magnus Group

JOINT EVENT ON

PRECISION MEDICINE AND ORPHAN DRUGS

VIRTUAL EVENT

17-18 AUGUST 2023

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BOOK OF ABSTRACTS

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17-18 AUGUST

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ABSTRACTS

JOINT EVENT ON

PRECISION MEDICINE AND ORPHAN DRUGS

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Institute for Biotech & Global Health of RosBioTech and A.I. Evdokimov MGMSU, Russian Federation

Thank You All...

ABOUT
MAGNUS GROUP

Magnus Group (MG) is initiated to meet a need and to pursue collective goals of the scientific community specifically focusing in the field of Sciences, Engineering and technology to endorse exchanging of the ideas & knowledge which facilitate the collaboration between the scientists, academicians and researchers of same field or interdisciplinary research. Magnus Group is proficient in organizing conferences, meetings, seminars and workshops with the ingenious and peerless speakers throughout the world providing you and your organization with broad range of networking opportunities to globalize your research and create your own identity. Our conferences and workshops can be well titled as 'ocean of knowledge' where you can sail your boat and pick the pearls, leading the way for innovative research and strategies empowering the strength by overwhelming the complications associated with in the respective fields. Participation from 90 different countries and 1090 different Universities have contributed to the success of our conferences. Our first International Conference was organized on Oncology and Radiology (ICOR) in Dubai, UAE. Our conferences usually run for 2-3 days completely covering Keynote & Oral sessions along with workshops and poster presentations. Our organization runs promptly with dedicated and proficient employees' managing different conferences throughout the world, without compromising service and quality.

BOOK OF ABSTRACTS

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DAY 01

KEYNOTE FORUM

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Precision pharmacotherapy in the treatment of epilepsy – use of antiseizure medications and therapeutic blood level monitoring?

This presentation will explore what happens to a Patient With Epilepsy (PWE) when (s) he attends the Emergency Department (ED) of the local teaching hospital which often includes the administration of an Antiseizure Medication (ASM) that is not the ASM that the patient was taking before the presentation. By far the most common reason for the PWE to attend the ED is: as a consequence of a failure of compliance (with a breakthrough seizure); exposure to a provocateur, such as infection or metabolic derangement; or the experience of a stressful situation which provoked a seizure. There is a rule of thumb which dictates that intervention should not confound the treatment by unnecessarily adding another ASM which may evoke medication interactions. It is more productive to determine the root cause of the presentation and address that. There is a need to arrest any seizures that may occur, during the admission, but to only interfere with short term therapy to stop the seizure, rather than change the ASM that has/had worked, prior to presentation. This should be achieved with a short acting ASM, such as a benzodiazepine followed by a longer acting ASM, namely the ASM that the patient was already taking but, prior to administering the long acting ASM, it is advisable to take blood samples to: determine compliance; seek cause of infection or sepsis; and assess metabolic status, including toxicity, hepatic function, renal function and electrolyte balance. It may be necessary to consider EEG or cerebral imaging. The ASM should be administered by the easiest route, acknowledging that midazolam can be applied topically, via the nose or gums, and carbamazepine can be given rectally but not parenterally. 1 hour after administering the long acting ASM, repeat levels, aiming for a therapeutic level and checking all the ASMs which the patient should be taking, remembering potential interactions. Once samples have been taken for ASM there is little worry about medication overdose as this can be easily managed in hospital.

Audience Take Away Notes

- This presentation should allow the audience to reconsider how to manage epilepsy which presents to the Emergency Department
- Use of the ASM which the patient was taking before presentation is the optimal ASM to use upon presentation.
- Take samples before loading the patient with long acting ASMs
- Treat to a therapeutic level rather than a predetermined dosage
- Don't be afraid to recheck levels and readminister the ASM which is/was subtherapeutic
- Try to determine why the seizures occurred and keep the patient as an inpatient until satisfied that (s)he is stable

Roy G Beran

South Western Clinical School, University of New South Wales, Sydney, NSW, Australia

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Sechenov, Moscow First State University, Moscow, Russia

Biography

Roy G Beran is a neurologist and sleep physician and: Conjoint Professor of Medicine - University of NSW; Professor, School of Medicine, Griffith University, Queensland; Conjoint Professor, Western Sydney University; Professor, Sechenov Moscow 1st State University, Russia. Following Russia's invasion of Ukraine, he refused to re-sign with Sechenov University. He was inaugural Visiting Professor - International Research Institute of Health Law Sciences, Southern Medical University, Guangzhou. He published: ~400 papers, book chapters and letters; presented > 420 papers at meetings; wrote or edited 17 books; served on numerous editorial boards; is the editor in chief of the international journal, Medicine and Law.

Personalized and Precision Medicine (PPM) as a unique healthcare model to be set up through biodesign-driven and inspired biotech, translational applications and upgraded business marketing to secure the human healthcare, wellness and biosafety

A new and upgraded approach to the diseased states and wellness, and to re-shape tomorrow's healthcare whilst doing it today, resulted in a new global trend in the healthcare services, namely, Personalized and Precision Medicine (PPM). PPM as a Unique Entity demonstrating an integration of Fundamental, Healthcare & Life Scienc- es, Biodesign-driven BioTech, Translational ART and IT Armamentarium, is based on the new developmental strategy driven by Biomarkers- and Biotargeting-related biomachines. So, it would be extremely useful to integrate data harvesting from different databanks for applications such as pre-early predictive diagnostics, precise prognosti- cation and personalization of further treatment to thus provide more tailored measures for the diseases bodies and persons- at- risk resulting in improved outcomes and more cost effective use of the latest health care resources.

PPM as being the Grand Challenge to forecast, to predict and to prevent is rooted in a big and a new SCIENCE generated by the achievements of (i) Systems & Synthetic Biology; (ii) Biodesign- driven Translational applications and Biotech- driven Biomanufacturing; (iii) Bioindustry and Biomarketing of the next step generation. The latter, being a Grand Brick laid into the frame of National Bioeconomy, says and confirms that the efficiency and efficacy of the Bioeconomy are determined and dictated by the innovative trends,generated by fresh knowledge and their transfer into the scientific, bioindustrial and social areas to maintain the national stability and extensive development of the country.

The core strategic tool to operate the transdisciplinary approach is rooted in a unique tandem consisting of (i) Inte- grated platforms of Fundamental Sciences (Basics) and innovative OMICs biotechnologies on one hand, and (ii) The algorithms of Bioinformatics, on the other one.

Healthcare is undergoing a transformation, and it is imperative to leverage new technologies to support the advent of PPM. This is the reason for developing global scientific, clinical, social, and educational projects in the area of PPM and TraMed to elicit the content of the new trend. The latter would provide a unique platform for dialogue and collaboration among thought leaders and stakeholders in government, academia, industry, foundations, and disease and patient advocacy with an interest in improving the system of healthcare delivery on one hand and drug discovery, development, and translation, on the other one, whilst educating the policy community about issues where biomedical science and policy intersect.

Sergey Suchkov[1-6]*, Daniel Scherman[10], Shawn Murphy[7,8], David Smith[11], Hiroyuki Abe[9], Holland Cheng[12], Noel Rose[8,13]

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[12]T College of Biological Sciences, UC Davis, CA, United States of America

Biography

Sergey Suchkov was born in the City of Astrakhan, Russia, in a family of dynasty medical doctors. In 1980, graduated from Astrakhan State Medical University and was awarded with MD. From 1989 through 1995, Dr Suchkov was being a Head of the Lab of Clinical Immunology, Helmholtz Eye Research Institute in Moscow. From 1995 through 2004 - a Chair of the Dept for Clinical Immunology, Moscow Clinical Research Institute (MONIKI). At present, Dr Sergey Suchkov, MD, PhD, is: Professor and Chair, Dept for Personalized Medicine, Precision Nutriciology and Biodesign, the Institute for Biotech & Global Medicine of RosBioTech, Moscow, Russia. Professor, Dept for Clinical Immunology, A.I. Evdokimov Moscow State University of Medical and Dentistry, Moscow, Russia. Member, New York Academy of Sciences, USA. Secretary General, United Cultural Convention (UCC), Cambridge, UK. Dr Suchkov is a member of the: American Chemical Society (ACS), USA; American Heart Association (AHA), USA; European Association for Medical Education (AMEE), Dundee, UK; EPMA (European Association for Predictive, Preventive and Personalized Medicine), Brussels, EU; ARVO (American Association for Research in Vision and Ophthalmology); ISER (International Society for Eye Research); Personalized Medicine Coalition (PMC), Washington, DC, USA.

[13]Center for Autoimmune Disease Research, John Hopkins University, Baltimore, MD, USA and Director of the Center for the Study of Systems Biology, Georgia Institute of Technology and School of Biological Sciences, Atlanta, GA, United States of America

Pharmacogenomics: Current status and future directions

The goal of personalized medicine is to provide individualized treatment and to predict the clinical outcome of different treatments in different patients. Pharmacogenomics (PGx) is one of the core elements in personalized medicine. The basic concept is that interindividual variability in drug response is a consequence of multiple factors, including genomics, epigenomics, the environment and patient characteristics, such as gender, age and/or concomitant medication. PGx research has led to fundamental discoveries in the last decade, and a large resource of PGx traits has been generated in which variation in the gene sequence and/or variation in the expression of genes involved in the metabolism, transport and other targets are associated with alterations in drug response. Clinical important cancer drugs related to PGx information are thiopurines, 5-fluorouracil, tamoxifen, irinotecan etc. Very recent efforts deal particularly with the implementation of PGx into clinical practice based on existing guideline recommendations such as CPIC or DPWG. A new generation of technologies commonly named -Omics permits assessment of the entirety of the components of biological systems and produces an explosion of data and a major shift in our concepts of disease. These technologies will likely shape the future of health care. One aspect of these advances is that the data generated documents the uniqueness of each human being with regard to disease risk and treatment response. These developments have reemphasized the concept of personalized medicine.

Audience Take Away Notes

- The clinical impact of pharmacogenomics (PGx)
- The implementation of PGx into clinical practice
- Consideration of various omics technologies to foster personalized drug therapy
- The high potential to integrate artificial intelligence approaches into future research activities

Matthias Schwab

Dr. Margarete Fischer-Bosch- Institute of Clinical Pharmacology, Stuttgart, Germany

Departments of Clinical Pharmacology, and of Biochemistry and Pharmacy, University Tuebingen, Tuebingen, Germany

Biography

Matthias Schwab is professor and chair of Clinical Pharmacology, and heads the department of Clinical Pharmacology, University of Tuebingen and the Dr. Margarete Fischer-Bosch-Institute of Clinical Pharmacology, Stuttgart, Germany. He studied medicine, holds board certifications in Pediatrics and Clinical Pharmacology. He was visiting professor at St Jude Children's Res. Hosp., Memphis, US. Schwab's scientific interests focus on personalized medicine and pharmacogenomics (PGx) and the contribution of ADME genes for better understanding of drug response. Special interests lies in the application of Omics-technologies (e.g. genomics, epigenomics, metabonomics). He is involved in programs for the clinical implementation of research findings and acts as principle investigator of academically initiated drug trials. Schwab received numerous awards, and is member of the German National Academy of Sciences Leopoldina, the Academy of Sciences and Literature, Mainz, Germany, and the Academia Europaea. His scientific accomplishments result in > 400 peer reviewed publications and he serves as Editor-in-Chief of Pharmacogenetics & Genomics, Drug Research, and as Section Editor of Genome Medicine.

Designing and managing intelligent and interoperable precision medicine ecosystems

For meeting the financial, quality and safety challenges as well as expectations of the patients, health and social care systems around the globe currently undergo a transformation towards personalized, preventive, predictive, participative precision medicine (5PM), supported by technology. It considers individual health status, conditions, genetic and genomic dispositions in personal social, occupational, environmental and behavioral context, understanding the pathology of diseases and turning health and social care from reactive to proactive. For enabling communication and cooperation between all actors from different disciplines involved, using different methodologies, perspectives, intentions, languages, we shall understand and formally and consistently represent the multidisciplinary, highly complex and dynamic 5PM ecosystem. The outcome is a system-theoretical, architecture-centric, ontology-based, policy-driven approach for designing and managing intelligent and ethical 5PM ecosystems.

Habil Bernd Blobel

University of Regensburg, Medical Faculty, Regensburg, Germany and Visiting Prof. at Charles University Prague, First Medical Faculty, Prague, Czech Republic

Biography

Prof. Blobel studied Mathematics, Technical Cybernetics and Electronics, Theoretical Physics, Biocybernetics, Informatics, and Medicine at different universities in East Germany. He received the PhD degree in Physics, a habilitation in Medicine, and a habilitation in Medical Informatics. He was Head of the Physical Laboratory in Environmental Medicine at the Medical University Magdeburg and thereafter Head of the Medical Informatics Department and then Director of the Institute for Biometrics and Medical Informatics at the Medical Faculty of the Otto-von-Guericke University Magdeburg. In 2004, he became Founder and Head of the Health Telematics Project Group at Fraunhofer Society, Institute of Integrated Circuits, Erlangen, and finally Head of the German National eHealth Competence Center at the University of Regensburg. He is author of more than 450 scientific publications.

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SPEAKERS

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Ahmed Raza Khan

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Monitoring folds localization in ultra-thin transition metal dichalcogenides using optical harmonic generation

Folding is an effective technique to alter the optoelectronic properties of two-dimensional (2D) materials such as interlayer coupling, bandgap, etc. Optical techniques such as PL, Raman were used in the past to probe the folds localization. Here, we show that optical Second Harmonic Generation (SHG), which is sensitive to the crystalline symmetry of 2D materials, is a powerful probe to monitor the fold localization in TMDCs. Two dimensional 2H Transition Metal Dichalcogenides (TMDC) are particularly well-suited for the study because their SHG investigation has already been done, in additional, they can be easily folded due to their high flexibility. Our study includes the fabrication of clean folds on ultra-thin layers of TMDCs, optical characterization of the folds using SHG imaging and theoretical calculations to prove our findings. We find that SHG from the folds is a coherent superposition of the SHG from the individual layers of the fold, with a very small phase difference depending on the folding angle. The SHG response is theoretically calculated as a function of the folding angle. Our results establish SHG as an effective tool to monitor folds localization in 2D TMDCs.

Biography

Ahmed Raza Khan did his PhD from Australian National University. He is working as postdoctoral researcher in School of Engineering, Australian National University. His research interests include linear and nonlinear optics, strain- engineering of nano- materials and non-conventional machining process. He has published many papers, including in high impact journals like ACS Nano, Science Advances, Materials today, and Nano Letters, etc.

Natasha A. Bujang, Kavitha Palaniappan*, Silke Vogel, John C. W. Lim

Centre of Regulatory Excellence, Duke-NUS Medical School, Singapore

A systematic review of regulatory approaches for Direct- To- Consumers (DTC) genetic testing

Background: Genetic testing can be categorised into clinical and non-clinical genetic testing. A clinical genetic testing involves predictive screening or testing for a disease as well as purposes that purport to assess, diagnose, prevent, alleviate or treat a medical condition or disorder. On the other hand, non-clinical genetic testing which are usually available Direct To Consumers (DTC) refers to genetic testing for non- clinical purposes such as general wellness and recreational purposes (e.g. relationship testing, ancestry, innate behavioural traits/ lifestyle testing, nutrigenomics testing) which are not used to assess, diagnose, prevent, alleviate or treat a medical condition or disorder. Singapore adopts a caveat emptor approach, similar to other overseas jurisdictions such as the US and Australia, wherein clinical genetic tests cannot be offered as DTC tests. As DTC genetic testing becomes increasingly popular, concerns have been raised about the safety, accuracy and reliability of these tests, as well as the potential for misuse of genetic information. Regulatory bodies have responded by implementing various regulations or guidelines to ensure that DTC genetic testing companies meet certain standards for safety, accuracy, privacy, and transparency. For example, the Therapeutic Good Administration, Australia issued a guidance document on nutrigenetic tests.

Objective: The objective of this study is to identify the current regulations and/or guidelines, the rationale behind them as well as the challenges faced to provide recommendations for future regulations for DTC GT.

Methods: A systematic review was conducted to review all the existing guidelines and regulations on DTC GT. The search terms used for this study were 'direct to consumer,' 'genetic testing', 'regulation,' and 'legislation' and we expanded the search to incorporate any document in English that had the terms anywhere within the title or text. The evaluation included any document or paper that presented a position statement, policy, guideline, or recommendation for the use of DTC GT in any country and was prepared by a professional organisation or relevant authorities. Results: The electronic database search retrieved 913 documents which were subjected to title and abstract screening, narrowing it down to 104 documents. Full-text screening of the 104 documents narrowed the eligible documents to 26 based on the inclusion criteria of the study. The final 26 articles were screened for statements pertaining to regulations in various countries and were tabulated in an Excel spreadsheet. The findings show that France, Germany, Portugal and Switzerland have specific legislations that defines that medically purposed DTC genetic tests can only be carried out by a medical doctor whereas Belgium and the United Kingdom allow the provision of DTC genetic tests1. In Canada, DTC GT is not regulated, however there are laws governing dissemination and use of consumers' DTC GT results2. Bill S-201 which received Royal Assent and will soon become law stated that it prohibits the requirement that an individual submit to genetic testing or disclose the results of genetic tests in order to receive goods or services or in order to enter into or continue a contract or agreement, and it prohibits submission to genetic testing or disclosure of test results from being used as the basis of any specific conditions in a contract or agreement. In contrast, certain countries including

Korea, Japan and China have very specific guidelines. The Korean government, for example, approved DTC GTs only on 42 genes related to 12 specific phenotypic traits such as body mass index, cholesterol, blood pressure3.

Conclusion: This study identified the different approaches in the existing legislations and guidelines with respect to DTC GT. Some recommendations provided in these studies would be for policymakers to decide whether the present regulatory framework is adequate and to regulate the DTC-GT in proportion to their risks. Interestingly, guidelines or regulation addressing consumer education, codes of practice and test registries, which could enable to maintain the safety, accuracy and reliability of DTC GTs, remain sparse.

1. Pascal Borry, Rachel E van Hellemondt, Dominique Sprumont, Camilla Fittipaldi Duarte Jales, Emmanuelle Rial-Sebbag, Tade Matthias Spranger, Liam Curren, Jane Kaye, Herman Nys and Heidi Howard, (2012) Legislation on direct-to-consumer genetic testing in seven European countries.

2. Cernat, A.; Bashir, N.S.; Ungar, W.J., (2022) Considerations for developing regulations for direct-to-consumer genetic testing: a scoping review using the 3-I framework.

3. Ilda Hoxhaja, Jovana Stojanovica; Michele Sassanoa; Anna Acamporaa; Stefania Bocciaa; (2020) A review of the legislation of direct-to-consumer genetic testing in EU member state.

Audience Take Away Notes

- Regulations/ guidelines in place in various countries
- Challenges faced in regulating DTC-GT e.g. how data privacy remains a concern in regulating DTC-GT
- Recommendations for future regulations of DTC-GT
- Recommendations in ensuring safety, welfare and privacy of consumers using DTC-GT

Biography

Assistant Professor Dr. Kavitha Palaniappan is the project lead for Health services Regulation at the Centre of Regulatory Excellence at Duke-NUS Medical School, Singapore. She is currently working on identifying the regulatory gaps with respect to the new trends in the health services sector. Apart from this, Dr. Palaniappan is also actively involved in multi-disciplinary research, including the prevalence of psychosocial illnesses and their impacts on society, economy and country. She also researches on the toxicity of nanomaterials, exposure measurements and hygiene requirements for nano-titanium dioxide. Educational Qualifications: BSc Microbiology (University of Madras, India), MSc Environmental Science (Anna University, India), MA French (English and Foreign Languages University, India), Bachelor of General Laws (Madurai Kamaraj University, India), Bachelor of Alternative System of Medicines (Indian Institute of Alternative Medicines, India), MA Public Administration (Tamil Naidu Open University, India), PhD Allied Health Sciences (Sri Ramachandra Medical University, India).

Awards:

Excellence in Teaching Award, University of Newcastle, Australia.

Masters (Public Administration) Gold Medal.

Career History:

2010 – 2022: Various positions from Associate Lecturer to Associate Professor and Academic Director, Newcastle Australia Institute of Higher Education (Singapore entity of the University of Newcastle, Australia).

2022 – Present: Assistant Professor, Centre of Regulatory Excellence, Duke-NUS Medical School.

Pei-Ting Sarah Chou
Taiwan Chapter of Regulatory Affairs Professionals Society, Hsinchu City, Taiwan

Regulatory framework of in vitro diagnostic and artificial intelligence for precision medicine

First, the existing regulatory frameworks for in vitro diagnostic and artificial intelligence medicinal products will be examined. Among those medicinal products of in vitro diagnostic and artificial intelligence, the ones characterized as precision medicine, or personalized medicine, will be evaluated from the aspects of the policy of health authorities and the needs of users. Second, the challenges encountered during the COVID-19 pandemic for developing and utilizing the medicinal products of in vitro diagnostic and artificial intelligence for precision medicine within the current regulatory framework will be pointed out and discussed. Third, recent breakthroughs of precision medicinal technology within the domains of in vitro diagnostic and artificial intelligence will be reviewed so that the evolving roles of regulatory agencies will be discussed. Next, concerns about the tolerance of the risk and the needs of the patients for these recent breakthroughs of precision medicinal technology within the domains of in vitro diagnostic and artificial intelligence will be raised and assessed, especially for the medicinal products of in vitro diagnostic and artificial intelligence with early interventions for life-threatening diseases. Corresponding to this part, the existing regulatory frameworks for in vitro diagnostic and artificial intelligence medicinal products will be reviewed and assessed accordingly. Last, several perspectives of precision medicinal products in terms of opportunities and challenges will be identified, which includes aspects of the good practice of precision medicine, the ethical consideration, the future advancement of regulatory framework, and the breakthrough of precision medicine technology within the realm in vitro diagnostic and artificial intelligence after the COVID-19 pandemic.

Audience Take Away Notes

- Current regulatory framework
- How practical approaches can be adopted to advance the development of precision medicine technology within the current regulatory framework
- Future advancement of regulatory framework and good practice to counteract the breakthrough of precision medicine technology and the needs of patients

Biography

Sarah is a U.S./Taiwan certified regulatory professional and ISO13485/ISO9001 lead auditor with European regulatory trainings funded by DAAD and British Council. She is the founding Board of Director at Regulatory Affairs Professional Society (RAPS) Taiwan and Quantic Law Society. As the author of International Regulatory Affairs books published by RAPS, she has led the teams at North American, European & Taiwanese firms as regulatory head to pass audits conducted by health authorities from around the globe. Having delivered some health authority training programs, she is also a reviewer of International Production Journal and a medical writer of scientific communication agency.

Nurul Syakima Ab Mutalib[1,2,3]*, Francis Yew Fu Tieng[1], Nadiah Abu[1], Sazuita Saidin[1], Zairul Azwan Mohd Azman[4], See Hui Shien[5], Edward Chee[6], Muhd Khairul Luqman Bin Muhd Sakaff[7], Learn-Han Lee[2,8]

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Unraveling cancer stem cell signatures in circulating tumor cells of metastatic colorectal cancer: Investigating ALDH1A1 and the repurposing potential of disulfiram via scRNA-seq

Colorectal Cancer (CRC) metastasis remains a significant challenge, and the presence of Cancer Stem Cells (CSCs) within Circulating Tumor Cells (CTCs) plays a critical role in this process. This study aimed to unravel the cancer stem cell signatures in CTCs of metastatic colorectal cancer, with a particular focus on investigating ALDH1A1 expression and exploring the potential repurposing of disulfiram as a therapeutic agent. Using single-cell RNA sequencing (scRNA-seq), we successfully captured and analyzed CTCs from a cohort of metastatic colorectal cancer patients. Initial results revealed the capture of 800 CTCs, with a median number of genes per cell of 560.5 and a median UMI count per cell of 1091. After stringent processing, the estimated number of cells became 548 CTCs, with a total number of genes of 20582, a median number of genes per cell of 846, and a median UMI count per cell of 1297. Through clustering analysis, we identified five distinct cell clusters within the CTC population. To investigate their stemness properties, we examined these clusters for the expression of 43 cancer stem cell-associated markers. Notably, ALDH1A1, a gene of increasing interest due to its potential in drug repurposing using disulfiram, emerged as a prominent marker in cluster 0 and cluster 1. ALDH1A1 expression was detected in more than 16% of cells, with 60 cells specifically expressing ALDH1A1. The identification of ALDH1A1- expressing CTCs provides valuable insights into the potential targeting of CSCs in metastatic colorectal cancer. Disulfiram, an ALDH1A1 inhibitor, has shown promise in inhibiting CSCs in other cancer types. The co-expression of ALDH1A1 in CTCs suggests the potential repurposing of disulfiram as a therapeutic strategy for targeting CSCs in metastatic colorectal cancer. This finding opens doors for further investigations into the efficacy and safety of disulfiram in preclinical and clinical settings. In conclusion, our study demonstrates the successful identification and characterization of ALDH1A1-expressing CTCs in metastatic colorectal cancer using scRNA-seq. The presence of ALDH1A1-positive CTCs suggests their potential role as CSCs in driving metastasis and therapeutic resistance. Moreover, the repurposing potential of disulfiram as an ALDH1A1 inhibitor highlights a promising avenue for precision therapy in metastatic colorectal cancer. Future directions include functional studies to validate the role of ALDH1A1- expressing CTCs as CSCs, elucidating the mechanisms underlying their metastatic potential, and investigating the efficacy of disulfiram in targeting ALDH1A1-positive CSCs. The findings presented here have implications for personalized treatment approaches and the development of novel therapies to combat metastatic colorectal cancer.

Audience Take Away Notes

- Audience can gain insights into the potential role of ALDH1A1-positive CTCs in driving metastasis and therapeutic resistance
- Audience can understand the implications of repurposing disulfiram and its potential impact on targeted therapy
- Audience can learn about the utility and potential of scRNA-seq in studying CTCs and cancer stem cells
- Researchers and clinicians can explore the use of ALDH1A1 as a potential biomarker or therapeutic target in metastatic colorectal cancer, enhancing their understanding of cancer stem cells' role in disease progression
- The findings can guide the development of future studies and clinical trials investigating the efficacy and safety of disulfiram as a targeted therapy in metastatic colorectal cancer
- Educators and faculty members can incorporate the research findings into their teaching and expand their curriculum on cancer stem cells and the potential repurposing of existing drugs
- Researchers and clinicians can gain insights into potential therapeutic strategies for targeting cancer stem cells and improving treatment outcomes in metastatic colorectal cancer
- The findings can contribute to the development of personalized treatment approaches and the identification of novel therapeutic targets
- The research may inspire further investigations and collaborations among researchers in the field of metastatic colorectal cancer and cancer stem cell biology
- Other benefits
    - The research presents a potential avenue for repurposing an existing drug, disulfiram, to target ALDH1A1- positive cancer stem cells, potentially providing a cost-effective and readily available therapeutic option
    - The findings highlight the importance of studying CTCs and cancer stem cells for a comprehensive understanding of cancer progression and treatment resistance
    - The research contributes to advancing the field of single-cell genomics and its application in characterizing CTCs and cancer stem cells, potentially benefiting future studies in various cancer types

Biography

Dr. Syakima is an accomplished researcher in Molecular Medicine, Molecular Biology, and Cancer Research, specializing in Noncoding RNA, Epigenetics, Molecular Diagnostics, and Next Generation Sequencing. She has published 105 journal articles, 6 book chapters, and authored 3 books, establishing her expertise. Her international recognition is highlighted through collaborations with esteemed institutions and as a visiting fellow at the Institute of Genomic Medicine. Dr. Syakima's contributions have been acknowledged with prestigious grants and awards from organizations like Qiagen Malaysia, the Korean Cancer Association, and the Hong Kong Institute of Digestive Disease. She is also an adjunct senior lecturer at Monash University Malaysia.

Francis Yew Fu Tieng[1]*, Nadiah Abu[1], Sazuita Saidin[1], Zairul Azwan Mohd Azman[2], See Hui Shien[3], Edward Chee[4], Muhd Khairul Luqman Bin Muhd Sakaff[5], Learn-Han Lee[6,7] and Nurul Syakima Ab Mutalib[1,6,8]

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Deciphering tumour heterogeneity and transcriptomic profiles of circulating tumor cells in archived metastatic colorectal cancer samples via single-cell mRNA sequencing

Molecular single-cell analyses have revolutionised the current understanding of complex biological processes by revealing rare cell populations, including Circulating Tumour Cells (CTCs), that were previously masked by bulk analyses. While CTCs have proven to be valuable prognostic markers for Metastatic Colorectal Cancer (mCRC), their characterisation at the singe cell level remains limited.

Purpose: This study aimed to perform an in-depth characterisation of CTCs in mCRC via single-cell RNA-sequencing (scRNA-seq).

Methods: Thirteen out of 60 CRC patients were identified via a CTC biomarker panel - the MILLIPLEX® MAP kit-human circulating cancer biomarker magnetic bead panel 4. Pure CTC suspension from pooled PBMC samples was then isolated via an antibody-free negative enrichment using the EasySep human CD45 depletion kit II. Single CTCs were sorted and barcoded using BD Rhapsody single-cell analysis system, followed by whole transcriptomics amplification and NextSeq sequencing. Bioinformatic analyses were performed using Seven Bridges, ICARUS and GeneCodis4 online analysis tools.

Results: Three potential serum markers for CTC screening (L1CAM, CA9, HPN) in mCRC were identified, and 507 single CTCs with a 0.9% cell multiplet rate were captured. Six distinct CTC clusters were identified, and differential expression analyses highlighted the significant overexpression of the MALAT1 gene across multiple clusters. A comparison between clusters 4 and 1 revealed four significant differentially expressed genes including SLC4A1 and BCL2L1, associated with CRC proliferation, cell cycle and apoptosis. Gene ontology and pathway analyses predicted the interference of PABPC1 in the nonsense-mediated decay pathway, potentially inhibiting MALAT1 degradation through NF-κB and TGF-β signalling pathways mediated by UPF1. Co-expression of PABPC1 and MALAT1 shows promise as a potential biomarker signature for mCRC CTCs. Additionally, CD74 was found to contribute to the survival of tumour cells by evading immune attacks through immunoediting surface antigen presentation.

Conclusion: scRNA-seq identified unique genes associated with CRC metastasis, highlighting the presence of tumour heterogeneity within CTCs from mCRC. These findings have significant implications for the development of liquid biopsy-based methods in identifying biomarkers for mCRC and guiding personalised treatment approaches in the future.

Keywords: Single-Cell RNA-Sequencing, Circulating Tumour cells, Colorectal Cancer, Archived Samples.

Audience Take Away Notes

- Cancer cells from blood samples of patients with late-stage colon cancer, contain important information that can help personalise cancer treatment
- This research demonstrates that archived Circulating Tumour Cells (CTCs), even those stored for over five years, can be effectively used for single-cell RNA sequencing. This finding is valuable for other researchers as it simplifies the sample collection process, allowing them to utilise existing archived samples for single-cell analysis. By showing the feasibility of using long-term stored samples, this study provides a cost-effective and efficient approach for future research in the field
- The identification of potential serum markers (L1CAM, CA9, HPN) for CTC screening in late-stage colon cancer, provide insights into the development of non-invasive diagnostic approaches
- The discovery of distinct CTC clusters and differential gene expression patterns related to cancer proliferation, metastasis, and drug resistance, highlights the existence of tumour heterogeneity

Biography

Francis Tieng Yew Fu holds a degree in Biomedical Science and a Master's degree in Medical Biotechnology from Universiti Putra Malaysia. He then joined the research group led by Assoc. Prof. Dr. Nurul Syakima Ab Mutalib at Universiti Kebangsaan Malaysia (UKM). Francis made a significant breakthrough by successfully capturing single cancer cells from the bloodstream of late-stage colon cancer patients. He obtained his PhD in 2023. Francis published over 12 journal articles, multiple pending copyrights, was awarded the Young Researcher Award at the International Microbe and Diagnostic Forum 2022 and serves as the Vice President of the UMBI Postgraduate club.

Yuji Yokouchi*, Takumi Era
Division of Stem Cell Modification, Institute of Molecular Embryology and Genetics, Kumamoto University, Kumamoto, Japan

Genome editing for precision medicine: Revolutionizing medicine

Precision medicine refers to personalized medicine that provides medical care tailored to the individual based on his or her individual constitution. One of the promising tools is genome editing with CRISPR-Cas system, which enables modification of specific genes in an individual's genome. In this presentation, we will explore the potential of precision medicine through genome editing, focusing on its applications, benefits, and ethical considerations. We will also introduce One-SHOT, an allele-specific single nucleotide substitution method we have developed, and discuss its limitations and future prospects.

Application of Genome Editing in Precision Medicine: Genome editing has the potential to revolutionize the treatment of various genetic diseases. By using genome editing tools to precisely modify genetic information, scientists can correct or eliminate disease-causing mutations. This approach is effective for diseases in which a single genetic mutation is the primary cause, such as sickle cell disease, cystic fibrosis, and muscular dystrophy. In addition, genome editing can be used in cancers where specific genetic mutations promote tumor cell growth, as a targeted therapy for cancer.

Advantages of Precision Medicine Through Genome Editing: precision medicine through genome editing has a clear advantage over conventional methods. It treats the genetic mutation that causes a specific disease at the genome level, thus enabling a fundamental cure. By applying this method to tissue stem cells, genomic medicine at the somatic cell level can be realized. Application of this method to germ cells will prevent the transmission of genetic diseases to offspring, which was not possible with the conventional method, and consequently eradicate genetic diseases from future generations.

Ethical Considerations: Ethical issues must always be considered regarding the application of genome editing in human cells. One such issue is the potential for genetic modification to have unintended and unknown effects on an individual's health. Furthermore, in the case of germline applications, a serious ethical dilemma arises. This is because there is concern that slight off-target effects could have potential, long-term effects on the gene pool. Therefore, clear guidelines and regulations for the use of this technology are needed before it can be operationalized as a formal therapy.

Challenges and future prospects: There are several technical challenges that need to be solved to realize precision medicine through genome editing. The first is that the performance of editing tools is still insufficient. Careful design and functional confirmation of the guide sequence is necessary to prevent off-target effects because of its insufficient target discrimination ability of the guide sequence of CRISPR-Cas, as we have reported in the One-SHOT. Second is the efficient delivery of genome editing tools to target cells. Researchers are actively exploring various delivery methods, such as viral vectors and nanoparticles, to optimize the efficiency of gene editing.

Looking ahead, precision medicine through genome editing has great potential to transform healthcare. Continued refinement and development of gene editing technologies will pave the way for personalized therapies that will improve patient quality of life and reduce the burden of hereditary diseases.

Audience Take Away Notes

- The audience will learn briefly about the issues to be considered in Precision Medicine through genome editing
- This presentation will provide information on the principle and overview of One-SHOT, an allele-specific single nucleotide substitution method invented by the author, which will be useful for the audience's research
- This presentation will provide information on simple screening methods to identify edits
- This presentation will provide information on the design of editing tools to improve the accuracy of genome editing

Biography

Dr. Yokouchi studied Biology at Tohoku University, Japan, then joined the research group of Prof. Obinata at the Research Institute for Tuberculosis and Leprosy, Tohoku University. He received his PhD degree in 1992. After post-doctoral fellowships supervised by Dr Kuroiwa at Nagoya University and supervised by Dr Clifford Tabin at Harvard Medical School, he obtained the position of an Professor at Kumamoto University in 2000. After conducting stem cell research at Fukushima Medical University, currently, he is deepening his research on repairing disease-specific stem cell. He has published more than 30 research articles in Developmental Biology and Stem Cell Biology.

Yongping Zhang[1], Shuting Jiang[2,3], Fuhong He[2,3]*, Yuanyuan Tian[1], Haiyang Hu[2,3], Li Gao1, Lin Zhang[2,3], Aili Chen[2,3], Yixin Hu1, Liyan Fan[1], Chun Yang[4], Bi Zhou[5], Dan Liu[2], Zihan Zhou[2,3], Yanxun Su[2,3], Lei Qin[2,3], Yi Wang[1], Hailong He[1], Jun Lu[1], Peifang Xiao[1], Shaoyan Hu[1], Qian-Fei Wang[2,3]

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Single-cell transcriptomics reveals multiple chemoresistant properties in leukemic stem and progenitor cells in pediatric AML

Background: Cancer patients can achieve dramatic responses to chemotherapy yet retain resistant tumor cells, which ultimately results in relapse. Although xenograft model studies have identified several cellular and molecular features that are associated with chemoresistance in Acute Myeloid Leukemia (AML), to what extent AML patients exhibit these properties remains largely unknown.

Results: We applied single-cell RNA sequencing to paired pre- and post-chemotherapy whole bone marrow samples obtained from 13 pediatric AML patients who had achieved disease remission, and distinguished AML clusters from normal cells based on their unique transcriptomic profiles. Approximately 50% of leukemic stem and progenitor populations actively expressed Leukemia Stem Cell (LSC) and Oxidative Phosphorylation (OXPHOS) signatures, respectively. These clusters had a higher chance of tolerating therapy and exhibited an enhanced metabolic program in response to treatment. Interestingly, the transmembrane receptor CD69 was highly expressed in chemoresistant Hematopoietic Stem Cell (HSC)-like populations (named the CD69+ HSC-like subpopulation). Furthermore, overexpression of CD69 resulted in suppression of the mTOR signaling pathway and promotion of cell quiescence and adhesion in vitro. Finally, the presence of $CD69^{+}$ HSC-like cells was associated with unfavorable genetic mutations, the persistence of residual tumor cells in chemotherapy, and poor outcomes in independent pediatric and adult public AML cohorts.

Conclusions: Our analysis revealed LSC and OXPHOS as two major chemoresistant features in human AML patients. CD69 may serve as a potential biomarker in defining a subpopulation of chemoresistant LSCs. These findings have important implications for targeting residual chemo-surviving AML cells.

Audience Take Away Notes

- Implications for targeted therapy and treatment strategies:
- By elucidating the chemoresistant properties of leukemic stem and progenitor cells, our research offers potential avenues for developing targeted therapies. The audience will understand how this information can be applied to design novel treatment strategies that specifically target and overcome chemoresistance, potentially improving the outcomes for pediatric AML patients
- Practical implications for clinical decision-making:
- The identification of multiple chemoresistant properties in leukemic stem and progenitor cells

has practical implications for clinical practice. The insights gained from our presentation may help clinicians make more informed treatment decisions, such as personalized therapy selection or the development of combination treatment approaches that target specific chemoresistant mechanisms

- Enhancing research and teaching in the field:
- Our research findings provide valuable insights for other faculty members and researchers working in the field of pediatric AML. By expanding their knowledge of the chemoresistant properties of leukemic stem and progenitor cells, they can incorporate this information into their own research projects and teaching materials, fostering further advancements in the field

Biography

Dr. Fuhong He pursued her studies in Genomics under the guidance of Dr. Jun Yu at the Beijing Institute of Genomics, Chinese Academy of Sciences (BIG, CAS). She successfully completed her Ph.D. in 2009. Subsequently, she joined the research group of Prof. Qian-fei Wang at BIG, CAS and China National Center for Bioinformation (CNCB). In 2015, she was appointed as an Associate Research Professor. Her research focus has revolved around the application of bio-informatic methods and high-throughput omics technologies to gain insights into the biology of leukemia. She has published over 20 research articles in SCI journals.

Guo Wei He*, Zhuo Chen, Huan Xin Chen, Hai Tao Hou, Xiu Yun Yin, Qin Yang

The Institute of Cardiovascular Diseases & Department Cardiovascular Surgery, TEDA International Cardiovascular Hospital, Tianjin University & Chinese Academy of Medical Sciences, Tianjin, China

Genetic variants of the CITED2 gene promoter in sporadic tetralogy of fallot patients with clinical implications

Background: Tetralogy Of Fallot (TOF) is a common congenital heart malformation. Genetic variants in the CITED2 coding region is known to be significantly associated with cardiac malformation, but the role of variants in the CITED2 promoter region in the development of TOF remains unclear.

Methods: In this study, we investigated CITED2 promoter variants in the DNA of 605 subjects, including 312 TOF patients and 293 unrelated healthy controls, by Sanger sequencing. The discovered variants were further verified by cellular functional studies to examine the pathological role. JASPAR database analysis was used to predict the possible transcription factor binding sites that may result in changes in CITED2 protein expression.

Results: We identified nine CITED2 gene promoter variants (including one novel heterozygous variant). Six were found only in patients with TOF and none in the control group. The transcriptional activity of CITED2 gene promoter in mouse cardiomyocytes (HL-1) was significantly altered by the 6 variants ($P<0.05$). The results of electrophoretic mobility change assay and JASPAR database analysis showed that these variants generated or destroyed a series of possible transcription factor binding sites, resulting in changes in CITED2 protein expression.

Conclusion: We conclude that CITED2 promoter variants in TOF patients affect transcriptional activity and may be involved in the occurrence and progression of TOF. These findings may provide new insights into molecular pathogenesis and potential therapeutic insights of precision medicine in patients with TOF.

Audience Take Away Notes

- The audience will be able to use genetic knowledge in the diagnosis of congenital heart disease
- To help precision diagnosis of tetralogy of Fallot
- To help other faculties enhancing genetic studies in congenital diseases
- Will improve the accuracy of diagnosis of congenital heart disease
- Will help understanding the role of gene promoter in physiology and pathophysiology of diseases

Biography

Dr. Guo-Wei Current research focused on genomics, transcriptomics, proteomics, and metabolomics in cardiovascular diseases. Performed more than 7,000 open heart operations. Obtained more than 80 research grants. “He Classification” and “He solutions” for CABG grafts. First Class Award, Tianjin Municipal Natural Science Award, 2012. First Class Award, Prize of Science & Technology, The China Medicine Education Association, 2021. Published 409 articles/reports in SCI(E)-index international journals. Ranked in World's Top 2% Scientists (1999, 2020, 2021, 2022) Google scholar citation = 10,654 H-index: 55 i10 Index: 200.

Isabella Friis Jorgensen PhD*, Soren Brunak PhD

Novo Nordisk Foundation Center for Protein Research, University of Copenhagen, Copenhagen, Denmark

Time-ordered comorbidity correlations identify patients at risk of MIS- and overdiagnosis

Unfortunately, diagnostic errors are common, and the increasing co-occurrence of diseases also increases the risk of erroneous diagnoses. We present a data-driven, generic approach for identifying patients potentially at risk of being mis- or over-diagnosed, here exemplified by Chronic Obstructive Pulmonary Disease (COPD). Literature based on a manual review of patient records estimated that 5–60% of all COPD cases are misdiagnosed. Hence, there is an urgent need to systematically identify patients at risk of mis- and over-diagnosis. Here, we have used the Danish National Patient Registry (NPR), which contains hospital diagnoses for 6.9 million patients for the entire Danish population over 21 years. We applied a previously published method to identify frequent disease trajectories comprising time-ordered comorbidities for the 284,154 patients diagnosed with COPD in the NPR. Interestingly, as many as 42,459 patients did not present with these time-ordered, common comorbidities. Comparing the individual disease history for each of these non-followers to the significant COPD trajectories, demonstrated that 9,597 patients were very unusual. Survival analysis demonstrated that this group of patients died significantly earlier than the 'average' COPD patients following a trajectory. Of the 9,597 patients, we identified one subgroup comprising 2,185 patients at risk of being misdiagnosed with COPD without the typical events of COPD patients. In all, 10% of these patients were diagnosed with lung cancer, and it seems likely that they are underdiagnosed with lung cancer as their laboratory test values and survival pattern are more like such patients than other COPD patients. Furthermore, only 4% had a lung function test registered in NPR to confirm the COPD diagnosis. Another subgroup with 2,368 patients was found to be at risk of "classically" over-diagnosed COPD as they survive more than 5.5 years after the COPD diagnosis, but without the typical complications of COPD. The method could, in the future, be used in a more real-time clinical setting by discovering patients with unusual disease patterns and subsequently clinicians could verify their COPD diagnosis with spirometry and consider other differential diagnoses more thoroughly. This method can also be used to investigate other cases of potentially mis- or over-diagnosed disease and stratify the diagnostic process to discover where errors might happen and thereby highlight the common pitfalls to prevent them in the future.

Audience Take Away Notes

- To the best of our knowledge, we are the first to systematically identify patients at risk of mis- and over-diagnosis
- The method takes advantage of time-ordered comorbidities for more than 250K patients and their disease history for more than two decades
- We hope this can highlight the topic of diagnostic errors and in the long term reduce the number of diagnostic errors happening in the clinics

Biography

Isabella completed her Msc.Eng. in Bioinformatics and Systems Biology from Technical University of Denmark in 2016. She, later in 2016, joined the research group of prof. Soren Brunak at the Translational Disease Systems Biology group, Novo Nordisk Foundation Center for Protein Research (CPR), University of Copenhagen. She received her PhD degree in 2019 at the same institution. After two years of postdoctoral fellowship, she continued an Assistant Professor also at CPR. She has specialized within temporal disease trajectories using the Danish National Patient Registry.

Stefania Di Mauro[1]*, Alessandra Scamporrino[1], Agnese Filippello[1], Maurizio Di Marco[1], Maria Teresa Di Martino[2], Francesca Scionti[3], Antonino Di Pino[1], Roberto Scicali[1], Roberta Malaguarnera[4], Francesco Purrello[1], Salvatore Piro[1]

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Mitochondrial RNAs as potential biomarkers of functional impairment in diabetic kidney disease

Background: Type 2 diabetes and renal damage are strictly linked. The progressive increase in T2D incidence has stimulated the interest in novel biomarkers to improve the diagnostic performance of commonly utilized markers such as albuminuria and eGFR.

Methods: Through microarray method, we analyzed the entire transcriptome expressed in 12 serum samples of diabetic patients, six without DKD and six with DKD; the downregulation of the most dysregulated transcripts was validated in a wider cohort of 69 patients by qPCRs.

Results: We identified a total of 33 downregulated transcripts. The downregulation of four mitochondrial messenger RNAs (MT-ATP6, MT-ATP8, MT-COX3, MT-ND1) and other two transcripts (seysnoy, skerdo) was validated in patients with eGFR stage G3 versus G2 and G1. The four messenger RNAs correlated with creatinine and eGFR stages, while seysnoy and skerdo were associated with white blood cell values. All transcripts correlated also with Blood Urea Nitrogen. The four mitochondrial messenger RNAs had a high diagnostic performance in G3 versus G2 discrimination, with AUC values above 0.8. The most performant transcript was MT-ATP6, with an AUC of 0.846; sensitivity = 90%, specificity = 76%, p-value = 7.8 × 10-5.

Conclusions: This study led to the identification of a specific molecular signature of DKD, proposing the dosage of RNAs, especially mitochondrial RNAs, as noninvasive biomarkers of diabetes complications.

Audience Take Away Notes

- This work shows to the audience a translational approach for biomarker discovery based on transcriptome analysis followed by result validation that could be applied for several kinds of diseases

Biography

Dr. Stefania Di Mauro studied molecular and cellular biology at the University of Catania, Italy and graduated in 2013. She then joined the research group of Francesco Purrello at the Department of Clinical and Experimental Medicine. She received her PhD degree in translational medicine in 2017 at the same institution. As a postdoctoral fellowship (from 2018 to date) she has been working on several projects mainly focused on the identification of non-coding RNAs as circulating noninvasive biomarkers or intracellular novel molecular targets of several kinds of diseases.

Boris Tankhilevich
Magtera, Inc, United States

Curative treatment of alzheimer's

(I) Alzheimer's Disease Facts and Figures, an annual report released by the Alzheimer's Association, reveals the burden of Alzheimer's and dementia on individuals, caregivers, government and the nation's health care system. Per the special report, More Than Normal Aging: Understanding Mild Cognitive Impairment (MCI), it is estimated 10% to 15% of individuals with MCI go on to develop dementia each year.

(II) Because of the narrow brain-blood barrier every medicine designed to treat Alzheimer's failed due to inability of complex and large molecules to penetrate this barrier.

(III) Three steps of Alzheimer's treatment by using proprietary Magtera Technology.

First step: Detect the THz modes for Aβ42 Oligomer. or any other micro bio structures proven to be responsible for Alzheimer's. The most probable THz modes would be intermolecular modes: librations, low frequency bond vibrations; hydrogen bond stretches and distortions; molecular rotations. There are plenty of such modes.

Second step: Find a THz window of penetration in brain fluids that corresponds to one of these modes by using the highly tunable THz Magnon Laser that bridges the THz Gap.

Third step: Apply high power THz radiation by using the THz Magnon Laser to Aβ42 Oligomer and eradicate it.

(Note: THz radiation is benign).

(IV) This could be done by using a helmet device with multiple THz Magnon lasers attached and spread around the skull so that all areas of the brain that are responsible for Alzheimer's can be covered.

In pioneering this approach, one needs a relatively small power source (up to milliwatt) of THz radiation; it must be highly tunable in order to cover the whole THz region. Also, it is necessary to find a THz propagation window that corresponds to the most attractive THz mode(s) of Aβ42 Oligomer intermolecular excitations.

Audience Take Away Notes

- The audience can start trials to treat Alzheimer's immediately as the prototype of the THz Magnon lasers has been fabricated and proof of principle has been demonstrated
- The proposed method could revolutionize the treatment of Alzheimer's
- Any hospital in the world can use this technology
- This technology can provide a practical solution to a problem of treatment of Alzheimer's
- Huge benefits to the society as huge resources are used to take care of Alzheimer's patients worldwide

Biography

Dr. Tankhilevich received his PhD in theoretical quantum magnetism from the Academy of the Sciences of former Soviet Union. After immigration to the USA, Dr. Tankhilevich founded a start-up Magtera. The prototype of the THz Magnon Laser has been fabricated in the UC Santa Barbra, USA. The proof-of principle has been demonstrated in the Terahertz Institute for Science and Technology located at the UC Santa Barbara, USA. THz Magnon Laser technology is protected by 21 US Patents, and several European and Chinese patents.

Thomas J. Webster

School of Health Sciences and Biomedical Engineering, Hebei University of Technology, Tianjin, China
Interstellar Therapeutics, Mansfield, MA United States of America

Artificial intelligence and precision medicine: A perfect combination

Artificial intelligence has already changed the world. Here, this invited talk, will provide a review of how Artificial Intelligence (AI) can be used in medicine. By learning from how patients respond to certain therapies, AI can be used to predict clinical outcomes for that specific patient. By doing so, AI can be used in the context of numerous nanoparticles and nanosensors to promote disease prevention, diagnosis, and therapy. Specific examples will be given in orthopedics where AI was used to improve sensor function to eliminate orthopedic implant infections. Further, AI was used to predict how patients respond to orthopedic surgery to make improved decisions on care. In this manner, this invited talk will provide strong evidence that AI can be used to improve medicine and thus patient healthcare.

Audience Take Away Notes

- What artificial intelligence is
- How artificial intelligence can be used in medicine
- How biomaterials and artificial intelligence can be used together to improve disease prevention, detection, and therapy

Biography

Thomas J. Webster's (H index: 119; Google Scholar) degrees are in chemical engineering from the University of Pittsburgh (B.S., 1995; USA) and in biomedical engineering from RPI (Ph.D., 2000; USA). He has served as a professor at Purdue (2000-2005), Brown (2005-2012), and Northeastern (2012-2021; serving as Chemical Engineering Department Chair from 2012 - 2019) Universities and has formed over a dozen companies who have numerous FDA approved medical products currently improving human health. He is currently helping those companies and serves as a professor at Hebei University of Technology, Saveetha University, Vellore Institute of Technology, UFPI, and others. Dr. Webster has numerous awards including: 2020, World Top 2% Scientist by Citations (PLOS); 2020, SCOPUS Highly Cited Research (Top 1% Materials Science and Mixed Fields); 2021, Clarivate Top 0.1% Most Influential Researchers (Pharmacology and Toxicology); 2022, Best Materials Science Scientist by Citations (Research.com); and is a fellow of over 8 societies. Prof. Webster is a former President of the U.S. Society For Biomaterials and has over 1,350 publications to his credit with over 53,000 citations. He was recently nominated for the Nobel Prize in Chemistry (2023).

David W. Hein

Department of Pharmacology & Toxicology, University of Louisville School of Medicine, Louisville, Kentucky, United States of America

Pharmacogenomic- guided therapy: Insights from n-acetyltransferase 2 genetic polymorphism

Recent investigations more clearly define the effects of N-acetyltransferase 2 (NAT2) haplotypes and genotypes on the expression of acetylator phenotype towards selected drugs within human hepatocytes in vitro, within human hepatocyte cultures in situ, and clinical measures such as bioavailability, plasma metabolic ratios of parent to N-acetyl metabolite, elimination rate constants and plasma half-life, and/or clearance determinations in human subjects. Several drugs (isoniazid, hydralazine, sulfamethazine, amifampridine, procainamide, sulfasalazine, amonafide and metamizole) have been identified for which NAT2 phenotype-guided therapy may be important. The value of pharmacogenomics-guided isoniazid therapy for the prevention and treatment of tuberculosis is presented as a paradigm for NAT2 phenotype-dependent dosing strategies. Studies in human subjects and cryopreserved human hepatocytes show evidence for rapid, intermediate and slow acetylator phenotypes, with further data suggesting genetic heterogeneity within the slow acetylator phenotype. Incorporation of more robust NAT2 genotype/phenotypes relationships, including genetic heterogeneity within the slow acetylator phenotype should lead to further advancements in both health outcomes and cost benefit for prevention and treatment of tuberculosis.

Audience Take Away Notes

- The effects of the N- acetylation polymorphism on metabolism, efficacy, and/or toxicity of numerous drugs will be described
- Studies in human subjects and cryopreserved human hepatocytes show evidence for rapid, intermediate and slow acetylator phenotypes, with further data suggesting genetic heterogeneity within the slow acetylator phenotype
- Point of care testing for NAT2 phenotype/genotype and providing dose guidance could improve safety and efficacy of isoniazid for tuberculosis prevention and treatment
- More robust methods for assessing N-acetylation genotype and/or phenotype should lead to further advancements in health outcomes and cost benefits

Biography

Dr. Hein serves as Peter K. Knoefel Endowed Chair, Professor and Chair of the Department of Pharmacology & Toxicology, and Distinguished University Scholar at the University of Louisville (USA). Dr. Hein's research program has been funded since 1983 by grants and contracts from the National Institutes of Health and other federal and private foundations and industry. He has coauthored over 275 publications with over 17,000 citations (h-index=67). He has presented about 150 invited research seminars in Australia, Austria, Canada, China, Czech Republic, Egypt, France, Germany, Greece, Italy, Norway, Switzerland, the United Kingdom and across the USA.

Wei Wu
UCSF, United States of America

Deficiency of the splicing factor RBM10 limits EGFR inhibitor response in EGFR-mutant lung cancer

Molecularly targeted cancer therapy has improved outcomes for patients with cancer with targetable oncoproteins, such as mutant EGFR in lung cancer. Yet, the long-term survival of these patients remains limited, because treatment responses are typically incomplete. One potential explanation for the lack of complete and durable responses is that oncogene-driven cancers with activating mutations of EGFR often harbor additional co-occurring genetic alterations. This hypothesis remains untested for most genetic alterations that co-occur with mutant EGFR. Here, we report the functional impact of inactivating genetic alterations of the mRNA splicing factor RNA-binding motif 10 (RBM10) that co-occur with mutant EGFR. RBM10 deficiency decreased EGFR inhibitor efficacy in patient-derived EGFR-mutant tumor models. RBM10 modulated mRNA alternative splicing of the mitochondrial apoptotic regulator Bcl-x to regulate tumor cell apoptosis during treatment. Genetic inactivation of RBM10 diminished EGFR inhibitor–mediated apoptosis by decreasing the ratio of (proapoptotic) Bcl-xS to (antiapoptotic) Bcl-xL isoforms of Bcl-x. RBM10 deficiency was a biomarker of poor response to EGFR inhibitor treatment in clinical samples. Coinhibition of Bcl-xL and mutant EGFR overcame the resistance induced by RBM10 deficiency. This study sheds light on the role of co-occurring genetic alterations and on the effect of splicing factor deficiency on the modulation of sensitivity to targeted kinase inhibitor cancer therapy.

Audience Take Away Notes

- Lung cancer mutational landscape
- Co-mutations in lung cancer
- Loss of function of RBM10 in lung cancer
- Novel polytherapy for lung cancer

Biography

Dr. Wei Wu received extensive training in cancer biology and computational biology. He is studying the intricate mechanisms of cancer development and progression, with a specific focus on 1) gene regulatory networks mediated by both protein-coding and non-coding transcripts within the mammalian genome; 2) the landscapes of common and rare somatic mutations and chromosomal structural variations and their genetic alterations occurring within and between tumors. Dr. Wu aims to gain a deeper understanding of the dynamic changes that shape the cancer genome during its evolution. Dr. Wu has published more than 60 research papers and edited 5 biomedical books.

Mehrbod Vakhshoori[1]*, Niloofar Bondariyan[2], Sadeq Sabouhi[3], Keivan Kiani[4], Nazanin Alaei Faradonbeh[5], Sayed Ali Emami[6], Mehrnaz Shakarami[7], Farbod Khanizadeh[8], Shahin Sanaei[9], Niloofaralsadat Motamedi[10], Davood Shafie[11]

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Platelet to Lymphocyte Ratio (PLR) and its association with heart failure clinical outcomes; A systematic review and meta-analysis

Background: Inflammation is believed to play a role in the pathogenesis of Heart Failure (HF). However, the potential role of Platelet- to- Lymphocyte Ratio (PLR) as a novel biomarker for assessing HF prognosis requires further investigation. The aim of this study was to evaluate the impact of PLR on clinical outcomes in HF.

Methods: We conducted a systematic review and meta- analysis of English published records from PubMed/ Medline, Scopus, and Web of Science databases up until May 2022. Relevant articles that assessed PLR in relation to clinical outcomes such as mortality, rehospitalization, HF worsening, and HF detection were included. We also performed a subgroup analysis based on death/survival status.

Results: A total of 16 articles involving 10,860 individuals were finally selected for analysis (mean age: 69.50 ± 12.80 years, males: 64.96%). The overall mean PLR among HF patients was 169.86 (95% confidence interval [CI]: 156.88 – 182.84). Fourteen articles (n = 7,570) reported mortality rates in HF, either during follow-up (PLR: 164.47, 95% CI: 149.48 – 179.46) or in-hospital (PLR: 192.83, 95% CI: 150.06 – 235.61), with a mean PLR of 169.44 (95% CI: 156.18 – 182.71). Further analysis revealed that PLR was significantly lower in survived HF patients compared to the deceased group (155.13, 95% CI: 130.13 – 180.13 vs. 203.08, 95% CI: 183.18 – 222.98; standard mean difference: -0.657, 95% CI: -1.002, -0.313; $p < 0.001$). However, PLR failed to show any association with mortality risk (hazard ratio [HR]: 1.19, 95% CI: 0.95 – 1.50; $p = 0.132$). Due to limited available studies, analysis of other clinical outcomes was not feasible.

Conclusions: This systematic review suggests that caution should be exercised when using PLR as a prognostic marker in HF patients, and further studies are warranted to explore the exact association.

Audience Take Away Notes

- Biomarkers are emerging prognostic factors in medicine
- Inflammatory biomarkers are widely available and could be used as valuable tools for prognosis assessment, especially in nations with limited health care resources
- PLR is an inflammatory biomarker with controversial relation with HF prognosis
- Our findings indicate PLR could be a potential prognostic biomarker to differentiate high risk HF patients. However, more evidence is still required to prove the exact prognostic capability of PLR in HF era

Biography

Mehrbod Vakhshoori completed his MD at Isfahan University of Medical Sciences (IUMS), Isfahan, Iran. He was the research assistant at heart failure research center, affiliated to IUMS, for more than 5 years. He is currently a postdoctoral research fellow at Loma Linda University, California, USA. Mehrbod has currently published more than 40 articles and has been invited by several medical journals to review more than 30 manuscripts. He is also the editorial board member of PLOS ONE journal, one of the well-known journals in medicine field.

Qianqian Song
Wake Forest University School of Medicine, United States

Gain spatial biology insight via graph- based artificial intelligence

Cell–cell communications are vital for biological signaling and play important roles in complex diseases. Recent advances in Single Cell Spatial Transcriptomics (SCST) technologies allow examining the spatial cell communication landscapes and hold the promise for disentangling the complex Ligand– Receptor (L–R) interactions across cells. However, due to frequent dropout events and noisy signals in SCST data, it is challenging and lack of effective and tailored methods to accurately infer cellular communications. To address these challenges, we have proposed a novel adaptive graph model with attention mechanisms named spaCI. spaCI incorporates both spatial locations and gene expression profiles of cells to identify the active L–R signaling axis across neighboring cells. Through benchmarking with currently available methods, spaCI shows superior performance on both simulation data and real SCST datasets. spaCI achieves to reveal hidden L–R interactions and their upstream transcription factors from different types of SCST data such as seqFISH+ and NanoString CosMx Spatial Molecular Imager (SMI) data. Collectively, spaCI addresses the challenges in interrogating SCST data for gaining insights into the underlying cellular communications, thus facilitates the discoveries of disease mechanisms, effective biomarkers and therapeutic targets.

Biography

Dr. Song is a tenure-track Assistant Professor at Wake Forest Unviersity School of Medicine. Her research aims to advance precision medicine through the development of innovative computational methods and graph-based artificial intelligence algorithms. With a specialization in large-scale biomedical data, her expertise spans from the molecular level, including genomics and transcriptomics data, to the cutting-edge single-cell and spatial omics data at the cellular level, and to the population level with EHR data. She has designed a series of tailored deep learning and statistical methods to facilitate data representation and interpretation in complex diseases.

Arun K. Rishi Ph.D

Department of Oncology, Karmanos Cancer Institute, Wayne State University, and Research Career Scientist, Department of Veterans Affairs, VA Medical Center, Detroit

A novel mechanism to inhibit NF-κB and enhance chemotherapy efficacy in breast cancer

NF-κB is a pro-inflammatory transcription factor that regulates pathways for DNA Damage repair, cell survival and apoptosis, and contributes to emergence of resistance to genotoxic chemotherapy in a variety of cancers. Cell cycle and apoptosis regulatory protein 1 (CARP-1 or CCAR1) is a perinuclear phosphoprotein that regulates signaling induced by anticancer chemotherapy and growth factors. CARP-1 is a part of the NF-κB proteome. Our studies show that CARP-1 binds with NF-κB activating kinase IKK subunit □ (NEMO or NF-κB essential modulator) as well as RIP1 Kinase (RIPK1). CARP-1 interactions with NEMO or RIPK1 regulate the chemotherapy-activated canonical NF-κB pathway. Importantly, blockade of NEMO-CARP-1 or RIPK1-CARP-1 Interaction diminished NF-κB activation, indicated by reduced phosphorylation of its subunit p65/RelA by chemotherapeutic agent adriamycin (ADR), but not NF-κB activation induced by tumor necrosis factor α (TNFα), interleukin-1β (IL-1β), or Epidermal Growth Factor (EGF). High-throughput screening of a chemical library yielded a small molecule inhibitor of NEMO-CARP-1 binding, termed selective NF-κB inhibitor 1 (SNI)-1). We noted that SNI-1 enhances chemotherapy-dependent growth inhibition of a variety of cancer cells including human Triple-Negative Breast Cancer (TNBC), and patient-derived TNBC cells, in vitro, and attenuates chemotherapy-induced secretion of the pro-inflammatory cytokines TNFα, IL-1β, and IL-8. SNI-1 also enhanced ADR or cisplatin inhibition of murine TNBC tumors, in vivo, and reduced systemic levels of pro-inflammatory cytokines. We conclude that NF-κB pathway can be selectively targeted to enhance responses of cancer cells to genotoxic chemotherapy.

Research Interest: Dr. Rishi is studying mechanisms regulating cell growth/survival and death/apoptosis in cancer cells. Dr. Rishi identified and characterized a novel, apoptosis inducing protein termed CARP-1/CCAR1 that regulates apoptosis induced by diverse chemotherapy agents including Adriamycin, Etoposide, Cisplatin, and EGFR Tyrosine Kinase Inhibitors (TKIs). The long-term goal of Dr. Rishi's research is to exploit this knowledge for development of strategies to inhibit a variety of cancers including the drug-resistant cancers.

Keywords: Cancers (Breast, Lung, Kidney), Chemotherapy Resistance, Apoptosis Signaling, CARP-1/CCAR1.

Acknowledgements: This Research was supported by the US Department of Veterans Affairs Merit Review.

Biography

Dr. Rishi obtained a M.Sc. in Biochemistry from University College London, UK, and a Ph.D. in Molecular Biology from Imperial College of Science Technology and Medicine, London, followed by post-doctoral training at MIT and the Brigham and Womens Hospital, Harvard University Medical School, Boston, USA. He has held faculty positions at the Pulmonary Center, Boston University, Boston, and University of Maryland Cancer Center, Baltimore, Maryland, USA prior to joining the current position. In addition, Dr. Rishi has been working as a Health Science Specialist at the US Department of Veterans Affairs (USDVA) since 2001, and appointed as a Research Career Scientist in 2017. Dr. Rishi's research has been supported by the Susan G. Komen Foundation for Breast Cancer Research and the Merit Review Awards from the Department of Veterans Affairs. Dr. Rishi is a course director as well as teaches in Wayne State Cancer Biology Graduate Program. In addition, Dr. Rishi serves as a scientific member of the committees for review of grants by United States Department of Defense, United States Department of Veterans Affairs, the Susan G. Komen Foundation for Breast Cancer Research, the National cancer Institute, and National Institutes of Health. Dr. Rishi is serving as an Academic Editor for PLoS One as well as a reviewer for a number of scientific journals.

Minskaia E*, Ryapolova A, Moroz V, Krapivin B, Gasanov N, Egorov A, Zhuravleva S, Ivanov R, Karabelsky A

Sirius University of Science and Technology, Russian Federation

Development of recombinant VSV- based oncolytics for cancer immunotherapy

Oncolytic Viruses (OV) are a relatively novel class of anti-tumor therapies. Their selective replication in tumor cells and activation of the host immune response lead to the death of only malignant cells setting OV-based therapies apart from the non-specific conventional chemo-/ radiotherapies and even target-specific antibody-based therapies.

Vesicular Stomatitis Virus (VSV) offers a promising platform for OV development, especially in combination with immunotherapeutic approaches. The optimized viral rescue protocol allowed the amplification of the virus in suspension cultures and did not rely on helper vaccinia virus. The oncolytic potency of rVSV-delM51-GFP was tested in syngeneic in vivo model with fifty-two male C57BL/6 mice injected subcutaneously with 1x106 murine melanoma (an aggressive tumor model) B16-F10 cells. Eight days post inoculation, the mice were injected intratumorally with 1x106 TCID of VSV-GFP per mouse (group 1), 1x108 TCID of VSV-GFP per mouse (group 2) or placebo control (group 3) at days 0 and 3. Tumor sizes were measured every 2 days for 31 days. Partially inhibited tumor growth was observed in group 1 and 2 mice as compared to group 3 mice (max 52,5% and 41,8%, respectively, on day 11). The TGI% index in group 1 remained positive at 20-30% until the end of the study, but fell to zero in group 2 by day 25. Statistically significant differences in tumor volumes between groups 1 and 3 remained for 12 days of the study (Mann-Whitney U-test, $p<0.05$). Overall, the morbidity of mice in group 3 exceeded that of mice in groups 1 and 2. The increase in the median survival of mice in group 1 was 6.1 days compared to group 3 (Kaplan-Meier survival analysis). Virus persisted in melanoma cells for at least 21 day as demonstrated by immunohistochemistry analysis of tumor tissue.

OV-induced tumor immunity can be enhanced by delivery of anti-tumor cytokines, such as IL-12 (interleukin -12) and GM-CSF (granulocyte-macrophage colony-stimulating factor). IL-12 induces T-helper 1 (Th1) differentiation and activates interferon (IFN)-□ production in Natural Killer (NK) cells, CD4+ and CD8+ T lymphocytes. GM-CSF induces the activation of Antigen-Presenting Cells (APCs) and promotes Dendritic Cell (DC) differentiation. Targeted cytokine delivery to the tumors avoids significant toxicity associated with systemic delivery while also boosting the immune response. To achieve this synergistic effect, a novel recombinant VSV (rVSV)-mIL12-mGMCSF, co-expressing mouse IL-12 and GM-CSF, was produced. The cytopathic effect was assessed in BHK21 cells with titer of 2 x 106 TCID50 / ml. Expression of the chimeric mIL12-mGM-CSF protein was detected by Western Blotting. Functional activity of IL-12 produced in viral supernatants of BHK21 cells was assessed by both ELISA and in HEK-Blue™ IL-12 reporter cell line stably expressing IL-12 receptor and signaling pathway genes, as well as the STAT4-inducible SEAP reporter gene. The levels of SEAP reporter expression induced by the rVSV-produced IL-12 were 1.3 times higher than those induced by the commercial IL-12 control used at 10ng/ml.

Biography

Dr. Ekaterina Minskaia worked on molecular virology projects at Wuezburg University (Germany) and University of Glasgow (Scotland, UK) where she obtained her PhD. She then worked as a molecular biologist on projects in the field of cell and gene therapy at Queen's University Belfast, University of St.Andrews and University College London (UCL) in the UK and also University of Lisbon, Instituto de Medicina Molecular, in Portugal. She regularly presented at various conferences, including ASGCT and ASH, and published articles in PNAS, Frontiers in Immunology and Journal of Clinical Immunology.

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17-18 AUGUST

DAY 01

POSTERS

JOINT EVENT ON

PRECISION MEDICINE AND ORPHAN DRUGS

Lina Carvalho[1,2,3]*, Ana Filipa Ladeirinha[1,2], Ana Alarcao[1,2], Maria Reis Silva[1,2], Teresa Ferreira[1], Catarina Eliseu[1], Maria Viseu[1], Vania Almeida[1,3], Guilherme Fontinha[1,3], Daniela Madama[4], Vitor Sousa[1,2,3]

[1]Institute of Anatomical and Molecular Pathology, Faculty of Medicine of the University of Coimbra, Coimbra, Portugal
[2]CIMAGO – Research Center for Environment, Genetics and Oncobiology, Faculty of Medicine, University of Coimbra, Coimbra, Portugal
[3]University Hospital Anatomical Pathology Coimbra, Portugal
[4]University Hospital Pulmonology, Coimbra, Portugal

Pulmonary adenocarcinoma: Questioning six years follow up of resistance mutations with anti- ALK therapy – case report

Background: ALK rearrangements are detected in 2–5% of NSCLCs (85% correspond to EML4-ALK) sensitive to ALK TKIs; resistance mutations schedule is unknown. A case demonstrates NGS as the actual methodology for recognition of rearrangements, amplifications, and point mutations.

Methods: Bronchial biopsies - 62-years old woman pulmonary adenocarcinoma (CK7/TTF1):

2016 – FISH [Zyto Light SPEC ALK/EML4 TriCheck Probe (2p23)] - 100 cells were validated.

2022 – NGS in Genexus (Thermo Fisher Platform). Microdissection performed before DNA/RNA extraction and nucleic acids obtained with MagMAX FFPE DNA/RNA Ultra Kit. Oncomine Precision Assay Panel: DNA Hotspots (SNVs/Indels), CNVs (polysomy/amplification), inter- genetic and intra-genetic fusions.

Results: 2016 – June - ALK positive (80% of cells with fusion). Patient started therapy-Crizotinib.

2018 – Sepetember - clinical and imaging progression; Ceritinib was prescribed and maintained without side effects, for 16 months.

2019 – December - Lorlatinib – Introduced due to brain metastisation on EC CT, maintained without side effects.

2022 – May - Clinical progression – Two missenses mutations were detected in ALK gene: [c.3607G>A;p.(Asp1203Asn) ; c.3586C>A;p.(Leu1196Met)] with 8,3% and 8,2% allelic frequency respectively. ALK Fusion (EML4-ALK.E20A20) and one ALK imbalance were detected. ALK fusions therapeutic response for TKIs, run without information about ALK imbalance; the referred missense mutations have been considered secondary resistance/acquired mechanism after Crizotinib treatment. The patient died in November 2022.

Conclusion: The introduction of next-generation sequencing for research of therapeutic targets has been detecting ALK gene imbalances beyond resistance point mutations, together with the predominant ALK fusions genes targeted by TKIs.

This 62-years woman tumour kept EML4-ALK fusion gene responding to Crizotinib for two years and the resistance missense mutations were determined four years later. Crizotinib induced heterogeneity might be questioned together with imbalances, beyond the original/primary mutations status of ALK gene, when FISH has now lost is role.

Audience Take Away Notes

- Discussion of molecular targets in Lung cancer
- Diferent molecular target detection methods
- Case report of a specific genetic mutation and therapy

Biography

Lina Carvalho, Mozambican, Portuguese, Doctor of Medicine, University Coimbra, 1982. Doctor of Philosophy of Pathology, University Coimbra, 1995. Professor of Anatomical Pathology, University Coimbra, Portugal, since 2002. Consultant University Hospital, Coimbra, 1991- 2023. Director of the Institute of Anatomical Pathology, Coimbra. She has published more than 50 research articles in SCI (E) journals.) Member of European Society Pathology.

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17-18 AUGUST

DAY 02

KEYNOTE FORUM

JOINT EVENT ON

PRECISION MEDICINE AND ORPHAN DRUGS

The foundation for rare disease and its role in the european rare disease research landscape

The French rare disease research and clinical field has been a pioneer by structuring itself through different action plans. Competence centres and Reference centres are organized within Rare Disease Health Networks (Filieres de Sante Maladies Rares), which have been the basis of the European Reference Networks in rare Diseases.

There are 23 FSMRs each covering a wide and coherent field of diseases, either similar in their manifestations, their consequences or their management, or responsible for damage to the same organ or system. In addition, several Rare Disease Regional Platforms offers specific methodologic and technical tools to RD clinicians and researchers.

The Foundation for Rare Diseases (FFRD) aims to promote the conduct of research projects and scientific excellence as well as the sharing and dissemination of knowledge in the field of rare diseases.

In particular, it pursues the following objectives:

- The coordination of national players in research on rare diseases.
- Accessibility to technology platforms and calls for projects, which are financed after selection by independent scientific panels.
- Rapprochement between the public sector of research, diagnostic products and innovative therapies.
- The representation of France in the implementation of European and international projects.
- Scientific support to Patient Advocacy Organizations.

Since its creation in 2012, FFRD has funded more than 400 research projects, including 60 projects in Social Sciences and Humanities. This expertise has been recognized by several Patient Advocacy Organizations (PAOs) and FFRD has now provided advice and guidance in building scientific strategy, policy and research calls for proposals for more than 80 different PAOs. FFRD has organized several scientific meetings each year since its inception. FFRD has also developed an active and broad communication and dissemination strategy with an European outreach.

FFRD main objectives include: Accelerating the translation of research into clinical development; detecting business development opportunities; enhancing access to innovative technologies; and facilitating cross-sector partnerships. With its close contacts with academic researchers and clinicians in the field, FFRD is contributing to early identification of proofs of therapeutic concept. Drug Repurposing is a topic of paramount interest to FFRD since 35% of the projects that FFRD supports and advises refer to it. This is why FFRD contributes with its ideas and joins work groups involved in that topic, and organizes webinars, publications, and meetings with various stakeholders (academia, industry) at national

Daniel Scherman

Foundation for Rare Diseases, France

Biography

Dr. Daniel Scherman is Exceptional-Class Research Director at the CNRS National Scientific Research Center at the Pharmacy Faculty of Paris University. He is Director of the Foundation for Rare Diseases. Fields: Rare Diseases, Gene therapy, Gene and Drug delivery, Biotherapy, Bioimaging (h-index: 69; 543 quoted articles in WoS). Additional functions: Head of Medicine and Life Sciences Division of the European Academy of Sciences EURASC Corresponding Member of the Acacademie Nationale de Pharmacie Editor-in-Chief of the Rare Disease and Orphan Drug Journal Editor of the "Advanced Textbook on Gene Transfer, Gene Therapy and Genetic Pharmacology (Worlf Scientific)."

and European. FFRD provides and facilitates the connection with other partners in the research value chain, namely SMEs, Pharmas, and TTOs.

From its inception, FFRD has been building an EU outreach. Currently FFRD is involved in the European Joint Program for Rare Diseases (EJP RD-Horizon 2020 Grant agreement N°825575), coordinating the development of the EJP RD online academic course (as a series of MOOCs) as well as two EU innovative calls for proposals: The Rare Diseases Research Challenge-bridging academic and industrial research-and the 2021 EJP RD Joint Transnational Call focusing on Social Sciences & Humanities.

Audience Take Away Notes

- Knowledge of the French and European granting system for Rare Diseases
- Knoweldge of the Foundation for Rare Diseases support action to research and training in the RD field
- Could help to identify funding opportunity for RD research in Biological and Humanities sciences

Overview of appendix cancer PMP (ACPMP) research foundation & epithelial appendiceal malignant neoplasms: A rare but challenging cancer with critical unmet medical need

Appendiceal cancer is a rare cancer for which there is critical unmet medical need. Although it is a rare cancer, findings from a 2020 study reflect that the overall incidence of malignant appendiceal tumors has significantly increased in the U.S. and Canada from 2000 to 2016. Singh H, Koomson AS, Decker KM, Park J. Demers AA. Continued increasing incidence of malignant aopendiceal tumors in Canada and the United States a population based study. Cancer 2020;126(10):2206-2216. One of the challenges of diagnosing appendiceal cancer is that it often presents with nonspecific symptoms and is often mistaken for colon cancer. By the time a proper diagnosis of appendiceal cancer is made, the disease is advanced. It has spread throughout the abdomen and, depending on histology, presents as pseudomyxoma peritonei (for low grade tumors) or peritoneal carcinomatosis (for high grade tumors). This is deemed Stage 4. For years, and continuing today, cytoreductive surgery and intraperitoneal heated chemotherapy with mitomycin C or another perfusion agent remains the standard of care. This procedure, known as CRS/HIPEC, however, is not an option for many patients due to a high-grade histology, tumor burden, or unresectable tumor due to location (e.g., small bowel). For these patients, quality of life is poor and the disease is fatal.

In terms of non-surgical options, patients are typically offered systemic chemotherapy (5FU-based) that are typically used to treat colorectal cancer. However, as shown by a team at MD Anderson in a recently published paper, this approach is not effective, particularly in the case of low grade appendiceal histologies. Shen JP, Yourself A, Zeneddine F et al. Efficacy of Systemic Chemotherapy in Patients with Low-grade Mucinous Appendiceal Carcinoma: A randomized crossover trial. JAMA June 2023. (Dr. Shen is a guest presenter for ACPMP's free June webinar on June 22 and will be discussing this study in greater detail.)

The ACPMP Research Foundation is a small, all-volunteer led 501(c)3 foundation whose mission is to fund educational programs to increase awareness among clinicians researchers, patients/families about appendix cancer and to fund research to discover innovative treatments for appendiceal cancer with the hope of one day finding a cure.

This presentation will provide a brief overview of appendiceal cancer with a focus on the current challenges, limited treatments options, and critical need for innovative therapies. It will also include an overview of the ACPMP Research Foundation and its research grant program and some of the more recent research funded, including this year a study

Deborah Shelton Esq.

Executive Director and Vice President, (ACPMP) Research Foundation, Springfield, Pennsylvania, United States of America

Biography

Deborah Shelton, Esq., has over 25 years of experience in drug and biotech development. She became Executive Director and VP of ACPMP, the Appendix Cancer Pseudomyxoma Peritonei Research Foundation after 25 years as an FDA regulatory consultant advising drug and device developers, research institutions, and legislative bodies. In her professional capacity, Deborah has helped this diverse group of stakeholders to navigate the complex considerations and regulations pertinent to clinical research, and the testing and commercialization of cutting-edge pharmaceuticals and medical devices directed at enhancing the timely diagnosis and effective treatments for cancers and other serious diseases. She is an honors graduate of the University of Maryland School of Law, a frequent presenter at FDA-related conferences and has authored numerous publications on various topics of interest in the regulatory sphere. As with other colleagues at ACPMP, Deborah's personal journey with appendix cancer inspired her

to explore a vaccine for a specific mutation often seen in appendiceal cancer that, to date has not been targetable.

Audience Take Away Notes

- Increase awareness of the rare cancer of appendiceal cancer and the critical need for targeted therapies
- Identify ACPMP funding opportunities for tinterested researchers
- Foster ongoing thinking and collaborations about how to leverage the promise of precision medicine for the purposes of earlier diagnosis, more efficacious treatments, and/or more reliable surveillance

to dedicate her time to ACPMP. Deborah's spouse is a survivor of appendix cancer. She was diagnosed in August 2018 and underwent CRS/HIPEC that October. For several years prior to her spouse being diagnosed, Deborah had been actively engaged in patient advocacy and issues involving the need to incentivize innovation for the development of therapies to treat cancers and other diseases where there is critical unmet medical need. Deborah's primary focus in her work at ACPMP is in further developing the ACPMPs research grant program, clinical trial network, and the organization's scientific and educational initiatives.

What does a technology-enabled patient concierge mean to the orphan drugs industry?

Traditional clinical research paradigms relying solely on brick and mortar in-person engagement between researchers and patients have failed to provide the scale and efficiencies needed in orphan products development. Patients with rare disease are geographically sparsely distributed globally, are already burdened by the disease they carry, often genetic and debilitating, are often dependent on a caregiver to take paid time off to support them, yet are still willing to travel across the globe to access a life-saving or altering treatment options such as gene therapies. But it is unfair to expect them to do so when it is really not necessary in this day and age of Telemedicine, Digital Health, and wearable devices. Unique to rare diseases R&D are patient registries and natural history studies. These multi-year studies are often necessary prerequisites for orphan product development as patients demonstrate significant heterogeneity of symptoms with limited medical literature and understanding of their physiological and molecular underpinnings. The traditional process of patient education, engagement, informed consent, screening, enrollment, retention, and evidence generation needs an overhaul. It is not just introducing digital tools and elements into the centralized brick-and-mortar paradigm. It is about finding and meeting patients where they are in the global communities through online social channels and multi-modal engagement. I will demonstrate how such as technology enabled patient concierge is helping connect patients with registries, natural history studies, clinical trials, other global resources and experts based on their specific needs.

Harsha K Rajasimha MS, Ph.D

Jeeva Informatics Solutions Inc., Indo US Organization for Rare Diseases, George Mason University

Biography

Harsha is a precision medicine data scientist by training with 17+ years of experience spanning academia, the National Institutes of Health, FDA, healthcare and life science consulting, and multiple startups. He is a social entrepreneur focused on accelerating the research & development of diagnostics and therapies for rare & common diseases. Harsha has founded numerous international organizations to address these challenges. Harsha is pioneering human-centric technology innovation to accelerate online recruitment of diverse patients for clinical research in a range of diseases including rare, chronic, infectious, and neurobehavioral disorders. Harsha has authored 17+ publications, book chapters, and patents.

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17-18 AUGUST

DAY 02

SPEAKERS

JOINT EVENT ON

PRECISION MEDICINE AND ORPHAN DRUGS

Guanhao Zheng[1], Jiaqi Cai[2,3], Han Deng[4], Haoyu Yang[5], Wenling Xiong[6], Hao Bai[7], Juan He[1]*

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[2]Department of Clinical Laboratory, Kunshan Hospital affiliated to Nanjing University of Chinese Medicine, Kunshan, China
[3]School of Medicine, Jiangsu University, Zhenjiang, China
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[5]Department of Pharmacy, Handan First Hospital, Handan, China
[6]Department of Infection Management, Chongqing University Cancer Hospital, Chongqing, China
[7]Department of Pharmacy, Chongqing University Cancer Hospital, Chongqing, China

Development of a risk prediction model for subsequent infection after colonization with carbapenem-resistant enterobacterales: A retrospective cohort study

Background: Colonization of Carbapenem-Resistant Enterobacterale (CRE) is considered as one of vital preconditions for infection, with corresponding high morbidity and mortality. It is indispensable to construct a reliable prediction model and develop preventive and therapeutic strategies for those high-risk infected CRE carriers.

Methods: A retrospective cohort study was conducted in two Chinese tertiary hospitals for patients with CRE colonization from 2011 to 2021. Univariate analysis and the Fine-Gray subdistribution hazard model were utilized to identify potential risk factors for CRE-colonized infection, while death was the competing event. A nomogram was established to predict 30-day and 60-day risk of CRE-colonized infection.

Results: 879 eligible patients were enrolled in our study and divided into training (n = 761) and validation (n = 118) group, respectively. There were 196 (25.8%) patients suffered from subsequent CRE infection within 20 (interquartile range [IQR], 14-32) days after detection of colonization. Multisite colonization, polymicrobial colonization, catheterization and receiving albumin after colonization, concomitant respiratory diseases, receiving carbapenems and antimicrobial combination therapy before CRE colonization within 90 days were reserved in final model. Model discrimination and calibration were acceptable for predicting the probability of 60-day CRE-colonized infection in both training (area under the curve [AUC], 74.7) and validation dataset (AUC, 81.1). Decision-curve analysis revealed a significantly better net benefit in current model. Our prediction model is freely available online at.

Conclusions: Our nomogram has a favorable predictive performance, which is deemed as a meaningful clinical tool for early identification of CRE carriers in high-risk status of subsequent infection.

Keywords: Carbapenem-resistant Enterobacterale, Colonization; Infection, Prediction model, All-cause mortality, Nomogram, Risk factors.

Biography

Dr. He Juan currently works at the Department of Pharmacy of Ruijin Hospital, Affiliated to Shanghai JiaoTong University School of Medicine, Shanghai 200025, P.R China. He is a well-known and renowned researcher. His research field includes Caco-2 cells; Antidotal pathway.

Fenglan Wang[1], Juan Liu[1], Yong lin Liu[1], Fuyong Jiao[2]*

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[2]Children's Hospital of Shaanxi Provincial People's Hospital, Shaanxi Province Kawasaki Disease Diagnosis and Treatment Center, Shaanxi Province, China

Progress related in genetic research on kawasaki disease

Kawasaki disease, it is a systemic vasioinflammatory disease in children of Asian descent, Coronary artery injury is its major complication, the disease has now become a major cause of acquired heart disease in children. The etiology of Kawasaki disease is not fully clear, and its pathogenesis is related to infection, immune damage and genetic susceptibility. Genetic research has made new progress in recent years, with the aim of trying to better discover the intrinsic link of pathogenesis and treatment, in order to better understand the pathogenesis and obtain better treatment. The exact etiology of KD is still unknown. However, increasing evidence supports that genetic factors play a key role in their occurrence and development. Studying the changes in related genes in children with Kawasaki disease will help to understand the relationship between the changes in this gene and the onset of Kawasaki disease and its coronary damage and the sensitivity of various treatments, and will contribute to the better treatment of Kawasaki disease.

Keyword: Kawasaki disease gene polymorphism Coronary vein injury

Biography

Fuyong Jiao is currently working as Professor and Head of Department of Pediatrics at Shaanxi Provincial People's Hospital, Xian Jiaotong Univeristy. He is the Editorial Advisor for Journal of Nepal Paediatric Society, Journal of Polish Paediatric Society, Temporary Consultant for WHO 2001, International Journal of Infection and Microbiology (Nepal). He completed his Bachelor's degree in the year 1971-1975 at Xian Medical University and he did his further education at Prince of Wales Hospital, Hong Kong during the year 1995-1996. He completed her further education: 1990 Dept of pediatrics Tokyo Women Medical Univ. under Professor Fukuyama Japan Further education:- 1998 - Royal Alexandra Hospital, Sydney, Australia under Professor R. Ouvrier Further education: May–June 1994: International Center for diarrhea disease research Bangladesh, Further education: June – August 2011: Medical University of Rome.

Fereshteh Sedaghat M.D. Ph. D

Neuroscience Private Clinic, Mashhad, Iran and Aristotle University of Thessaloniki, First department of Neurology, Greece

Covid-19 seems to be initiated by the heparan-sulfate dysregulation by coronavirus: The use of low-molecular- weight heparin (LMWH) can prevent and treat covid-19 when it is used in early stages, as a heparan-sulfate-regulating medicine

The proteoglycan named heparan sulfate (HS) is found in the extracellular matrix and also on cell surface and may represent one of the most biologically important glycoconjugates, playing essential role in a variety of different events at molecular level. Heparanase is an endo-glucuronidase enzyme expressed in all tissues and play role in diseases mainly through degradation of HS. HS has important regulatory functions in several pathophysiological conditions, including neuroinflamation, synaptic development, regulation of leukocyte activation, modulation of a variety of proteins in the lungs, lipoprotein metabolism in the liver, also in red blood cell adhesion events occurring with pathogens such as herpes simplex virus and P falciparum. The time to thrombosis has shown to be significantly lower in the heparanase-overexpressing mice and showed a powerful mediator of thrombosis in vascular injury. HS is found at different concentrations and structures, some gender, organ and age specific differences in murine HS was observed in the body of mice. Heparanase has shown to be elevated in covid-19 patients. In COVID-19 different cells and organs are aggravated including lungs, brain, heart, kidneys, gastrointestinal system, skin, erythrocytes, and endothelial dysfunction and loss of endothelial barrier function is well demonstrated. No specific clinically approved heparanase inhibitors are currently available. Hypothesizing that heparin-sulfate dysregulation contributes in starting covid-19 syndrome as the early pathogenesis of COVID-19, LMWH has been used in three groups: A) ten volunteers as preventive B) Fifty-one covid-19 patients in different stages of the disease C) 18 patients with side effects of the disease. In the group A, 7 volunteers experienced a very mild disease in comparison with the other members of the family and one male remained disease-free. The patients in group B recovered significantly faster regarding the ones that didn't used LMWH with the easing of their symptoms. Significant improvement of the side effects was achieved in the group C.

The conclusion is that Heparan-sulfate dysregulation may initiate covid-19 pathology and can be intervened by early administration of LMWH as preventing, easing the symptoms and treating the disease as a regulator of heparan-sulfate system.

Biography

Fereshteh Sedaghat, M.D. Ph. D from Neuroscience Private Clinic, Mashhad, IRAN and Aristotle University of Thessaloniki, First department of Neurology, Greece.

Magali Taiel
GenSight Biologics, Paris, France

Lumevoq gene therapy in leber hereditary optic neuropathy

Leber hereditary optic neuropathy (LHON) is a rare, maternally inherited mitochondrial genetic disease with a continued high unmet medical need. Three primary point mutations in the mtDNA are responsible for LHON in approximately 90% of subjects: G3460A, G11778A and T14484C, located respectively in the ND1, ND4 and ND6 genes. The m.11778G>A ND4 mutation is known to cause the most severe clinical form of LHON, and is also the most frequent mutation, as it accounts for about 75% of LHON in North America and Europe. Lenadogene nolparvovec (Lumevoq) is a recombinant adeno-associated viral vector, serotype 2 (rAAV2/2), containing a cDNA coding the human wild-type mitochondrial NADH dehydrogenase 4 protein (ND4), which has been specifically developed to treat MT-ND4 LHON subjects, and is targeting the root cause of the disease. Restoring the expression of the ND4 protein could correct the deficiency due to the m.11778G>A ND4 mutation, leading to the improved activity and assembly of Complex I of the mitochondrial respiratory chain, helping to protect RGCs, eventually halting and reversing the disease. The three Phase-3 multi-center clinical trials RESCUE, REVERSE and REFLECT showed sustained bilateral improvement of best-corrected visual acuity (BCVA) following unilateral or bilateral intravitreal injection of lenadogene nolparvovec (rAAV2/2 ND4) gene therapy for the treatment of leber hereditary optic neuropathy (LHON) caused by the m.11778G>A mitochondrial DNA mutation in the MT-ND4 gene. Overall, 189 MT-ND4 patients were treated with lenadogene nolparvovec in clinical trials. Early expanded access programs have been granted in the US and Europe. Lenadogene nolparvovec brings a novel and efficacious treatment option, fulfilling an ongoing unmet medical need whilst restoring visual function in MT-ND4 LHON patients.

Audience Take Away Notes

- LHON, a rare disease, with unmet medical need
- Insights on clinical development of lenadogene nolparvovec to treat MT-ND4 LHON patients
- US and Europe regulatory pathways
- Next steps for lenadogene nolparvovec registration
- Key learnings

Biography

Dr. Taiel completed her doctorate in Medicine with board certified in Ophthalmology from Lariboisiere Saint Louis University, Paris, France, in 1993, and her Associate Professor degree in 1998. Dr. Taiel completed her internship at academic Paris hospitals, was an Associate Professor of Ophthalmology, served as an Ophthalmology Department Head, and ran Surgical and Medical Ophthalmology private practice. After 13 years of Ophthalmology public and private practice, Dr. Taiel has been engaged in the Pharma Industry for 20 years; she brings extensive experience and expertise in drug clinical development, gene therapy, and medical affairs. She started her carrier at Servier company headquarter, and then worked in Ophthalmology area at Pfizer for several years; she then held international and management positions in various therapeutic areas, including both technical and supervision duties, at Eli Lilly Company for many years. Then, as VP Clinical Development, she led Clinical Development and Operations, to develop antisense oligonucleotides in Inherited Retinal diseases at ProQR Therapeutics. She then moved to GenSight-Biologics in 2018, to supervise the Medical Department and lead Gene Therapy programs in Inherited Retinal and Neuro-Ophthalmology diseases, as the CMO of the company. Dr. Taiel has authored numerous protocols and articles published in peer reviewed journals, and made critical contributions to successful clinical development and launch of many products. She brings extensive years of experience from both academic medicine and pharma industry.

J. Somasekar
Professor, Department of Computer Science and Engineering, Faculty of Engineering and Technology, Jain University, Bangalore, India

Drug recommendation system using a collaborative filtering in machine learning

A drug recommendation system using collaborative filtering in machine learning is a system that suggests drugs to users based on the preferences and patterns of similar users. Collaborative filtering is a popular technique in recommendation systems, and it can be applied to drug recommendations by leveraging the historical data of drug usage and user preferences. The following steps are used to built drug recommendation system using collaborative filtering approach in machine learning.

Data Collection: Gather data on drug usage and user preferences. This data could come from electronic health records, patient surveys, or other sources that capture information on which drugs were prescribed or used by patients and their feedback or ratings on those drugs.

Data Preprocessing: Clean and preprocess the data to handle missing values, remove duplicates, and ensure the data is in a suitable format for collaborative filtering.

User-Item Matrix: Construct a user-item matrix, where rows represent users, columns represent drugs, and the cells contain user ratings or usage information for each drug. If explicit ratings are not available, implicit feedback (e.g., number of times a drug was prescribed) can be used.

Similarity Calculation: Calculate the similarity between users based on their drug usage patterns. Various similarity metrics can be used, such as cosine similarity or Pearson correlation coefficient.

Neighborhood Selection: Identify a subset of similar users (i.e., neighbors) for each target user based on the calculated similarity scores.

Prediction: For each drug not yet used by the target user, predict their preference or likelihood of using the drug based on the ratings or usage patterns of their neighbors.

Top-N Recommendations: Generate a ranked list of top-N drug recommendations for each user, considering the predicted preferences.

Evaluation: Evaluate the performance of the recommendation system using metrics such as precision, recall, or Mean Average Precision (MAP).

Deployment: Deploy the drug recommendation system in a healthcare setting, integrating it with electronic health records or other relevant systems to provide personalized drug suggestions to healthcare professionals or patients. It's important that healthcare recommendation systems, especially for drugs, need to adhere to strict privacy and security regulations to protect patient data. Additionally, medical professionals should always review and validate the recommendations before making any decisions regarding patient treatments. Collaborative filtering is just one approach to building drug recommendation systems. The overview of training dataset for drug recommendation is as follows.

Audience Take Away Notes

- Role of machine learning and recommendation system for health care
- Drug recommendation system using machine learning techniques
- Types of recommendation system
- Collaborative filtering approach for drug recommendation system
- Research directions

Biography

Dr. J.Somasekar received a Ph.D. degree in CSE with specialization on Medical Imaging from JNTUA, Andhra Pradesh in 2017, and M.Tech. degree from the National Institute of Technology Karnataka (NITK), Surathkal in 2010. He is currently working as a Professor at the CSE Department, Jain University, Bangalore, India and Post-doctoral researcher at University of south Florida, USA. As a resource person, he has delivered 154 Technical Talks in the emerging technologies. He got an All India Rank of 43 in the GATE exam. He is having more than 16 years of experience in teaching and 6 years of experience in research. He has published more than 35 research articles in leading journals (SCI & SCOPUS indexed), and conference proceedings. His research interests include Image Processing, Medical Imaging, Data Science, Machine Learning, and ML for Cyber security.

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Blockers of β2-adrenergic receptors reduce inflammation and oxidative stress in von ippel-lindau rare tumor

Lack of expression or the inefficient function of the VHL protein raises the rare inherited cancer Von Hippel-Lindau (VHL). This multi-systemic rare disease affects mainly CNS and retina (hemangioblastomas, HBs), pancreas, and kidneys (cysts and clear cell renal cell carcinomas, ccRCC). The constitutive pseudo-hypoxic state in which the mutated cells subsist is triggered by the accumulation of HIFs.

Since standard therapies have shown limited response, remaining surgery as the only possible treatment, the use of β2-adrenergic receptor (ADRB2) antagonists, such as propranolol or ICI-118,551, have also shown antitumor therapeutic benefits in a clinical trial and a retrospective analysis of patients by decreasing HIFs nucleation and downstream target gene activation.

HIF promotes glycolytic and inflammatory pathways; therefore, we addressed the effects of propranolol and ICI-118,551 on: (i) changes in the inflammatory response of ccRCC cells; and (ii) modulation on the Warburg effect (glycolytic metabolism), specifically, on the expression of genes involved in the balance and levels of cellular reactive oxygen species (ROS). Accordingly, in vitro studies were performed using primary VHL-ccRCC and 786-O cells, measuring ROS levels, expression of detoxifying enzymes, and expression of p65/NF-κB targets, by RT-PCR. Furthermore, histological analyses of ccRCC samples, from heterotopic mouse xenografts, were performed.

The results obtained show that the blockade of ADRB2 in ccRCC cells reduces oxidative stress levels and stabilizes the inflammatory response. Therefore, these data further support the idea of targeting ADRB2 as a promising strategy for the treatment of VHL and other non-VHL tumors.

Audience Take Away Notes

- A new application of a beta-blocker to reduce inflammation and, therefore, normalize the cellular homeostasis
- Can serve as an example of thinking a different way to reach the point (therapy)
- Obviously, it's an example of drug repurposing and direct application to a rare disease
- Does not provide a practical solution to a problem that could simplify or make a designer's job more efficient
- No it will not improve the accuracy of a design, or provide new information to assist in a design problem

Biography

Dr. Cuesta studied Biology at the Autonomous University of Madrid (Spain). In 2003, he joined to Dr. Alvarez-Vallina at the Puerta de Hierro University Hospital, Madrid. After his PhD degree in 2009, in 2011 he moved with Dr. Acker-Palmer at the Buchmann Institute for Molecular Life Sciences (Goethe University Frankfurt, Germany). In 2017 he returned to Spain and combined his research in rare diseases with Dr. Botella at Centro de Investigaciones Biológicas Margaritas Salas- CSIC with lectures as Associate Professor at the Complutense University of Madrid (UCM). In 2021, he obtained a lecturer position at UCM. 11 out of more than 30 research articles in SCI(E) journals are related with rare disease and drug repurposing.

Kondakova O. B*, Savostyanov K.V, Kazakova K.A, Lyalina A.A, Grebenkin D.I, Davidova Y.I, Kanivets I.V, Khachatryan L.G, Pushkov A.A

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Rare forms of primary enzyme defects in monoamine biosynthesis: AADCD and TH-deficient progressive infantile encephalopathy

Neurotransmitter deficiencies are rare neurological disorders with clinical onset during childhood. Its classical signs are hypotonia, movement disorders, autonomous dysregulations, and impaired development. The clinical symptoms of inherited neurotransmitters disorders often overlap with features of other neurological syndromes. It's particularly important to diagnose the diseases in this group early because of the good response to symptomatic therapy and the significant improvement in patient condition.

We present the case of 6-year old boy with a severe form of autosomal recessive Segawa syndrome and the case of 1-year boy with aromatic L-amino acid decarboxylase deficiency (AADCd). DNA diagnostic was performed using full exome sequencing and was confirmed by Sanger sequencing.

The boy with TH-Deficient Progressive Infantile Encephalopathy had normal development before 3 months of age. At the age of 3 months he became weak, stopped holding his head and playing with toys. He had a tremor of the head, lethargy, the child's appetite deteriorated at the age of 6 months. He had severe motor development delay. He was able to control his head at 5 months, sit up straight at 18 months. He had severe hypokinesia, truncal hypotonia, dystonia, intellectual disability, ptosis, increased sweating and drooling. At the 32 month we start treatment with a low dose of L-dopa/carbidopa (1/32 part of pill). The patient's condition improved immediately: activity increased significantly, ptosis and salivation disappeared, at 34 months he walked independently. Now he has normal development and intelligence and going to enter school. He takes 1/3 part of pill L-dopa/carbidopa. He has a bit hyperactive.

Our second patient with AADCd had psychomotor development delay. At the age of 2.5 months his attacks began from episodes of movement of head and eyes up and to the side. Patient had marked delay in motor development, truncal hypotonia, dystonia, severe hypokinesia, ptosis, somnolence, increased sweating and drooling at the age of 10 months. We start treatment with high dose by pyridoxal- 5′-phosphate (100 mg/d). The condition of our patient improved in 24-48 hours. He had less somnolence, ptosis of his eyelids decreased, he became more active. The therapy was continued by pramipexole 5 μg/kg/d and are planning to selegilinea by dose 0,1 mg/kg/d.

Brain MRI and EEG were normal in both patients.

We identified homozygous missense mutations c.1040G>A (p.Arg347Gln) in the DDC gene in first patient and c.1546G>A (p. Glu516Lys) in TH gene in second. The first one was previously described in the HGMD database. High concentration of 3-OMD 1181.60 ng/ml is detected in dry blood spots in patient with AADCd (normal < 305 ng/ml).

Clinical and genetic features were described in Russian patients with aromatic L-amino acid decarboxylase deficiency due to DDC mutations and TH-Deficient Progressive Infantile Encephalopathy due TH mutations. The case shows the first description with an effective therapy of pyridoxal-6-phosphate in the patient with AADCd in Russia.

Biography

Kondakova O. B from National Medical Research Center for Children's Health Federal state autonomous institution of the Russian Federation Ministry of Health, Russian Federation.

Kranthi Kumar Singamaneni
Associate Professor, Department of Computer Science and Engineering,
Chaitanya Bharathi Institute of Technology (CBIT), Hyderabad, Telangana, India

Cyber security role for rare diseases and pharmaceutical industry

Cyber security is the practice of defending computers, servers, mobile devices, electronic systems, networks, and data from malicious attacks. It's also known as information technology security or electronic information security. Cybersecurity plays a vital role in the context of rare diseases and the pharmaceutical industry, ensuring the protection of sensitive data, patient privacy, and intellectual property related to rare diseases and pharmaceutical research. The following are some specific aspects of the cybersecurity role in this domain.

Patient Data Protection: For patients with rare diseases, their medical records and personal information are highly sensitive. Cybersecurity measures are crucial in healthcare institutions to safeguard patient data from unauthorized access, data breaches, and potential identity theft.

Research Data Security: Rare disease research involves extensive data collection and analysis. Cybersecurity safeguards help protect research data, ensuring the integrity and confidentiality of clinical trial results, genomic data, and other research findings.

Intellectual Property Protection: The pharmaceutical industry invests significant resources in research and development of rare disease treatments. Cybersecurity is essential to protect valuable intellectual property, trade secrets, and proprietary data related to potential drug candidates and their formulations.

Clinical Trial Security: Cybersecurity measures are critical during clinical trials of rare disease treatments to prevent data manipulation, unauthorized access to trial results, or any tampering that could impact patient safety and drug efficacy.

Preventing Counterfeit Drugs: Cybersecurity plays a role in preventing the distribution of counterfeit drugs, especially for rare disease medications. Implementing secure supply chain management and digital tracking systems can help verify the authenticity of drugs.

Medical Device Security: Some rare diseases require specialized medical devices. Ensuring the security of these devices is vital to prevent cyber threats that could compromise patient safety or privacy.

Data Sharing and Collaboration: Collaboration among researchers, pharmaceutical companies, and healthcare institutions is essential for rare disease research. Cybersecurity measures enable secure data sharing, fostering collaboration without compromising sensitive information.

Pharmaceutical Infrastructure Protection: Cyber threats can target pharmaceutical companies and research institutions directly. Robust cybersecurity measures protect against data breaches, ransomware attacks, and other cyber incidents that could disrupt operations or compromise sensitive data.

Patient Trust and Reputation: Strong cybersecurity practices instill confidence in patients and stakeholders, enhancing the reputation of pharmaceutical companies and healthcare institutions involved in rare disease research and treatment.

Remote Healthcare Technologies: The increasing use of telemedicine and remote healthcare technologies in rare disease management requires robust cybersecurity to protect patient data during online consultations and remote monitoring.

By addressing these cybersecurity aspects, organizations involved in rare diseases and the pharmaceutical industry can ensure the confidentiality, integrity, and availability of critical data, promote patient trust, and contribute to advancements in research and treatments for rare diseases.

Audience Take Away Notes

- Cyber security basics
- Cyber security role for rare diseases
- Significance of cyber security for pharmaceutical industry
- Future directions

Biography

Dr. S. Kranthi Kumar is a faculty member with a Ph.D. in Applied Cryptography and Cloud Security from GITAM Deemed to be University. He has M.Tech degrees in Information Technology and Computer Science from JNTU Kakinada and Acharya Nagarjuna University, respectively. With 16 years of experience in teaching, industry, and research, Dr. Kranthi Kumar brings a comprehensive skill set. He worked as a Data Specialist at IBM and focuses his research on Applied Cryptography, Network, and Cloud Security. He has published 25 research papers in reputable journals indexed by SCI, WOS, SCOPUS, and UGC. As a member of professional societies such as ISTE, CSI, IFERP, and IAENG, Dr. Kranthi Kumar actively engages with the academic community and stays updated with the latest advancements in Computer Science.

Priyanka Wadhwa
Rare Disease Division, Ikris Pharma Network, Noida, U.P, India

Unlocking hope: India's initiatives to improve rare disease healthcare

Rare diseases are a significant healthcare challenge worldwide, with an estimated 350 million people globally affected by one of over 7000 rare diseases. India, with the population of over 1.48 billion, is no exception. It is estimated that we have more than 70 million people affected by rare diseases in India. Although progress has been made in recent years in terms of policy implementation and access to healthcare services, challenges remain, particularly regarding the availability of treatments and therapies for rare diseases.

The Indian government has taken steps to address this issue, including the launch of the National Policy for Treatment of Rare Diseases (NPTRD) in 2021. The policy provides financial support for the treatment of rare diseases. The policy also establishes a framework for the development of rare disease treatment centers, with the aim of improving access to specialized care for patients with rare diseases. In addition to government initiatives, there are several organizations working towards addressing rare diseases in India.

India is also a potential market for rare disease drug manufacturers. The growing prevalence of rare diseases in India, coupled with the government's focus on improving access to healthcare and promoting research and development, makes it an attractive market for pharmaceutical companies.

Overall, while challenges remain, there are positive developments in India in terms of policy implementation, access to healthcare services, and the availability of rare disease drugs. The government's commitment to addressing rare diseases, coupled with the effects of organizations such as the ICMR, provides hope for the future of rare disease care in India. The growing market for rare disease drugs also represents a significant opportunity for pharmaceutical companies to make a difference in the lives of millions of people affected by rare diseases in India.

Audience Take Away Notes

- Any Rare Disease company who is willing to enter the India market will be benefitted by this
- This will help in understanding the potential of the Indian market
- Yes, this information can be used by other faculty to expand their research or teaching
- Yes, it will help in understanding the Indian healthcare market especially Rare Disease market
- This will help Rare Disease pharma companies in exploring Managed Access Programs or Compassionate Programs for Indian and other SAARC regions

Biography

Dr. Priyanka Wadhwa, a medical graduate with an MBA in healthcare administration. She has dedicated more than 12 years of her career to working in the space of rare diseases, breast cancer and women hormone therapies, etc. She works closely with all the Centers of Excellence Centers in India. Currently, she is working on Named Patient programs through which unregistered rare disease medicines can be made accessible for Indian Rare Disease patients.

Arti Sharma[1,2]*, Sarkaraisamy Ponmariappan[3], Syed I. Alam[4]

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[2]Research Scholar, Biotechnology Division, Defence Research & Development Establishment, Gwalior, India
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Immunoproteomic approach towards vaccine development against botulism of C botulinum type B

Botulism is a neuroparalytic disease caused by botulinum neurotoxins (BoNTs) and has been reported as a potential bio warfare agent due to its extreme toxicity (~100 billion times more toxic than cyanide). BoNTs is produced by Gram positive; an obligate anaerobic and endospore forming bacteria called Clostridium botulinum. There is no licensed vaccine available commercially for the treatment of botulism. An immunoproteomic-based approach was used to screen the immunogenic proteins of C. botulinum type B. The identity of immunogenic proteins is important to develop the vaccine candidates and diagnostic markers against the botulism. Using a proteomics-based approach, whole cell proteome were separated by two-dimensional gel electrophoresis and immunoreactive proteins were revealed by reaction with antisera against whole cell proteins of C. botulinum type B. The identity of immunoreactive proteins were recognized by mass spectrometry. Fifty six pre dominant proteins were identified in total. Out of total proteins, 13-proteins were identified as immunogenic. These proteins may be potential vaccine/diagnostic candidate molecule against botulism.

Audience Take Away Notes

- The audience will be able to learn about the botulism
- Knowledge of immunoproteomic study
- Vaccine development against infant and wound botulism

Biography

Arti Sharma working as assistant professor in Govt. P.G. College Prithvipur, India. She has published national and international papers in immunoproteomics. She had also worked in Defence Research & Development Establishment, Gwalior. She had developed diagnostic system as well as vaccine markers against botulism. She had also worked on Biodiesel in Indian institute of Technology, Roorkee, India as research scientist.

Zeynep Unluturk
University of Health Sciences Kocaeli Derince Training Hospital, Derince, Kocaeli, Turkey

Neiman-pick disease type C- early onset dementia

Neiman pick disease type-C (NPC) is a rare lysosomal lipid storage disorder. NPC has a wide variety of clinical manifestations from rapidly fatal neonatal form to adult onset chronic neurodegenerative form. It is traditionally known as a childhood onset autosomal recessive, visceral, metabolic disorder. The neurological features of NPC are vertical supranuclear ophthalmoplegia, ataxia, dysarthria, mental-motor retardation and seizure. Nowadays more patients presenting with organic psychosis, early-onset cognitive decline and movement disorders are diagnosed with NPC. Although it does not seem possible to assess the true prevalence of the disease due to the heterogeneous clinical presentation and the large number of undiagnosed adult cases the insidace of NPC is estimated at about 1/100000.

Here it is presented a thirty-four year old man with dizziness and attention deficiency. A genetic test run by a neurologist and he is diagnosed with NPC after the years of the psyhchiatric treatment for adult attention-deficit/hyperactivity disorder and depression.

Diagnosing of a rare disease with a possible cure for such disorders, which often does not have a definitive cure, increases the hope both of the patients and clinicians.

There is no specific cure for NPC although research into disease modifying therapies such as miglustat has been ongoing. It is hoped that the treatment of the NPC will be provided by gene therapy, which will result in correction of the genetic defect in the future.

Audience Take Away Notes

- This is a case based rare disease presentation that give the audience a different perspective to look to the neurometabolic disorders
- The audience will keep their mind that metabolic disorders can be seen also in adults
- This presentation is a clinical experience sharing

Biography

Dr. Zeynep Unluturk studied Medicine at the Dokuz Eylul University, Izmir, Turkey and graduated as MD in 2013. She then joined resident Neurology at the Pamukkale University, Denizli, Turkey. She started to work as a clinical neurologist in Giresun University Prof. Dr. A. Ilhan Ozdemir Training Hospital in 2020. After two year public obligator duty in there she started to work University of Health Sciences Kocaeli Derince Training Hospital as a clinical neurologist in 2022.

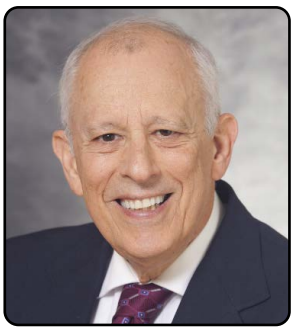
Vicki Ratner
ESSIC - International Society for the Study of BPS, United States

Interstitial cystitis/bladder pain syndrome - A rare disease?

Interstitial cystitis/bladder pain syndrome (IC/PBS) was once thought to be a rare disease as well as a psychosomatic disorder in women. As a result, the disease went undiagnosed for hundreds of years. IC/BPS is a condition of the bladder that can cause severe pain, urinary urgency and frequency of the bladder. However, laboratories report urine cultures as negative and there does not appear to be an infection. It wasn't until 1987 that IC/BPS was considered a medical condition highlighted by the first NIH (National Institutes of Health) research conference on the subject. This recognition was triggered by the tremendous efforts on the part of a patient advocacy group, the Interstitial Cystitis Association (ICA), formed in 1984. Even today, female patients often consult multiple urologists before getting the proper diagnosis. Unfortunately, despite 35 years of research by an excellent cadre of researchers, we are no further along in categorizing the disease, or finding a uniformly effective treatment.

Biography

Vicki Ratner, M.D. completed her undergraduate studies at Columbia University in New York City (NYC), medical school at Upstate Medical Center in Syracuse, New York, and completed her orthopedic surgery residency at Montefiore and Albert Einstein School of Medicine in NYC. She is Founder and President Emeritus of the Interstitial Cystitis Association, serving from 1984-2008. She now works with ESSIC (International Society for the study of Painful Bladder Syndrome) as co-chair of the Patient Advocacy Committee.



Paul L. Kaufman MD

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United States of America

Gene and stem cell therapy for glaucoma

Glaucoma is a degenerative optic neuropathy that is the leading cause of preventable blindness worldwide. Roughly 3% of the adult human population has or will have glaucoma, and the prevalence increases with age. All races, both genders, and all 6 inhabitable continents comprise the current 80 million sufferers, many of whom do not know that they have it. Predictions are that by 2040 more than 110 million people will have glaucoma. Intraocular pressure (IOP) is a major and treatable risk factor, and reducing IOP is the only therapeutic.

We hypothesize that in live non-human primates (NHPs), administration of viral vector-transgene constructs incorporating the C3 or caldesmon transgene directly into Schlemm's canal will decrease conventional aqueous humor outflow resistance in the conventional aqueous humor outflow and thereby reduce intraocular pressure. This may constitute potential human therapeutics for open-angle glaucoma (the most common cause of irreversible vision loss and blindness worldwide), and also provide the basis for a platform to deliver genes that would increase outflow resistance to create a live NHP molecular glaucoma model.

In human eyes there is an age-dependent loss of trabecular meshwork (TM) cells. Glaucomatous human eyes start out with fewer TM cells and have the same age-dependent loss as normal eyes. Presumably, they reach a critical margin and the conventional outflow pathway resistance increases, increasing IOP which in turn damages the optic nerve. In anterior segment eye organ culture, the TM can be 'wiped clean' of cells with saponin, increasing outflow resistance. Injecting human TM cells into the anterior chamber restores normal function and IOP. Injecting iPSC grown up in normal media has no effect, but injecting iPSC grown in TM cell media restores normal function. HUVEC and fibroblasts have no effect.

Gene and stem-cell therapy have great potential as glaucoma therapeutics, removing the unreliable patient from the drug delivery system that now involves the patient self-administering therapeutic eye drops.

Audience Take Away Notes

- The audience will be able to learn the future of glaucoma therapy
- Can explain future therapeutic delivery & targets
- Absolutely other faculty could use to expand their research or teaching
- Yes, this provide a practical solution to a problem that could simplify or make a designer's job more efficient
- Yes, it will improve the accuracy of a design, or provide new information to assist in a design problem
- List all other benefits
- Eliminate the patient from the therapeutic delivery system

Biography

Dr. Kaufman, Barany Prof of Ocular Pharmacology and past Chair, Dep't of Ophthalmology and Visual Sciences, Univ of Wisconsin, is a glaucoma physician-scientist exploring the mechanisms of aqueous drainage and presbyopia. He is past President and Executive Vice President of ARVO and ISER, and has served on the US National Advisory Eye Council and numerous foundation and corporate scientific advisory boards. He has authored over 375 original scientific articles and 95 book chapters/review articles, co-edited the most recent editions of Adler's Physiology of the Eye, and was past Editor in Chief of IOVS. He has received numerous honors and awards, including ARVO's Friedenwald Award & ISER's Balazs Prize.

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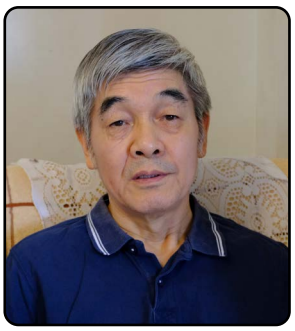

Huaixiu Wang[1]*, Aimei Wang[2], Fengyun Hu[1]

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The effect of eupalinolide b on amyotrophic lateral sclerosis: A case report

Objective: To investigate the effect of Eupalinolide B (EB) on amyotrophic lateral sclerosis (ALS).

Case description: The 66-year-old femele patient experienced progressive right upper limb weakness and slowed speech speed in November, 2021. One month later, weakness of lower limbs and left upper limb followed. Physical examination and neurologic check showed slight interosseus atrophy between thumb and index finger in both hands. Biceps reflex, triceps reflex, knee reflex and ankle reflex graded +++. Ankle clonus and Hofman's sign showed +. Babinski's sign was negative. Mascular tension in four limbs graded ++ according to Ashworth standard. Electromyogram showed neurogenic injury in cervical and lumbar section. Pulmonary function and cerebral spinal fluid test were normal. Based on the above data, the patient was diagnosed clinicaly as ALS. Since then, Riluzole 50 mg twice daily and Butylphthalide soft capsule 0.2 g thrice daily were prescribed. The disease progressed steadily. The mascular strength of four limbs worsened. Eating and getting up could not be accomplished by herself. Constipation was experienced and sometimes glycerol was used as lubricant. ALSFRS-R went down all the way and scored 17 before experiment.

Result: Three days after EB administration, the abnormally lower mascular tension of lower limbs turned to basically normal. At the same time, the mascular strength of lower limbs improved. She could walk under assistance for about 45 meters. Sinteen days after EB administration, ankle clonus disappeared. Biceps reflex, triceps reflex, knee reflex, ankle reflex graded ++. Hofman's sign showed +. Babinski's sign remained negative. Constipation resolved and glycerol has not been used since experiment. ALSFR-R score stopped declining and scored 19-30 days since the start of experiment. As DMSO is irritating and was unpleasant when orally administered, the patient refused to accept further treatment with EB 30 days after the beginning of experiment. About 10 days after discontinuation of EB, muscular tension of lower limbs went back to abnormally low. Muscular strength decreased and ALSFR-R worsened.

Experiment: In January 2023, EB dissolved in Dimethyl Sulfoxide (DMSO) was orally administered 20 mg daily. Riluzole 50 mg twice daily and Butylphthalide soft capsule 0.2 g thrice daily were continued. Before experiment, neurologic check was repeated. Neural reflexes showed the same results as above but ankle clonus seemed stronger. The mascular tension in upper limbs graded +. But it was abnormally lower in lower limbs. She could walk at most 5 meters per day with caregiver's help.Written consent was signed using an inked thumbprint in lieu of sigature. The experiment was authorized by Ethical Committee of Shanxi Provincial Hospital.

Discussion: EB might be effective on ALS and deserves further investigation.

Key words: Eupalinolide B, Amyotrophic lateral sclerosis, Sesquiterpenes, Eupatorium Lindleyanum, Chinese herbs.

Audience Take Away Notes

- As far as I know, this is the first clinical report describing the application of EB in ALS patient
- As EB was reported to restore the Nissl body in motor neuron of ALS animal model and Nissl body is a special apparatus in motor neuron, EB might have special role to pathalogical mortor neurons in ALS patients
- EB deserves further experiment with large sample to investigate its efficacy, safety. If it is effective and safe for ALS patient, pharmacokinetics and medication route should be researched

Biography

Dr. Wang Huaixiu graduated from Shanxi Medical College in 1981 and worked in Shanxi Provincial Hospital in China. He worked in Universith of Sydney and University of Adelaide in Australia as a visiting scholar in 1992-1993. Now he worked in Neurology Department in Shanxi Provincial Hospital in China.

Daniel Wainstock
Georgetown University-PUC-Rio, Brazil

Advancing rare disease policy in latin America: A call to action

People living with a rare disease are amongst the most vulnerable groups in society. They have been historically marginalized and systematically stigmatized, especially in middle and low-income countries. It is estimated that 300 million people worldwide live with a rare disease. Despite that, many countries today, especially in Latin America, still lack consideration of rare diseases in public policies and national laws. Based on interviews with patient advocacy groups in Latin America, we aim to provide recommendations for lawmakers and policymakers in Brazil, Peru, and Colombia on how to improve public policies and national legislation for persons living with rare diseases in these three countries.

Biography

Daniel Wainstock is a Rare Disease Patient Advocate and Health Law Researcher at the Pontifical Catholic University of Rio de Janeiro (PUC-Rio), in Brazil. He advises lawmakers and policymakers in Latin American countries on Rare Disease-related policies. He has also worked as a Volunteer at Rare Diseases International (RDI), on advocacy efforts for the WHO Resolution on Rare Diseases.

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"We wish to meet you again at our upcoming events next year..."

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