used to build the ML algorithms. Random Forest (RF), Support Vector Machine (SVM), and Bayesian Network Classifiers (BNC) models with and without CT scan results were trained and compared to CT

scan results alone and the Alvarado score using area under the Receiver Operator Curve (ROC), sensitivity, and specificity measures as well as calibration indices from 500 bootstrapped samples.

Results: Among the cases that underwent appendectomy, 88% had pathology-confirmed appendicitis. All the ML algorithms had better sensitivity, specificity, and ROC than the Alvarado score. SVM with and without CT had the best indices and could predict if imaging would be necessary in diagnosis of appendicitis.

Conclusion: This study demonstrated that SVM with and without CT results can be used for selective imaging in the diagnosis of appendicitis. This study serves as the initial step and proof-of-concept to externally validate these results with larger and more diverse patient population.

“
**The impact of
 cooperative
 R&D and
 advertising on
 innovation and
 welfare**
 ”

P. Pourkarimi¹ and G. Atallah²

¹*Carleton University, Canada*

²*University of Ottawa, Canada*

This paper studies the impact of cooperative R&D and advertising on innovation and welfare in a duopolistic industry. The model incorporates two symmetric firms producing differentiated products. Firms invest in R&D and advertising in the presence of R&D spillovers and advertising spillovers. Advertising spillovers may be positive or negative. Four cooperative structures are studied: no cooperation, R&D cooperation, advertising cooperation, R&D and advertising

cooperation. R&D spillovers and advertising spillovers always increase innovation and welfare if products are highly differentiated and/or spillovers are sufficiently high. The ranking of cooperation settings in terms of R&D, profits and welfare depends on product differentiation, R&D spillovers and advertising externalities. Firms always prefer cooperation on both dimensions, which is socially beneficial only when advertising and R&D spillovers are sufficiently high.

“ Training in clinical research ”

Donato Bonifazi¹ and Ana Dilo²

¹*Consorzio per Valutazioni Biologiche e Farmacologiche, Italy*

²*Consorzio per Valutazioni Biologiche e Farmacologiche, Albania*

Background: Training is a key factor in the clinical research field. To gain the needed skills and confidence, persons involved in clinical research should be well trained.

Objectives: The EUCROF (European CRO Federation) events and training working group aims to deliver activities to build relationships across organizational boundaries; provide high quality training services like webinars, training courses, podcasts, roundtables and forums of discussion, in order to enable participants to develop skills, expertise and grow within their role in clinical research field; promote good practices in education in clinical research.

A forum of discussion, available on the Moodle e-learning platform, enables the participants to get in direct contact with the speakers to ask questions or provide their insight on different topics. EUCROF offers training on topics of high interest for the participants taking into

consideration the latest developments in the field of clinical research and selects speakers with a broad knowledge on the specific topic.

Results: During a period of 3 years, more than 20 webinars, 2 one-day training courses and 4 podcasts have been organized with more than 1300 attendees and 44 speakers making EUCROF a trusted platform where high quality training is provided.

Conclusions: Events and trainings organized so far have always been successful and scientifically adequate to promote the role of EUCROF as a qualified player in the European clinical research scenario, allowing its members to become more and more appreciated as experts in the most relevant fields and as excellent partners for pharma companies, regulators, researchers, institutions and patients.

“
Protein sequence alignment showed that the SARS-CoV-2 may be a chimeric virus
 ”

Mohammed Elimam Ahamed Mohammed

King Khalid University, Saudi Arabia

The determination of the SARS-CoV-2 origin is important so as to take prevention actions to avoid future RNA viruses' pandemics. This article carried out sequence alignment for the proteins of SARS-CoV-2 (NCBI Reference Sequence: NC_045512.2), and Pangolin coronavirus (GenBank: MT121216.1) and compared the results to the published sequence alignment of the SARS-CoV-2 and the BatCoV RaTG13. Protein sequence alignment was done using the online free service of the European Molecular Biology Open Software

Suite (EMBOSS). Sequence alignment of the proteins of the SARS-CoV-2, BatCoV RaTG13 and pangolin coronavirus enforced the bat origin of the SARS-CoV-2 over the pangolin origin. Furthermore, both of the SARS-CoV-2 and the pangolin coronavirus contain the orf10 accessory protein with the identity of 97.4% and similarity of 100% whereas it is not found in the BatCoV RaTG13. The obtained results strongly favor the chimeric nature of the SARS-CoV-2 over the bat or pangolin origin alone.

“
**Saliva biomarkers
 in diagnostics
 of early stages
 of Alzheimer’s
 disease**
 ”

A. N. Kodintsev^{1,2}, O. P. Kovtun¹ and L. I. Volkova¹

¹*Ural State Medical University, Russia*

²*The Institute of High Temperature Electrochemistry of the Ural Branch of the Russian Academy of Sciences, Russia*

Diagnosis of Alzheimer’s disease (AD) is based on clinical examination of patient’s cognitive state. In 2016, the A/T/N system was developed, which expanded a spectrum of biomarkers recommended for AD diagnostics. However, the high price and low availability of the suggested methods, including lumbar puncture or positron-emission tomography, limit their use in daily clinical practice. An active search for other diagnostic tools led to studies on biomarkers in peripheral tissues, such as the blood and saliva. Development of ultrasensitive methods allowed detecting minimal alterations of concentrations of various substances, proteins, or metabolites, which can be used

for AD diagnosis at the preclinical stage. Saliva is one of the most important biological fluids and potential candidates for study of various biomarkers. However, the absence of a single protocol for collection and conservation as well as the effects of multiple confounding factors make the development of diagnostic panels difficult. In this review, we consider and analyse the main difficulties in saliva investigation and the results of studies on the possibility of using beta-amyloid, tau-protein, acetylcholinesterase, lactoferrin, and metabolome as the markers of the early stages of AD.

“ **Prevalence of diabetes mellitus among HIV-positive patients under ARVs attending in Rwanda, A case study of university teaching hospital of Butare** ”

Venuste Kayinamura¹, V. Iyamuremye¹, A. Ngirabakunzi¹, L. Dusengemungu³ and G. Nzeyimana²

¹*Catholic University Rwanda (CUR), Rwanda*

²*University Teaching Hospital of Butare (CHUB), Rwanda*

³*The Copperbelt University, Zambia*

Anti-retroviral therapy (ART) for HIV patient can cause a deficiency in glucose metabolism by promoting insulin resistance, glucose intolerance, and diabetes, diabetes mellitus keep increasing among HIV-infected patients worldwide but there is limited data on levels of blood glucose and its relationship with antiretroviral drugs (ARVs) and HIV-infection worldwide, particularly in Rwanda. A convenient sampling strategy was used in this study and it involved 323 HIV patients (n=323). Patients who are HIV positive under ARVs were involved in this study. The patient's blood glucose was analyzed using an automated machine or glucometer (COBAS C 311). Data were analyzed using Microsoft Excel and SPSS V. 20.0 and presented in percentages. The highest diabetes mellitus prevalence was 93.33 % in people aged >40 years while the lowest diabetes mellitus prevalence was 6.67% in people aged between 21-and 40

years. The P-value was (0.021). Thus, there is a significant association between age and diabetes occurrence. The highest diabetes mellitus prevalence was 28.2% in patients under ART treatment for more than 10 years, 16.7% were <5 years while 20% of patients were on ART treatment between 5-10 years. The P-value here is (0.03), thus the incidence of diabetes is associated with long-term ART use in HIV-infected patients. This study assessed the prevalence of diabetes among HIV-infected patients under ARVs attending the University Teaching Hospital of Butare (CHUB), it shows that the prevalence of diabetes is high in HIV-infected patients under ARTs. This study found no significant relationship between gender and diabetes mellitus growth. Therefore, regular assessment of diabetes mellitus especially among HIV-infected patients under ARVs is highly recommended to control other health issues caused by diabetes mellitus.



A case of muscoli peroneus tertius anatomic variation



Han Yang, Fan Xue and Yikai Li

Southern Medical University, China

Scope: In the routine dissections study for medical postgraduates, we came across an anatomical variation between the right leg and the ankle. The specimen was observed in an approximately 40 years old male fresh cadaver of Asian origin.

Case report: A case of muscoli peroneus tertius (PT) anatomic variation was observed in the routine dissections study. The PT is closely associated with the extensor digitorum longus (EDL) in the leg. At the dorsum of the foot, the EDL tendon divided into three tendinous slips for the second, third and fifth toes. The most common PT insertion sites were the base of the fifth metatarsal. Still, the PT muscle divided into two tendons in this case: the first tendon was attached to the base of the fifth metatarsal bone, and the second tendon was inserted into the base of the fourth metatarsal bone. (Figure 1)

Objectives: The purpose of this paper is to provide detailed anatomical case reports, and to discuss the possible causes and mechanisms of the variation by reviewing relevant literature, so as to provide some reference for

future anatomical and clinical related disease research.

Conclusion: A case of the PT variation has been reported in our paper. Although the causes of anatomical variation and the exact contribution of the PT in the periankle musculature remain unclear. There is no doubt that the PT is an important functional anatomical structure in the evolution, function, and morphology. It might play an important role in the well-functioning muscle system around the ankle, which urges us to explore it in the future further.

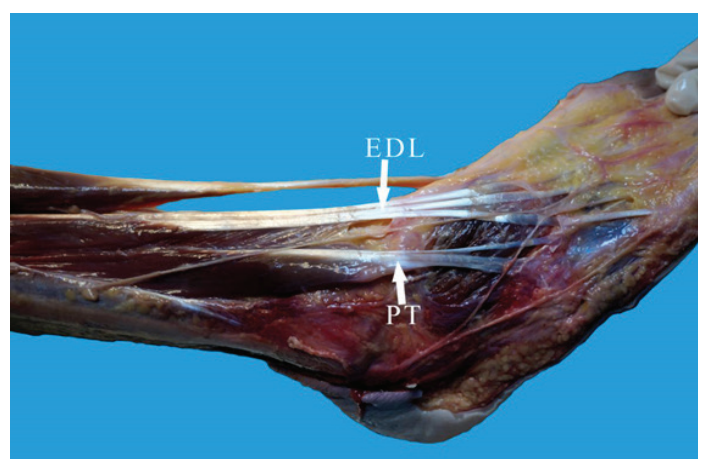


Figure 1:
EDL: Extensor digitorum longus; PT : peroneus tertius

“ On the relation of personality, emotion, and choices ”

G. Gilboa Freedman, S. Schlimoff and D. Trigman

Reichman University, Israel

The current study explored the combined influence of personality and emotions on decision-making under uncertainty. We took a novel approach that emphasizes the fact that personality traits are more stable than emotions. To capture this difference, we designed a machine-learning algorithm to identify a two-layer structure of (1) personality traits (stable parameters) that influence (2) emotions (unstable parameters), which in turn influence decisions.

The proposed approach can improve the performance of systems and services that work under conditions of uncertainty and involve emotionally driven decisions. One of these is healthcare services, where these insights can be useful to encourage wise health-related choices, such as increasing the number of vaccinated individuals in the population and influencing adherence to taking medications.

We considered the Ellsberg and Allais paradoxes. For each paradox, we performed an experiment with 200 participants who were rewarded with payments and recruited through the Prolific recruitment platform. The collected data included information on participants' choices, emotions, and personality factors, and we used it to train a machine learning algorithm (decision tree).

By employing this methodology, we identified

certain groups of personalities in which the connection between emotions and decision-making is unique to each group.

For example, we examined the emotions reported for the first option in the first decision game of Allais paradox (see the game in the following figure).

Participants who are Stable (stability > 11.5) demonstrated that emotion anticipation induced a tendency to behave irrationally (chose option 1). Neurotics who reported the same emotion did not demonstrate such a tendency.

We also found that the effect of the relationship between emotions and decisions is different for people with different degrees of locus of control. This study expands the existing literature on decision-making under uncertainty and has the potential to offer significant value for this field.

DECISION GAME

- **Option 1 -**
certainty of \$1 Million.
- **Option 2 -**

1%	0\$
89%	1M\$
10%	5M\$

“DNA nanotechnology for modulating the growth and development of neurons”

Mirza Muhammad Faran Ashraf Baig

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Late prenatal growth, early postnatal growth, and layering of the neocortical neurons (NC-Ns) play determining roles in the development of the cerebral cortex (CC). Here, we systematically explore the interactive role of neuronal surface receptors (NSRs) on cytoskeleton activation (CA) and the piconewton (pN) force generation (P-FG) and their influence on the proper development, growth, and functioning of neurons using a designed DNA nanomechanical device (DNA-NMD).

This DNA-NMD, functioning as a molecular tension probe (MTP), can be used to selectively bind the different NSRs (β -NGFR, Reelin, and

Integrin) to mono-, bi-, and trispecifically activate the receptors on the NC-Ns surface for imaging and calculating the P-FG involved in various processes. Measurements *in vivo* on the brain of newly born Institute of Cancer Research mice (early postnatal) or *in vitro* after extracting neurons from the fetal brain of pregnant Institute of Cancer Research mice (late prenatal) reveal that there are augmented interactive roles of the β -NGFR with Integrin and Reelin receptors (RR) on the CA and P-FG, resulting in enhanced directional migration of the neuronal endings (M-NEs), layering, and the somal terminal translocation (S-TT) followed by early postnatal growth.



Laparoscopic natural orifice specimen extraction surgery versus conventional surgery in colorectal cancer



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Natural orifice specimen extraction surgery (NOSES) is regarded as an important advance recently for surgical treatment of colorectal cancer (CRC). Nevertheless, introduction of NOSES to laparoscopy is not a simple conceptional or technical combination but requires additional validations. Therefore, we initiated some first studies in China since 2015 by enrollment of consecutive patients with CRC who underwent laparoscopic surgery with or without successful NOSES attempt in the department of colorectal surgery, Shanghai East hospital. In order to setup a workflow, we modified and reported two major NOSES procedures for CRC, namely the PISTA surgery and specimen dissection with trans-rectal extraction followed by intracorporal anastomosis using staplers. To make more accurate candidate selection, we established a preoperative nomogram to predict the feasibility of NOSES in CRC and highlighted several key factors restricting reasonable application of NOSES, such as increased BMI, tumor/specimen diameter and decreased pelvic metrics. In order to evaluate and

optimize the safety of NOSES in technology and oncology based on the workflow, we compared the perioperative clinical-pathological characteristics and outcomes between CRC patients receiving conventional laparoscopy (conventional group) and NOSES (NOSES group). Results showed that patients in the NOSES groups tended to experience a decreased operating time, intraoperative blood loss, analgesic use, visual analogue scale score, shortened recovery time (i.e., first bowel motion, hospital stay), comparably low chance of common postoperative complications (i.e., bleeding, surgical site infections, intestinal obstruction, anastomotic leak and stenosis), and no serious postoperative complications (i.e., fecal incontinence), not excepting a cosmetic advantage of NOSES. Moreover, there were no significance differences between the two groups regarding local recurrence rate, disease-free survival (DFS) and overall survival (OS). In keeping with all the results, application of NOSES in surgical treatment of CRC is demonstrated as a safe, efficient and economic procedure.



The efficacy of honey as an alternative to standard antiseptic care in the treatment of chronic pressure ulcers and diabetic foot ulcers in adults



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Objective: A chronic wound fails to progress through the phases of wound healing in an orderly and appropriate process, and poses a major challenge to wound care professionals. Pressure ulcers (PUs) and diabetic foot ulcers (DFUs) are classified as chronic wounds. Antiseptics, such as Povidone-iodine (PVP-I), are often used to treat bacterial infections in chronic wounds, however, their efficacy and ability to accelerate wound healing has come into question. As a result, current medical research is now focusing on alternative and natural antiseptic agents, such as honey, for the treatment of chronic wounds.

The aim of this study was to analyse the wound healing effects of honey in PU and DFU treatment in comparison to standard antiseptic care.

Methods: A systematic literature search of PubMed, Science Direct and Clinical Key was conducted to identify all published data of clinical trials and narrative reviews that investigated or reported the use of honey and standard antiseptics in the treatment of PUs and DFUs in adults. A keyword search was then performed using the following keywords: "pressure ulcers", "diabetic foot ulcers", "antiseptics", "Povidone-iodine", "honey", "Manuka honey", and "wound healing". Database restrictions

were implemented based on the inclusion and exclusion criteria, notably the report's availability, completion status and language, the sample populations age, as well as, the date of publication. A preferred reporting items for systematic review and meta-analysis (PRISMA) diagram was constructed illustrating the study selection process. The eligibility of articles was assessed by the screening of titles, abstracts and full texts. A total of 12 articles were included in this study comprising of 775 patients with PUs, DFUs or a combination of PUs and DFUs.

Results: Results indicated that honey reduced bacterial infection, reduced pain and oedema experienced by patients, reduced the odour of the wound and promoted wound healing in the treatment of chronic ulcers. Honey was also found to be effective in the process of debridement and exudate removal.

Conclusion: Honey was found to be highly effective in the treatment of PUs and DFUs and should be considered as an alternative to standard antiseptic care in the treatment of chronic wounds. However, the literature in this study is limited and so further research into honey and its antiseptic-promoting activity in wound healing is recommended.

“
**Gastrointestinal
 manifestations
 and outcomes
 in hospitalized
 covid-19 patients:
 A retrospective
 study**
 ”

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Region I Medical Center, Philippines

Background: Various gastrointestinal (GI) symptoms including diarrhea, nausea/vomiting and abdominal pain have been reported in patients with Coronavirus disease 2019 (COVID-19). In this context, the presence of GI symptoms is variably associated with poor clinical outcomes in COVID-19. We aim to determine the outcomes of hospitalized COVID-19 patients with gastrointestinal symptoms.

Methodology: This is a retrospective cohort study which used medical records of admitted COVID-19 patients from March 2020- March 2021 in a tertiary hospital in Pangasinan. Data records were evaluated for the presence of gastrointestinal manifestations including diarrhea, nausea, vomiting and abdominal pain at the time of admission. Comparison between cases or COVID-19 patients presenting with GI manifestations to controls or COVID-19 patients without GI manifestation was done.

Results: Four hundred three patients were included in the study. Of these, 22.3% presented with gastrointestinal symptoms while 77.7% comprised the study controls. Diarrhea was the most common GI symptom (10.4%). No statistically significant difference was observed in comorbidities and laboratory findings. Mortality as the primary outcome of the study did not reach statistical significance between cases and controls (13.33% vs. 16.30%, $p = 0.621$). There were also no significant differences observed in the secondary outcomes, mean length of stay, (14 [12-18 days] in cases vs 14 [12- 17.5 days] in controls, $p = 0.716$) and need for mechanical ventilation (12.22% vs 16.93%, $p = 0.329$).

Conclusion: The results of study revealed no association of the GI symptoms to poor outcomes including high rate of mortality, prolonged length of stay and increased need of mechanical ventilation.

“
**Breathing and
 supporting
 mechanical device
 clinical trial on
 novel coronavirus
 (COVID-19)
 infected patients in
 pandemic**
 ”

A. Shukla

Indus University, India

Severe acute respiratory distress syndrome (ARDS) is a complications of health, in this condition lungs cannot provide enough oxygen to the vital organs. Prone positioning is a used to treat COVID-19 as a first line intervention, mechanical ventilation an invasive device to provide the patient lifesaving support. This device improves gas exchanges and reduce mortality.

Respiratory system primarily affected by the SARS-CoV-2, and organ system damaged by

virus. Mechanical ventilation is required for the support organ system in body.

Mechanical ventilation with face masks (FM) or high flow nasal therapy (HFNT) has been significantly reduced the airborne infection in different condition. A clinical studies suggest mechanical device improve gas exchange and better lung aeration when used in spontaneous or long term. These techniques also reduce the patients admit time in the hospitals.

“
Covid-19 and ear surgery: Treatment strategies and triage during the post-lockdown period
 ”

Akriti Sharma

SGT University, India

Introduction: The accumulated disease burden during lockdown period, due to postponement of regular surgeries, is expected to put additional pressure on surgeons during the post-lockdown period. Due to the contagious nature of SARS-CoV-2 and its suspected presence in middle ear mucosa and mastoid, ear surgeons are bound to face a challenging situation in present times as well as in times to come. Through this article we aim to streamline fresh management strategies particularly for the post-lockdown period keeping in mind that immunity after vaccination may take a few months to develop due to various factors discussed in the article.

Method: The ENT Cochrane, Pubmed and Web of Science databases were searched extensively using the terms Covid-19 and SARS-CoV-2 in conjunction with Ear surgery and Otology. Data collected from these, put together with our experience helped us in putting forward fresh management strategies to deal with the

current situation being experienced worldwide.

Results: To reduce the risk of infection to the healthcare staff, we have suggested a new triage strategy for ear surgeries to reduce the accumulated disease burden in the post-lockdown period until immunity by vaccination develops amongst a good number of Ear surgeons. Also we have put forward certain operating guidelines that might prove helpful for the Ear surgeon during these times.

Conclusion: Fresh Triage guidelines mentioned in this article are particularly meant to help ear surgeons reduce the accumulated disease burden in the post lockdown-period with ease and efficacy. Since ear surgery poses a risk of infection to the healthcare workers, specific guidelines pertaining to ear surgery during the pandemic are mentioned in detail which in our opinion can be of immense help to all the healthcare professionals involved in ear procedures till the time the vaccine is administered on a large scale.



Carfilzomib-Pomalidomide-Dexamethasone (KPd) in Relapsed/Refractory Multiple Myeloma (RRMM) patients in a tertiary care hospital in India



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Rajiv Gandhi Cancer Institute and Research Centre, India

Purpose: Carfilzomib is a second-in class Proteasome Inhibitor and has been approved for Relapsed/Refractory Multiple Myeloma (RRMM).

Methodology: We retrospectively retrieved and analyzed data of kPD combination both biweekly and weekly regimens at our centre from 1st August 2017 and 31st May 2020.

Results: Sixty-nine patients were treated with KPd with median age of 58 years. Median prior lines of chemotherapy were 2 (1-15). Twenty-eight (40.5%) patients underwent autoSCT.

Median no. of cycles were 4(1-12) and 3 (1-13) with median time to response of 4(2-12) and 2 (2-6) months in biweekly and once weekly regimen cohorts respectively. At last follow-up, overall response rate (ORR) in biweekly KPd regimen was 51.2% with n=11 (28.2%) had PD and 13(59.1%) had relapse whereas ORR in once weekly KPd regimen was 33.3% with n= 03(10%) patients had PD and 11(36.6%) patients had relapse.

Thirty (43.4%) patients received maintenance therapy {n=21(70%)} or autoSCT {n=9(30%)}.

Common toxicities were anemia {n=11(15.9 %)}, thrombocytopenia (n=15(21.7%) and neutropenia (n=16 (23.2%)), hypertension {n=28 (40.5%)}, peripheral neuropathy (grade1/2) {n=15(21.7%)}, infections [n=18(26%) {bacterial [n=9(13%), viral n=7(10.1%), fungal n=8(11.6%)}]

At a median follow-up of 21 and 12 months, estimated median PFS was 10months (95% C.I. 6.7– 13.2) and 14.8months (95% C.I. 2.0- 25)and estimated median OS was 28months (95% C.I. 20.1-35.8) and not reached with mortality rate of 2.5% and 10% in two cohorts respectively. Commonest cause of death was PD and sepsis.

Conclusion: KPd is a well-tolerated regimen for RRMM, which can be a bridge to ASCT, however with significant side effects.



***In vitro* screening of growth inhibitory activity of medicines for malaria venture pathogen box compounds against *Leishmania aethiopica* clinical isolate**



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Treatment of cutaneous leishmaniasis (CL) in Ethiopia heavily depends on limited drugs, together with drawbacks like toxicity and microbial resistance. Finding new compounds or chemical entities that overcome the limitations of existing drugs remains an urgent task. The current research

aimed to investigate MMV-Pathogen Box (MMV - PB) compounds against *L. aethiopica* clinical isolate.

Methodology: Four hundred MMV - PB compounds were screened against clinical isolate of *L. aethiopica* using resazurin based colourimetric assay. Compounds with

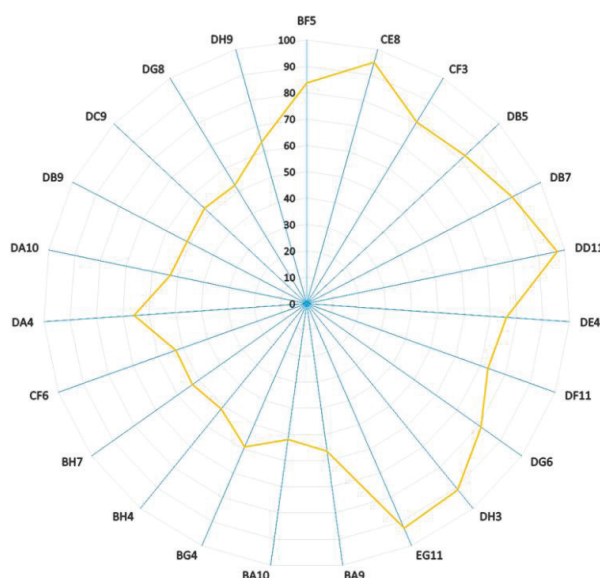


Figure 1: Pathogen box compounds showing > 50% inhibition against *L. aethiopica* promastigotes at 1 M. Compounds represented by their plate and well location. The experiment was conducted using amphotericin B and Pentamidine as standard.



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>70% inhibition were further tested using macrophage based intracellular amastigote assay. Cytotoxic and hemolytic activity of candidate hits were assessed on THP1- cells and sheep red blood cells (RBCs), respectively.

Results: At the test concentration of 1 μ M, twenty-three compounds showed >50% inhibition of promastigotes parasite growth, of which 11 compounds showed >70% inhibition. The 50% growth inhibition (IC₅₀) of the 11 compounds was ranged from 0.024 to 0.483 μ M in anti-promastigote assay and from 0.064 to 0.899 μ M in intracellular amastigote assay. Candidate compounds demonstrated

good safety on sheep RBCs and THP-1 cell lines. MMV688415 demonstrated a slight hemolytic activity on sheep RBC (5.3% at 25 μ M) and THP-1 cell line (CC₂₀ = 25 μ M) while MMV690102 inhibited half of THP-1 cells at 36.5 μ M (selectivity index = 478).

Conclusion: The present study identified a panel of compounds that can be used as a novel starting point for lead optimization. MMV690102 appears to be the most potent inhibitor against clinical isolate of *L. aethiopica* promastigotes and amastigotes. Future works should investigate the antileishmanial mechanism of action and *in vivo* antileishmanial activities of identified hits.

“ AI for covid19 disease management ”

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Coronavirus disease 2019, an infectious disease with acute intense respiratory syndrome impacted the way of life with drastic uncertainty and rapidly reached almost every nook and corner of the world. The health care institutions around the globe are looking for viable and real-time technological solutions to handle the virus. Importantly, the artificial intelligence tools and techniques are playing a major role in fighting the effect of virus on the economic jolt. In this paper AI strategies and techniques applied in public sphere using big-data analysis to prevent the dissemination of unexpected COVID-19 pandemic are discussed in detail. The disease prevention in public sphere is attained by improving health infrastructure, enhancing surveillance, strengthening contact tracing, intensifying social distancing, augmenting social media and upgrading industrial applications through

the AI techniques. It is noticed that, bigdata generated from chatbots, digital health records, contact tracing mobile applications, robotic platforms, image and thermal sensors can be used to train efficient and fast AI networks to deduce useful information regarding the impact of virus spread. Moreover, the advanced AI techniques such as machine learning, deep learning and regression models are also modified and applied in various pandemic mitigation measures. This review is expected to show light into the merits and demerits of the AI strategies adopted. Most importantly, in this digital era, automated decision making on certain specific areas might come as a big relief for the Governments and non-governmental agencies to concentrate more on the most essential and critical areas connected with pandemic prevention.

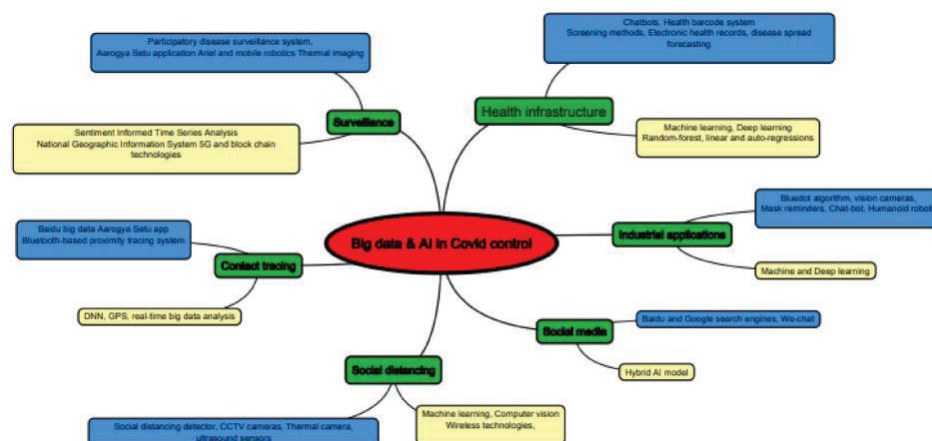


Figure1: Contribution of AI in public sphere



Understanding patients willingness to pay for biphasic insulin as part 30/70 in a pen device for type 2 diabetes treatment in an out-of-pocket payment market



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Objective: The objective of this study was to investigate willingness to pay (WTP) for biphasic insulin aspart 30/70 (BIAsp 30) in patients with type 2 diabetes mellitus (T2DM) in India.

Methods: A multicenter, prospective, non-interventional, preference study was conducted that assessed WTP for BIAsp 30 in an insulin pen (FlexPen® or Penfill® device) in patients in India with T2DM previously treated with biphasic human insulin (BHI) in vials and believed to be able to pay for treatment. The primary endpoint was the proportion of patients willing to continue to pay for BIAsp 30 after 12 weeks treatment. Secondary endpoints included the change from baseline in treatment and device satisfaction and patient preferences for treatment attributes as assessed by a nested discrete-choice experiment.

Results: Overall, 54.9% (n = 277/505) of participants were male; the mean age was

56.4 years; diabetes duration was 10.9 years; 63.8% had a body mass index ≥ 25 kg/m²; > 75% had an annual household income > 150,000 Indian rupees (INR). After 12 weeks' treatment, 96.4% of patients were willing to pay for BIAsp 30. Mean treatment and device satisfaction significantly improved from baseline (p < 0.0001). Patients were willing to pay INR3576 (95% confidence interval [CI] 2755–4398) for improved glycemic control, INR688 (95% CI 383–994) for a device upgrade (vial/syringe to an insulin pen), or INR327 (95% CI 95–560) to avoid major hypoglycemia. Patients would need to be compensated INR44 (95% CI 56–32) per minor hypoglycemic event.

Conclusions: In India, patients with T2DM previously treated with BHI were willing to pay for BIAsp 30 in an insulin pen. Furthermore, treatment and device satisfaction improved after this therapeutic switch.



**Preventive strategies
against novel
corona virus disease
(covid-19) by
natural compounds
& involvement of
immune cells**



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SARS CoV-2 emerges from Wuhan, China to the rest of the World. Wild type SARS CoV-2 has spread all around the world but their mutants were emerging nowadays and more deaths were recorded, these mutants can escape the immune response and help in increasing viral load in the respiratory system and lead to death. In this review, we discuss the Natural compound and metabolite for the treatment of SARS CoV-2 with Ashwagandha, Propolis, Vitamin D, Vitamin C, Zinc, Lead-based compounds, Chloroquine, Hydroxychloroquine, etc. A brief account on Mutation and their severity, Site of concern apart from S gene, Immune suppression which is a leading problem of post-Covid-19 event,

Immune response against Covid, etc. Mutation shows high transmission and mortality due to change in S subgenome and the efficacy of vaccine reduced. It is necessary to boost our immunity with natural compounds and metabolites and use them in treatment. Other sites and proteins which also play a huge role in virus viral replication and immune suppression, also have an ideal site of action for the treatment, action of these compounds have been discussed. Corona spreads worldwide so there is a need to conserve biodiversity and understand how anthropogenic actions occur in nature and their effect on nature because there is a link between biodiversity and disease transmission.



Fermatean fuzzy soft aggregation operators and their application in symptomatic treatment of COVID-19 (case study of patients Identification)



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The main focus of this paper is the application of aggregation operators (AOs) in the environment of Fermatean fuzzy soft sets (FFSS). The unique feature of the work is its application in the symptomatic treatment of the COVID-19 disease. For this purpose, the idea of FFSS is introduced which is based on the Senapati and Yagar's Fermatean fuzzy set. Next we have defined Fermatean fuzzy soft aggregation operators (FFSAOs) like, Fermatean fuzzy soft weighted averaging (FFSWA) operator, Fermatean fuzzy soft ordered weighted averaging (FFSOWA) operator, Fermatean fuzzy soft weighted geometric (FFSWG) operator and Fermatean

fuzzy soft ordered weighted geometric (FFSOWG). The prominent properties of these operators are given in details. We have also developed some approaches to solve multi-criteria decision making (MCDM) problems in Fermatean fuzzy soft (FFS) information. An introduction to the novel pandemic, safety measures, and then its possible symptomatic treatment is also provided. The developed operators are utilized in the symptomatic treatment of COVID-19 disease in order to show the practical applications and importance of these AOs as well as Fermatean fuzzy soft information. The stability of the proposed work is also proved by the comparative analysis.

“ A modification of the standard Grisotti flap ”

Harish Kumar Kabilan and Ashok.B.C

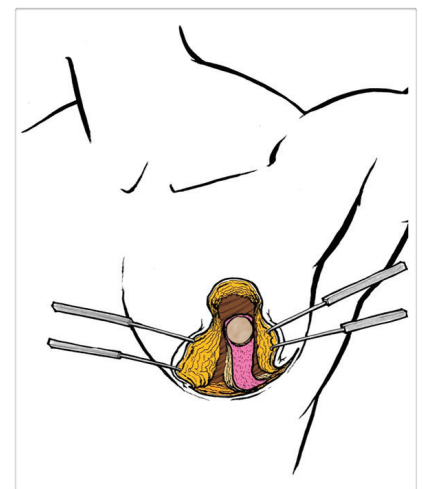
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The inception of breast conservation surgery and advances in oncoplastic techniques have transformed the management of retro areolar breast tumours. Cancers in this location were conventionally managed with central excision and primary closure or mastectomy. Lately, oncoplastic breast-conserving techniques such as the Grisotti mammoplasty have been increasingly encouraged as an alternative option as it allows oncological safe margin resections while restoring cosmesis. Using a Grisotti flap allows for safe resection of a retro areolar tumour with the simultaneous reconstruction of the defect using a local rotational advancement dermoglandular flap, allowing acceptable

results in terms of aesthetics contour and projection. The most common issues with the standard Grisotti were skin puckering and NAC asymmetry.

We describe a modification of the standard Grisotti flap is made such that it gives a fuller and ptotic lower pole appearance, avoiding both skin puckering of the tissues or skin, as well as any mismatch in the normal NAC (nipple-areola complex) size.

This study discusses Andrea Grisotti's original advancement-rotation flap and provides a technical modification made in our breast unit that aids wound closure and may improve the final aesthetic result of this operation.





***Rhus toxicodendron* extracts mimicking structure of staphylococcal protein A (SpA)**



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Background: *Staphylococcus aureus* secretes different surface membrane proteins amongst which staphylococcal protein A (SpA) is significant. The attachment of SpA to the Fab heavy chain (VH) region of immunoglobulin is a key factor in staphylococcal infections. Such a specific interaction is mediated by a number of identical repeats located at N-terminal region of SpA. Each repetition forms a triple helix structure, where the C-terminal helices interact with the target; thereby causing the opsonophagocytic killing of the B cells, serves to meddle with safe transformation, and its reaction towards a microbe. On the other side, this liking to bind with immunoglobulin goes about a possible contributing variable for the advancement in the treatment of auto-immune diseases. Alcoholic extracts of *Rhus toxicodendron* (RT) at various dilutions namely Mother Tincture (MT), 6CH, 30CH and 200CH, are regularly utilized in various skin, soft tissue infections and joint problems in clinical homeopathic practice. Urushiol is the most active component of RT which has many uses in drug industry. In this study we explored possibility of the Urushiol for an antagonistic action to SpA by docking and virtual screening study of Urushiol against SpA

besides laboratory study.

Materials and Methods: Initially we observed reactions when human IgG coated with Latex particle was challenged with alcoholic extracts *Rhus toxicodendron*. Thereafter we added 20µL buffy-coat suspension with leucocytes infected with *S. aureus* and 20µL alcoholic extracts of each dilutions of RT (MT, 6CH, 30CH & 200CH) one by one on glass slides. The resulted clumping were examined directly, under light microscope and under scanning electron microscope (SEM). We, then, characterized the optimized Urushiol compounds by molecular descriptors and molecular docking and virtual screening against the minimized target (SpA). After getting sufficiently stable score we also went for extraction of plant DNA from 10% ethanolic extracts of *Rhus tox* and analyzed their different sequences.

Results: Formation of clumps of latex particle coated immunoglobulin with RT extracts almost similar to binding of SpA was suggestive of structural similarity of SpA and active component of RT like Urushiol. Thereafter light microscope and SEM studies indicated reduction of leukocyte destruction with different dilutions of RT extracts when challenged directly. To explain this peculiar



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phenomenon, docking and virtual screening studies were done which demonstrated that Urushiol family of compounds are particularly effective in antagonizing D-domain's Fab binding region. Such interaction activity of Urushiol is largely determined by its descriptor properties.

Conclusion: The finding of our examinations are reminiscent of anti-staphylococcal properties of alcoholic extracts of RT and it additionally proposes that the extract impersonates the structure of SpA. To prevent pathogenicity of SpA, Urushiol family of compounds are, indeed, an effective lead molecule.

“Methylene blue for treatment of hospitalized covid-19, phase1, 2 and 3 clinical trials and rescue therapy”

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Objectives: Finding a safe and effective antiviral drug for treatment for COVID-19, since there is no consensus on specific pharmacological intervention.

Scope: Application of an oral Methylene blue mixture for treatment of hospitalized COVID-19 patients in randomized clinical trials (RCTs): phase 1, 2, 3 and rescue therapy study.

Results: Phase 1 showed the safety of MB (1); phase 2 showed that in the MB-group, a significant improvement was observed in SpO₂ and respiratory rate (RR) on the third-day and also the fifth-day. In the control-group, there was not a significant improvement of SpO₂ and RR on the third-day; but there was a significant improvement of SpO₂ and RR on the fifth-day. In the MB-group in comparison to the control-group, the rate-ratio of increased SpO₂ was 13.5 and 2.1 times on the third and fifth days, respectively. In the MB-group in comparison to the control-group, the rate-

ratio of RR improvement was 10.1 and 3.7 times on the third and fifth days, respectively. The hospital stay was significantly shortened in the MB-group, and the mortality was in the MB-group and control-group 12.5%, 22.5%, respectively (2); Phase 3 showed the hospital stay was significantly shortened in the MB-group in comparison to the control-group, and a marginal significant decrease in mortality was seen in the MB-group (12.2%) in comparison to control-group (21.4%) (3); In the rescue therapy study, 83 severe patients (in critical condition) who did not respond to antiviral drugs (Remdesivir, Interferon- β , and Favipiravir) underwent to MB therapy. 72 patients recovered completely, and 11 patients did not survive (4).

Methods: Patients were administered oral MB (1 mg/kg every 8 hours for two days, followed by 1mg/kg every 12 hours for the next days).



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Conclusion: MB is a low-cost and FDA-approved drug. It can be used as an adjunct therapy along with standard care protocols for the treatment of COVID-19. MB encapsulates many of the required mechanisms for treatment: 1) Antiviral activity against the SARS-CoV-2 virus; 2) Anti-hypoxemia activity in methemoglobinemia by converting the ferric (Fe^{3+}) state to the ferrous (Fe^{2+}) state; 3) Anti-

respiratory distress activity (bronchodilator property); 4) Inhibitor of nitrite production by inhibiting nitric oxide synthase and guanylate cyclase in activated macrophages; 5) Antimicrobial agent; 6) Inhibitor of reactive oxygen species; 7) Inhibitor of xanthine oxidase (which produces superoxide anion); 8) Anti-platelet aggregation drug; 9) Anti-inflammatory agent; 10) Antifungal agent.



Interleukin-6 differential expression in cancer patients of different clinical stages: A possible biomarker of cancer progression



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Purpose: The study investigated interleukin-6 expression pattern across all stages of cancer. The research questions raised in the study were: Is there differential expression of Interleukin-6 across all cancer stages? and what relationship exists between serum interleukin-6 level and cancer stage?

Methods: The prospective case-control study comprised sixty two (62) purposively selected cancer participants across all stages and age range 18 years to 72 years as well equal number of healthy volunteers from two medical centres in Nigeria. Three milliliters (3mls) of blood samples was collected intravenously from the participants and centrifuged after 30 minutes of collection at 3000rpm for 10 minutes to obtain serum. The serum level of Interleukin-6 was determined spectrophotometrically by

Enzyme linked immunosorbent assay (ELISA). Data obtained were expressed as mean and standard error of the mean. One way Analysis of variance and t-test were employed to test for significance difference between the groups and the significant level was considered at $P < 0.05$.

Results: Findings from the study revealed significant ($P < 0.05$) higher mean serum interleukin-6 levels in stage IV cancer participants as compared to other disease stages. In the same way, significant higher mean Interleukin-6 level of stage III cancer participants as compared to that of stage I cancer participants was observed. Furthermore, the study revealed a significant correlation ($P < 0.01$) between serum Interleukin 6 concentration and cancer stage.



The omega-3 and nano-curcumin effects on vascular cell adhesion molecule (VCAM) in episodic migraine patients: A clinical trial study



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Background: Migraine is a neurologic illness characterized by attacks of mild or severe headache and elevated level of blood endothelial factors such as vascular cell adhesion molecule (VCAM).

This study examined the effect of W-3 fatty acids (FAs), nano-curcumin and the combination of FAs and nano-curcumin on serum concentration and mRNA expression of VCAM in patients with episodic migraine.

Methods: This study was double-blind controlled trial. 80 patients were recruited and then were randomly divided into 4 groups to receive 1) W-3 FAs (N=19), 2) nano-curcumin (N=19), 3) combined W-3 FAs and nano-curcumin (N=17) and 4) placebo (control group) (N=19) for 2 months. VCAM-1 serum level and its gene expression were measured through ELISA and Real-time polymerase chain reaction (PCR) methods, respectively. Moreover, semi-3-day dietary recall method was used to assess energy intake. VCAM gene expression and serum concentration were measured by

real-time polymerase chain reaction (PCR) and ELISA method, respectively.

Results: Serum levels ($P=0.02$) and gene expression ($P=0.05$) of VCAM had remarkable decreases in the group 1. Furthermore, VCAM gene expression had stronger statistically significant reductions in people in group 3 ($P=0.001$ and $P=0.004$ for serum level and gene expression, respectively). Near to significant reduction in both serum level and gene expression of VCAM was observed in people in group 2 ($P=0.06$). However, no significant change existed in VCAM serum level and gene expression in patients in group 4 (control group).

Conclusion: According to the present findings, it appears that the W-3 and combined W-3 and nano-curcumin can relieve VCAM serum level and its gene expression in patients with episodic migraine. Moreover, the combination of W-3 FAs with nano-curcumin might cause more significant declines in these factors in these patients compared to when W-3 FAs are administered alone.



**Fractionated CO₂
laser treatment
for pearly penile
papules: Evaluation
of clinical results
and sexual health
quality of life
improve**



Pérez Rivera and Fabián

Private Practice, Argentina

Pearly penile papules (PPP) are acralangiofibromas, lesions in the epithelium of the corona of the glans penis. Although asymptomatic, benign and non-infectious nature, PPP can be a source of significant psychological distress to the patient and his sexual partner with a significant alteration of their sexual health quality. Between April 2017 and December 2019 a total of 20 male patients, ages from 18 to 54 yo (average of 29 yo), with PPP diagnosis, treated by fractionated CO₂ laser and evaluated for a period between 3 to 12 months completed a self-administered survey looking for changes in their sexual health quality of life (SHQL).

70% of enrolled patients indicated they had suffered, at least once in their life an embarrassing sexual situation due to their PPP, and 60% of them rated the way PPP altered their SHQL as very important to extremely important.

80% of patients had previously consulted

with another physician (70% by urologist). In the 75% of the cases the answer from the colleagues was that PPP are benign, non-treatable lesions.

The total of the 20 patients included in this study got a clinically successful treatment.

90 % of the patients evaluated the level of improve in their SHQL as successful: 45 % as extremely successful, 45 % as a lot successful and only 10 % reported poor results.

2 bleedings during the procedures were observed, which resolve only by compression.

In conclusions, PPP altered in an important grade young male SHQL and deserve a medical treatment. Majority of physicians minimize psychological effect and the impact of PPP in this population, and are not aware of available PPP treatments.

Fractionated CO₂ laser demonstrate to be a safe and effective PPP treatment.



Low post-arthroplasty infection rate is possible in developing countries: Long-term experience of local vancomycin use in Iran



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Background: Utilizing intrawound vancomycin powder in TKA surgery has yielded rather contrasting results in the current literature. Furthermore, CDC criteria, although effective in general, are not specifically designed for post-TKA infections. Here, we present a 7-year experience of vancomycin use in primary TKA in a high-volume tertiary knee center in Iran. Also, new criteria are proposed to detect suspected superficial post-TKA infections.

Methods: This is a retrospective analysis of primary total knee arthroplasties performed in a tertiary knee center, from March 2007 to December 2018, by a single senior knee surgeon. All patients with follow-up periods of less than 1 year were excluded from the study. Since March 2011, all patients received vancomycin (powder, 1 g) before water-tight closure of the joint capsule. A comparison

was made between this group and historical control subjects (operated from March 2007 to March 2011).

Results: Altogether, 2024 patients were included in the study. The vancomycin and the control groups included 1710 and 314 cases respectively. Patients were mostly women (male to female ratio, 1 to 4), with a mean age of 65.20 (SD = 10.83) years. In the vancomycin group, the rate of suspected SII (1.87%) and PJI (0.41%) was significantly lower than the control group ($P = 0.002$).

Conclusions: Our experience shows that application of local vancomycin during TKA surgery could be a reasonable infection prevention measure, although prospective randomized studies are required to evaluate its efficacy.



Correlations of mRNA-miRNA interaction between tumor and margin tissues in patients with breast cancer



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Background: Breast cancer is one of the three most common cancers worldwide. MicroRNA(miRNA) has been connected to kinds of cancer types like breast cancer. In this analytical article, we constructed an initial attempt to address the differential expression of the mRNA-miRNA interaction map between tumor and margin tissues samples.

Materials and Methods: The gene expression profiles for miRNA and mRNA were collected from Gene Expression Omnibus (GEO). Datasets related to genes (GSE61724, GSE86374, GSE37751) and miRNAs (GSE40525, GSE42072, GSE45666, GSE143564) were separately downloaded and analyzed by "R" software with the usage of "LIMMA". By using Cytoscape, the miRNA-

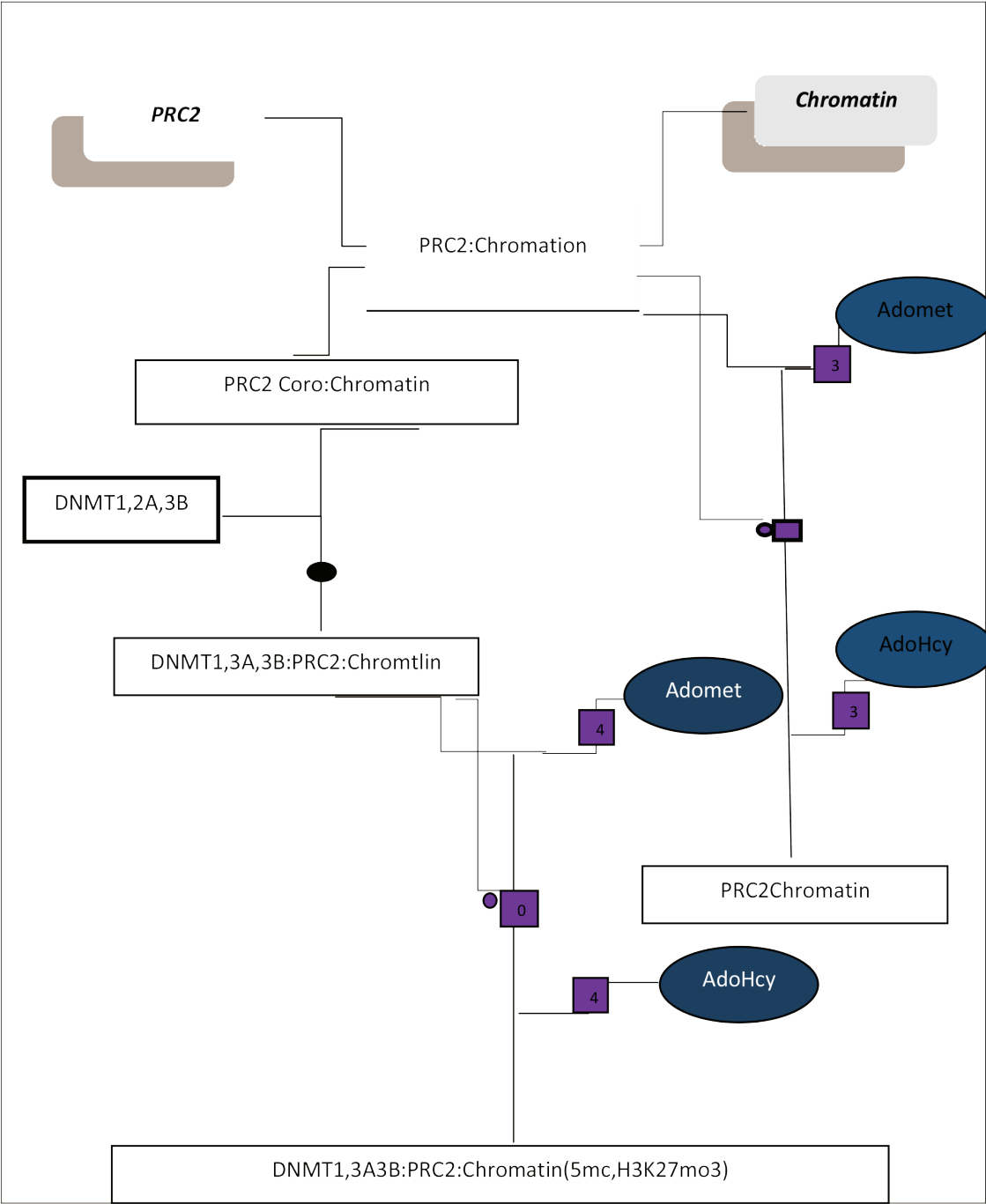
mRNA interaction and regulatory network were built. Enrichr and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analysis was applied to estimate the possible molecular mechanisms of DEGs. Dysregulated miRNAs were predicted by miRTarBase.

Results: Based on our result, 270 miRNAs and 325 mRNAs were differentially expressed. The enrichment results from analyzingDEmRNAs were shown to be associated with Methylation pathways.

Conclusion: Results show the prominent roles of miRNA- mRNA regulatory networks in breast cancer and revealed new prognostic and diagnostic approaches for better and more efficient treatment.

Mrna			miRNA			
GSE86374	GSE61724	GSE37751	GSE42072	GSE40525	GSE143564	GSE45666
325			270			

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Serum inflammatory markers in patients with multiple sclerosis and their association with clinical manifestations and MRI findings



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Inflammation in a myelinated portion of the nervous system is the mainstay of multiple sclerosis (MS). Elevation of inflammatory markers such as procalcitonin, ESR and hs-CRP is suspected to occur in MS patients. However, their prognostic role and their relationship with the severity of clinical symptoms of MS and MRI evidences has remained unnoticed in the literature. Hence, we aim to evaluate the serum level of inflammatory markers in the acute attack of MS patients and demonstrate the potential prognostic role of these inflammatory markers. This study was carried on case and control groups of definite MS patients. The cases were patients with active MS and were further allocated into four subgroups, while as control group included patients with non-active MS. Furthermore, all the participants underwent brain and cervical magnetic resonance imaging (MRI) using a contrast

agent. A significant difference was detected in hs-CRP level ($p = 0.009$) across the subgroups of the cases. The highest level of hs-CRP was reported in patients with cerebellar and brain stem symptoms (mean = 6998.13 ± 3501.16), while the lowest in patients with pyramidal and urinary incontinence symptoms (mean = 1958.91 ± 2662.16). Moreover, correlation coefficient between values of MRI contrast-enhanced lesions and ESR level was statistically significant ($R_s = 0.503$ and $p = 0.001$). Elevation of ESR serum level positively correlates with disease activity evidenced by values of contrast-enhanced plaques of MRI in relapsing–remitting MS patients which may predict the disease activity. In addition, MS relapse with cerebellar and brain stem symptoms is associated with a high concentration of hs-CRP plasma level.



Anti- β 2-glycoprotein i autoantibody expression as a potential biomarker for strokes in patients with anti-phospholipid syndrome



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Anti-phospholipid syndrome (APS) is an autoimmune disease. Cerebral ischemia associated with APS occurs at a younger age than typical atherothrombotic cerebrovascular disease and is often recurrent.

This study sought to determine the frequency rates of anti-cardiolipin (aCL) dependent on the presence of β 2-GPI, anti- β 2-glycoprotein I (a β 2-GPI), and anti-phosphatidyl serine (aPS) IgG autoantibodies among stroke patients. Stroke patients and control subjects recruited from Mosul, Erbil, and Dohuk provinces in Northern Iraq were evaluated. All cases were under 50 years-of-age and had no recognizable risk factors.

Using ELISA, the results indicated that the frequency of a β 2-GPI was 14/50 (28%), aCL was 11/50 (22%), and aPS was 9/50 (18%) among stroke patients. In contrast, aCL was

detected in 2/30 (6.7%) of control subjects; each of the other anti-phospholipid antibodies (APLA) was never observed. Of all the a β 2-GPI+ cases, the incidence of stroke patients having the combined profile of a β 2-GPI + aCL was 11/14 (78.6%) and of a β 2-GPI + aPS was 9/14 (64.3%). Only 2/14 (14.3%) of these a β 2-GPI+ patients also expressed aCL in the absence of aPS. In none of the APS/stroke patients were aCL or aPS expressed in the absence of the a β 2-GPI. Conversely, a β 2-GPI as a sole marker was seen in 3/14 (21.4%) of these patients (i.e., in absence of either other marker).

It can be concluded from these studies that among the three major forms of APLA examined, the presence of a β 2-GPI IgG autoantibodies appeared to correlate best with stroke in patients who were concurrently suffering APS.



Delays in the surgical pathway in breast cancer patients in Tunisia: A descriptive prospective study



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Background: With the increase of breast cancer incidence and the growing complexity of surgical treatments, there has been an increase in awareness of possible long delays for care access. In this context, exploring this surgical process is necessary in order to identify dysfunctions that may impact the quality and continuity of care.

Objectives: Describe the surgical pathway and identify the different waiting times to surgery of women with breast cancer in the Gynecology Department of the University Hospital of Sousse in Tunisia.

Methods: It is a descriptive prospective study based on an assessment of professional practices using the process approach method. The study focused on the surgical management of women with breast cancer followed and

scheduled for surgical treatment. The data were collected using a data collection sheet, developed according to a literature review.

Results: The sample consisted of 77 women. Ten waiting times have been calculated. Global time to first treatment (surgical treatment) was 78.5 days with an interquartile range (IIQ) of [55.5-113.25 days]. The information period was 10 days with an IIQ of [3-19 days]. The global time of access to surgery was 43.5 days with an IIQ of [40-54.75].

Conclusion: Delays in access to care appear to be a potential marker of inequalities in access to care and an indicator of the performance of the health care system and can influence patient prognosis. The reduction of these delays must be integrated into a continuous quality improvement approach.



**Clinical characteristics
of acute liver failure
associated with Hepatitis
A infection in children
in Mogadishu, Somalia:
A hospital-based
retrospective study**



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Background: Hepatitis A is one of the most common infectious causes of acute hepatitis, and currently, a neglected global public health problem necessitating an urgent response in Somalia. Hepatitis A infection and its rare complication of acute liver failure in children are largely based on very limited data. The aim of the study was therefore to investigate the Hepatitis A infection and its rare complication of acute liver failure in children in Somalia.

Methods: This retrospective study was conducted on children aged 0–18 years who were admitted to the pediatric departments of the Somalia Mogadishu-Turkey Training and Research Hospital, Somali, from June 2019 and December 2019. Patients who were tested for hepatitis A infection during the study period and had complete data were included. Children with chronic disease, primary or secondary immunodeficiency, blood transfusion history, and missing data were excluded. Abstracted data including patients' demographics, clinical presentation, laboratory results, ultrasonographic findings, length of hospital stay, clinical course and outcome were retrieved

from the hospital database system.

Results: Of the 13,047 children, 219 were analyzed. Of the 219 Hepatitis A cases, 25 (11%) were diagnosed with pediatric acute liver failure (PALF). The mean age of children with Hepatitis A was 6.7 years. The majority of cases were reported in the 5–9 (39.7%) year age range. Hepatic encephalopathy, length of hospital stay, levels of albumin, and values of PT, aPPT, and INR were significantly higher in children with acute live failure. The presence of cholecystitis and cholecystitis with ascites in the sonographic evaluation were poor prognostic markers for acute liver failure.

Conclusions: This study revealed hepatitis A virus infection and its related acute liver failure among hospitalized children in Somalia of which 11% had PALF. Hence, the introduction of Hepatitis A vaccination, which is the main public health tool, into the national immunization program, the improvement of hygiene conditions, raising awareness of the disease, and increasing health literacy are necessary to prevent the consequence of the Hepatitis A virus in children.



***Ginkgo biloba* extract
modulates hippocampal
signaling pathways
related to the regulation
of feeding behavior
in ovariectomized rats**



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Several studies have demonstrated that menopause contributes to the triggering of energy homeostasis disturbances, including in feeding behavior, which favor the development of obesity. However, there is no effective treatment that might be used as appetite modulator without generate important side effects. We have previously observed that Ginkgo biloba Extract (GbE) attenuated ovariectomy-related obesity, improving the hypophagic response of serotonin in the hypothalamus, and reducing serum leptin levels. Moreover, several anti-obesogenic properties of GbE were reported in diet-induced obese male rats, as well as the activity of GbE in increase anorexigenic effectors in the hypothalamus of normal male rats. Therefore, the present study investigated the GbE activity on hippocampal protein levels of 5-HT1A, 5-HT1B, 5-HTT, and leptin receptor

(LepR) in ovariectomized rats. 2-month-old Wistar female rats were ovariectomized (OVX) or Sham-operated. After 2 months, daily oral gavages were performed once a day with 500 mg.kg⁻¹ of GbE or vehicle for 14 days. GbE restored ovariectomy-induced decrease of 5-HT1A, and 5-HT1B protein levels in the hippocampus. Moreover, LepR hippocampal levels increased after GbE treatment, presenting similar levels of Sham rats. No changes were identified in 5-HTT levels. In summary, the present findings indicated that GbE improved the effectiveness of pivotal mechanisms involved in hippocampal generation of the negative feedback of food intake that were impaired by ovariectomy. Thus, GbE might be used to alleviate disturbances related to energy homeostasis in menopause, which may also favor the improvement of body profile.



**Effect of pomegranate
supplement on
menopausal symptoms
and quality of life in
menopausal women: A
double-blind randomized
placebo-controlled trial**



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Background: Menopausal symptoms have negative effects on different aspects of quality of life and impose a high cost on the health system. In traditional Persian medicine, pomegranate is recommended to alleviate menopausal symptoms.

Material and Methods: A randomized double-blind placebo-controlled trial was performed among 78 healthy women. Participants were interviewed three times: Before receiving the supplement/placebo, after completing the treatment, and after 3 weeks with no intervention. They filled out the demographic information sheet, modified-Kupperman index, and Menopause-Specific Quality of Life (MENQOL) questionnaires.

Results: The mean scores of the modified-Kupperman index and MENQOL characteristics before and after the treatment and after the follow-up period were significantly different between pomegranate and placebo groups in both modified-Kupperman and MENQOL scores ($P < 0.001$).

Conclusion: This study demonstrated that 4 weeks treatment with the pomegranate supplement significantly ameliorates the irritating symptoms of menopause and improves the quality of life in menopausal women even after 4 weeks medicine deprivation.



PeriOrbital hyperpigmentation's relation to neurology and mental health: Psychosis accompanying maladaptive daydreaming, and its treatment methods



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Kafrelsheikh University, Egypt

Objective: To test the hypothesis of the relation between POH and mental health.

Methods: We have studied the relationship between Psychosis accompanying MD and POH to a 17 years old female individual. We established some physical exercises to strengthen the eye and the eyelid muscles and to develop and construct new dopaminergic and excitatory neurotransmitters pathways in new neural networks; to enhance the effort of the visual cortex and the primary motor cortex to see the results if they would support the hypothesis. A 22-inquiries questionnaire was conducted on 22 participants about Maladaptive daydreaming accompanying mental health issues and Peri-Orbital Hyperpigmentation.

Results: In brain stimulation, POH decreased which means the individual has developed new circuits participating the visual cortex neurons in them. The muscles strength increased increasing the eyes' plasticity in addition to increasing the

plasticity/action potential of the frontal cortex. 68% of the individuals said they had POH which support the hypothesis consistency. $p\text{-value} = .06$. $p < .10$.

Conclusion: After analysis of the leading causes of POH and the experiment of the physical exercises and the ratio of confirming individuals with MD of having POH, we postulate that POH is related to mental illness due to insufficient effort on them that is caused by the low eyes activity and that frequently occur in Psychosis symptom (according to the 17 yo female individual), or any other mental disorder.

Discussion: The excess amount of Dopamine may lead to the hyperpigmentation of the eyelids due to the synthesis of eumelanin from levodopa in eyelids due to the lack of neural effort (Dopamine neurotransmitter consumption). It is supposed that the presence of ROS molecules in the eyelids area is a reason for the occurrence of POH.



Drug delivery system through alginate dermal scaffold loaded with hydroalcoholic extract of daphne mucronata improves dermal excisional wound healing: An experimental research



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Daphne mucronata (DM) has regenerative features. Alginate hydrogel (Alg), as a natural scaffold, acts as a drug delivery system. This study aimed to assess the probable regenerative effects of DM encapsulated in Alg dermal scaffold on skin wound healing. Seventy-two male mice were grouped as: control (normal skin with no experimental treatments), sham (only punched skin), margarine (only margarine ointment administration), Alg group (Alg hydrogel with no DM), margarineDM (margarine-based ointment with DM), and Alg-DM (DM encapsulated in Alg scaffold). DPPH assay was applied for phytochemical screening of DM. Cranial and cranial incisions of back were conducted for histological and gene expression evaluations, respectively. Alg scaffold was placed on wound and supported by a dressing pad. Tissue sampling was applied on 3, 7, 12, and 22 days of treatments. Collagen deposition, regeneration rate, angiogenesis and granulation, respectively, were assessed through hydroxyproline assay, caliper instrument, CD31

immunohistochemistry staining, and ImageJ software. Also, gene expression of MMP13, EGF, and bFGF was evaluated by real-time PCR. Data were analyzed using SPSS (V. 16), and graphs were drawn by GraphPad Prism (V.9, 2020) software. Antioxidant agents of DM were approved by the DPPH assay. Besides, it was found that DM restored the damaged dermal tissue and increased the expression of genes involved in wound healing significantly ($p < 0.05$) in 7 and 12 days of experiment in both groups of margarine-DM and Alg-DM than control. Application of hydroalcoholic extract of DM encapsulated in alginate hydrogel scaffold can accelerate skin tissue regeneration by induction of genes expression and histological tissue indices in dermal injuries. This study found that the Daphne mucronata extract encapsulated in alginate gel can accelerate wound healing by modulation of the expression of genes and tissue factors. This technique can be used in other pathologic skin-related conditions like diabetes or other non-skin injuries disorders.



Citrus flavonoids as covid-19 therapeutic agents



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The COVID-19 pandemic caused by SARS-CoV-2 that globally, as of 4:59pm CEST, 1 April 2022, there have been 486,761,597 confirmed cases of COVID-19, including 6,142,735 deaths, reported to WHO.

New evidence suggests that therapeutic drugs from safe natural sources focusing on antiviral agents may enhance the host immunity. Specific natural compounds like flavonoids, as phenolic compounds, demonstrated antiviral, whether they could inhibit SARS-CoV-2. Citrus fruit peel or wild citrus are rich in flavonoids and assumed to possess immunomodulatory activities against coronaviruses.

Based on experimental studies, naringin, major active constituent of citrus fruits, could inhibit the expression of the proinflammatory cytokines (COX-2, iNOS, IL-1 β and IL-6). The other mechanisms are suggested including the inhibition of COVID-19 main protease, 3C-like

protease (3CLpro), and reduction of angiotensin converting enzyme receptors activity.

The evidence indicates that hesperidin, a bioactive flavonoid abundant in citrus peel, could act as a high potent inhibitor of 3CLpro. Reductions in inflammatory markers was reported in human trials of hesperidin. Overall, the different combinations of herbs with multifaceted mechanism appear to be synergistic to attain desired therapeutic effects.

The use of plant extracts, as flavonoids, is assumed as useful for health, due to their synergistic effects, such as antioxidant, antiviral, anti-inflammatory, among others that must be considered and studied intensively. Therefore, future and more comprehensive studies are needed to help understand the role of flavonoids consumption in humans during a viral infection, especially in SARS-CoV-2 infection. However, the beneficial effects of citrus flavonoids still need to be confirmed in clinical trials.



How deep learning is empowering semantic segmentation



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²Northeastern University, China

Semantic segmentation involves extracting meaningful information from images or input from a video or recording frames. It is the way to perform the extraction by checking pixels by pixel using a classification approach. It gives us more accurate and fine details from the data we need for further evaluation. Formerly, we had a few techniques based on some unsupervised learning perspectives or some conventional ways to do some image processing tasks. With the advent of time, techniques are improving, and we now have more improved and efficient methods for segmentation. Image segmentation is slightly simpler than semantic segmentation because of the technical perspective as semantic segmentation is pixels based. After that, the detected part based on the label will be masked and refer to the masked

objects based on the classes we have defined with a relevant class name and the designated color.

In this paper, we have reviewed almost all the supervised and unsupervised learning algorithms from scratch to advanced and more efficient algorithms that have been done for semantic segmentation. As far as deep learning is concerned, we have many techniques already developed until now. We have studied around 120 papers in this research area. We have concluded how deep learning is helping in solving the critical issues of semantic segmentation and gives us more efficient results. We have reviewed and comprehensively studied different surveys on semantic segmentation, specifically using deep learning.



Piezo-surgery technique and intramuscular dexamethasone injection to reduce postoperative pain after impacted mandibular third molar surgery: A randomized clinical trial



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Background: Surgical extraction of the impacted mandibular third molar is commonly associated with postoperative pain, swelling, and trismus. Usually, rotatory instruments have been used for osteotomy, while Piezosurgery is an innovative technique introduced to overcome the weaknesses related to the conventional technique. Dexamethasone administration before the extraction of impacted third molars is an efficient way to reduce postoperative pain. The purpose of the study is to evaluate the effect of piezo-surgery and dexamethasone injection on postoperative sequelae after the surgical extraction of impacted mandibular third molars, and ultimately to compare their effect on reducing postoperative pain.

Methods: A randomized controlled clinical trial was conducted with a sample of 80 patients. Participants were divided into four groups: Group 1 (Conventional rotatory), Group 2 (Conventional rotatory with 8 mg dose of dexamethasone 30

min before surgery), Group 3 (Piezo-surgery), and Group 4 (Piezo-surgery with 8mg dose of dexamethasone 30 min before surgery). The outcome variables were surgical working time calculated in minutes, maximal mouth opening measured in millimeters using Vernier Caliper at baseline and day 3 and postoperative pain assessed using a Visual Analog Scale (VAS) on days 1, 3, and 7.

Results: The surgical working time was longer in piezo-surgery groups compared with the conventional rotatory instruments groups (15.82 ± 3.47 vs 23.33 ± 2.54 ; $P\text{-value} < 0.0001$). The lowest reduction in mouth opening between baseline and 3rd-day post-op was found in the Piezo-surgery with Dexamethasone group (mean difference = 5.0, $SD = 3.9$, $p\text{-value} < 0.0001$) followed by the Piezosurgery without Dexamethasone group (mean difference = 5.8, $SD = 4.5$, $p\text{-value} < 0.0001$) and the highest average was reported by the Conventional

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rotatory without Dexamethasone (mean difference =9.7, SD= 4.5, p-value <0.0001). In the four groups, the mean pain score was highest on the 1st day and gradually decreased over the following days. Comparison of the 1st and 3rd postoperative pain between groups revealed a lowest mean pain score in the Piezo-surgery with Dexamethasone group, followed by Conventional rotatory with Dexamethasone

group and a highest mean score in the Conventional rotatory without Dexamethasone group (P-value <0.0001).

Conclusion: The association of Piezosurgery osteotomy and Dexamethasone intramuscular injection could be an effective combination to reduce postoperative pain and trismus after impacted third molar surgery.



Photoluminescence of L-valine irradiated with 12.5 MeV electrons



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The processes of interaction of slow electrons with molecules that are part of DNA and RNA are the subject of intensive research [1]. Of particular interest is the study of the properties of valine molecules, an important component of DNA. Valine is important as a radioprotector in radiation therapy [2], with its participation, enzymes and nucleic acids are synthesized, which are involved in energy redox reactions at the cellular level. In addition, valine can be used as a model structure in studying the processes of interaction of ionized radiation with more complex biomolecular complexes (proteins, peptides).

We have studied the photoluminescence spectra of powdered L-valine (in the spectral region 400÷700 nm) excited by photons in the range 250÷380 nm. The experiment and measurement technique are described in detail in [3]. Here are the results of measuring the photoluminescence spectra of the L-valine, irradiated at room temperature by electrons with an energy of 12.5 MeV (density from $6.25 \cdot 10^{10}$ to $4.37 \cdot 10^{11}$ el/cm²) on the M-30 microtron. The range of

radiation doses was in the range of 0÷100 kGy. The photoluminescence spectra measured by us show two maxima at 445 and 503 nm. The intensity of the luminescence spectrum of irradiated valine differs significantly from that of non-irradiated. The dependence on the radiation dose is non-linear and has a maximum at 40÷50 kGy. In addition, the spectral intensity distribution changes on the wavelength scale, which may be associated with structural changes in the irradiated valine molecules. This suggests that the final state of valine molecules after irradiation depends not only on the absorbed dose, but also on the time of irradiation. To test this assumption, we measured the photoluminescence spectra of valine (dose 50 kGy, obtained during 6 min and 15 min), which differ. Thus, the final state of irradiated valine molecules depends not only on the absorbed dose, but also on the conditions (beam intensity, irradiation time). In the future, it is necessary to elucidate the role of structure restoration processes due to self-organization, chemical interaction, and clustering of structural segments of the valine molecule.



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