GOVERNMENT OF MALTA
MINISTRY FOR HEALTH AND ACTIVE AGEING

National Alliance for Rare Diseases Support
MALTA

L-Università ta' Malta

10 YEARS OF
STRENGTH & HOPE.
10 YEARS TOGETHER

The 2nd Joint
National Conference
on Rare Diseases 2026

National Conference on Rare Diseases

TOGETHER THROUGH THE UNCOMMON.

UNDER THE AUSPICES OF HER EXCELLENCY THE PRESIDENT OF MALTA

AGENDA

AGENDA

8.30 AM — **REGISTRATION & COFFEE**

9.00 AM — **INTRODUCTORY SPEECHES**

Address by Hon. Dr Jo Etienne Abela, Minister for Health and Active Ageing

Address by Mr Clarence Pace, Chief Medical Officer within the Ministry for Health and Active Ageing

Address by Dr Renzo De Gabriele, Permanent Secretary for the Ministry for Health and Active Ageing

Address by Founder and President of Rare Diseases Malta Michelle Muscat: Together Through the Uncommon and celebrating the 10-year anniversary of the National Alliance for Rare Diseases Support – Malta (including Memorial Speech in memory of Prof Alex Felice)

Address by Prof. Ing. Simon G. Fabri, Pro Rector for Research and Knowledge Transfer, University of Malta: Together Through the Uncommon: the importance of local research

9.45 AM — **TOGETHER THROUGH THE UNCOMMON**
The Foreign Perspective: Together Through the Uncommon Internationally.

Dr Antonio González-Meneses López: Artificial Intelligence in Rare Diseases

Dr Peter Schielen: Current neonatal screening scenario's globally and in Europe

Dr Kirsten Johnson: Chair of Rare Diseases International, Board member of EURORDIS, Chair of Fragile X International

10.30 AM — **COFFEE BREAK**

DISCUSSION 1

11.00 - 11.45 AM — **NEWBORN SCREENING AND EARLY DIAGNOSIS**

Mr Ian Brincat: Newborn Screening-the Local Scenario

Panel Discussion chaired by Dr. Miriam Azzopardi

Patient Experiences:
Mrs Charmaine Farrugia – mother of a child with a rare disease

Mrs Therese Attard – mother of three boys living with PKU

Dr Antonio González-Meneses López

Dr Peter Schielen

Dr Christopher Barbara – Clinical Chairperson Pathology Department Mater Dei Hospital

Mr Ian Brincat

BREAK

DISCUSSION 2

12.00- 12:45 PM — **EQUAL ACCESS TO CURE AND CARE**
(cross border healthcare, access to medicine & ERN's)

Dr Anthony Gatt: Cross Border Healthcare and Rare Diseases

Ms Isabelle Zahra Pulis: Access to Medicines for Rare Diseases

Panel Discussion chaired by Dr. Anthony Gatt

Patient Experience: Abigail Ellul
Ms Isabelle Zahra Pulis
Patient Advocates: Michelle Muscat, Dr Gertrude Buttigieg

AGENDA

BREAK

DISCUSSION 3

13.00- 13.45 PM BEYOND CURE: A HOLISTIC APPROACH

Ms Daniela Grima Bezzina: Ministry for Education, Sport, Youth, Research and Innovation – Supporting Learners with Rare Conditions in Educational Settings

Panel Discussion chaired by by Mr Oliver Scicluna – Aġenzija Sapport

Patient Experiences:

Ms Maria Schembri

Mrs Daniela Attard Seychell mother of Mason Vella Attard – CCHS & Hirschsprung Disease

Mrs Tanya Cuschieri Cascun: living with CVID Hypogammaglobulinemia and CVID Enteropathy

Ms Elizabeth Cauchi: lives with Addison's disease

Ms Allison Zammit – Commission for the Rights of Persons with Disability

Ms Daniela Grima Bezzina – Ministry for Education, Sport, Youth, Research and Innovation

QUESTIONS AND INTERVENTIONS FROM THE FLOOR

13.45 PM LUNCH

SCIENTIFIC & RESEARCH PRESENTATIONS HOSTED BY THE UNIVERSITY OF MALTA

14.30 – 14.35 PM OPENING REMARKS

Dr Joanna Vella

14.35 – 14.50 PM

TOWARDS HEMATOPOIETIC STEM CELL KNOCK IN GENE EDITING TRANSFER TO THE CLINIC

Jose-Carlos Segovia Sanz, Head, Cell Technology Division (CTD) and of the Flow Cytometry and Cell Separation Laboratory (LACISEP), at the Center for Energy, Environmental and Technological Research (CIEMAT), Centro de Investigación Biomédica en Red de Enfermedades Raras (CIBERER) e Instituto de Investigación Sanitaria Fundación Jimenez Díaz (IIS-FJD), Madrid, Spain.

14.50 – 14.55 PM

CARDIOMYOPATHY AND CHANNELOPATHY RESEARCH IN MALTA

Dr Mark Abela, Department of Medicine, Faculty of Medicine & Surgery, University of Malta

14.55 – 15.00 PM

MALTESE CORNEAL DYSTROPHY GENE VARIANTS AND TGFBI KNOCKDOWN AS A POTENTIAL THERAPEUTIC STRATEGY

Dr Gabriella Guo Sciriha, Department of Surgery, Faculty of Medicine & Surgery, University of Malta

AGENDA

15.00 – 15.05 PM

THE A30P ALPHA-SYNUCLEIN MUTATION AS A RARE CAUSE OF PARKINSON'S DISEASE

Prof. Neville Vassallo, Department of Physiology & Biochemistry, Faculty of Medicine & Surgery, University of Malta

15.05 – 15.10 PM

MALTA ALS/MND RESEARCH PROGRAMME: GENES TO THERAPEUTIC INSIGHTS

Ms Francesca Grech, Department of Physiology & Biochemistry, Faculty of Medicine & Surgery, University of Malta

15.10 – 15.25 PM

BBMRI-ERIC'S ROLE IN ADDRESSING RARE DISEASES AS A PRIORITY OF THE EUROPEAN RESEARCH AREA

Prof. Jens Habermann, Director General, and Ms Jana Pavlič-Zupanc, Head of Public Affairs, Biobanking and BioMolecular resources Research Infrastructure (BBMRI-ERIC)

15.25 – 15.30 PM

RARE EPLIEPSY SYNDORMES IN MALTA

Prof. Edith Said, Department of Anatomy, Faculty of Medicine & Surgery, University of Malta

15.30 – 15.35 PM

INVESTIGATION OF THE STEM CELL COMPARTMENT IN PATIENTS WITH CHRONIC CYTOPENIAS AND LOW-RISK MDS

Ms Stephanie Magri, Department of Pathology, Faculty of Medicine & Surgery, University of Malta

15.35 – 15.40 PM

GENOMICS OF RARE DISEASE: HOW RESEARCH CAN INFORM DIAGNOSTICS

Prof. Rosienne Farrugia, Department of Applied Biomedical Science, Faculty of Health Sciences, University of Malta

15.40 – 15.55 PM

UPDATES FROM THE EUROPEAN RARE DISEASE RESEARCH ALLIANCE (ERDERA)

Mr Clément Moreau, Project Manager for National Alignment, ERDERA

15.55 – 16.00 PM

EARLY-ONSET OSTEOPOROSIS: GENOMICS AND FUNCTIONAL MODELLING

Ms Marichela Schembri, Department of Applied Biomedical Science, Faculty of Health Sciences, University of Malta

16.00 – 16.05 PM

LESSONS FROM SPACEFLIGHT: GLOBIN GENE CONTROL AND THERAPEUTIC PATHWAYS FOR RARE ANEMIAS

Prof. Joseph Borg, Department of Applied Biomedical Science, Faculty of Health Sciences, University of Malta

16.05 – 16.25 PM **QUESTIONS**

16.25 - 16.30 PM **CLOSING REMARKS**

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SPEAKERS

HON. JO ETIENNE ABELA

Dr Jo Etienne Abela graduated in medicine and surgery at the University of Malta in 1999. He trained as a general surgeon in Malta and the United Kingdom and was appointed consultant surgeon in 2010. He is a visiting senior lecturer and examiner at the University of Malta and a member of the court of examiners of the Surgical Division of the UEMS. He is the recipient of the International Gold Medal of the Royal College of Surgeons of Edinburgh. His academic and clinical interests are preventive endoscopic care in oesophageal cancer (Barrett's Oesophagus), minimally invasive laparoscopic and robotic procedures and multi-organ retroperitoneal cancer surgery. He was appointed Minister for Active Ageing in 2022 and his remit was expanded to include the Health portfolio in 2024.

DR RENZO DEGABRIELE

Dr Renzo De Gabriele was appointed as Permanent Secretary in the Ministry for Health and Active Ageing in May 2025. He is a family doctor by profession, with over 30 years of experience working in the public service.

He graduated as a Doctor of Medicine and Surgery from the University of Malta in 1995 and was awarded a Certificate in Diabetes from the Irish College of General Practitioners in 2008. He is also a Specialist in Family Medicine, and a Fellow of the Malta College of Family Doctors. He is also an expert trainer in family medicine and delivered various national and international courses at various levels to train family doctors as trainers in family medicine.

In 2011, Dr De Gabriele was appointed Assistant Director Administration in the Primary HealthCare Department within the Ministry for Health. In 2013, he was appointed Chief Executive Officer of the Primary Healthcare Department within the Ministry for Health. In 2019, he was then appointed Chief Executive Officer of Active Ageing and Community Care where he was instrumental in strengthening existing services as well as developing new ones. New services launched since 2019 include the Telecare on the Move service, the domiciliary phlebotomy service, a nationwide free transport service for the elderly (the Silver T service), community psychotherapy services for the elderly, renting of motorised beds for homebound clients, the home helper of your choice scheme, and domiciliary dietitian services. Dr De Gabriele also planned and executed the opening of several new active ageing centres, as well as two new dementia activity centres. Residential care services saw the introduction of various new services like speciality nursing and palliative care. A programme of renovation of all government homes was one of his visions, with Floriana Residential Home being renovated and all other government-run residential homes undergoing radical refurbishment. Active Ageing and Community Care was instrumental in the ongoing implementation of the National Strategic Policy for Active Ageing 2023 – 2030 and, through its Dementia Care Directorate, in the publication and current implementation of the National Dementia Strategy 2024 – 2031.

In 2023, Dr De Gabriele was awarded the Best Manager Award in the National Worker of the Year Awards and led Active Ageing and Community Care to achieve another three national awards with the Silver T service being awarded the Best Innovative Service Award in the Malta National Transport Awards; the Dar Padova Project was awarded the Best Project Award in the Public Service Awards; and the Dementia Directorate was awarded the Best Unit Award in the National Worker of the Year Awards.

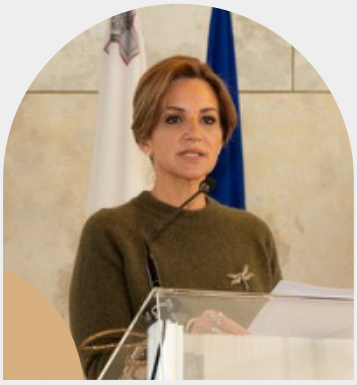
MR CLARENCE PACE

Mr Clarence Pace is a Consultant Maxillofacial/Head and Neck Surgeon. He graduated as a dental surgeon from the University of Malta in 1999 and later earned his Doctor of Surgery and Medicine in 2005. Mr Pace obtained the memberships of the Royal College of Surgeons and later was honoured with the Fellowship of the Royal College of Surgeons of England in Oral & Maxillofacial Surgery. In 2015, he was appointed as a Consultant at Mater Dei Hospital in Malta. Mr Pace has published numerous articles in peer-reviewed journals. He serves as an examiner for the Royal College of Surgeons of England and as a Senior Lecturer at the University of Malta. Following his ten year tenure as Director General for Health Care Services, Mr Pace currently holds the position of Chief Government Medical Officer at the Ministry for Health and Active Ageing in Malta.

PROF. ING. SIMON G. FABRI

Prof Ing. Simon G. Fabri is Professor of Control Engineering with the Department of Systems and Control Engineering at the University of Malta. His research interests focus on adaptive and intelligent control systems, artificial intelligence, automation, and robotics. He is a member of the Editorial Board of the International Journal of Systems Science, principal author of the Springer book "Functional Adaptive Control: An intelligent systems approach" and of numerous academic papers published in international journals and conference proceedings. He has a track record of participation in several funded research projects at the University of Malta.

Simon is a Senior Member of the Institute of Electrical and Electronics Engineers (IEEE), and holder of the Maltese Engineering Warrant. Over the years, he has held several leadership roles at the University of Malta, including headship of the Department of Electrical Power and Control Engineering, the Department of Systems and Control Engineering, Deputy Dean of the Faculty of Engineering and member on several University boards and committees. He is currently the University Pro-Rector for Research and Knowledge Transfer.



MS MICHELLE MUSCAT

Michelle Muscat, Spouse of the Former Prime Minister (2013-2020), is an advocate for healthcare and sustainability, particularly in the realm of rare diseases. As the founder and driving force behind The Marigold Foundation and The Alliance for Rare Disease Support Malta, Michelle has played an instrumental role in raising awareness, fostering collaboration, and mobilizing resources to address challenges faced by individuals with rare diseases.

Contributions to Healthcare and Rare Disease Advocacy Founder of the National Alliance for Rare Diseases Support Malta: Michelle Muscat established this initiative to provide a platform for patients, caregivers, researchers, and policy-makers to come together and address the unique challenges of rare diseases. Her efforts have improved access to treatment, enhanced patient care, and promoted research.
Founder of The Marigold Foundation: Through this foundation, Michelle has spearheaded projects focusing on health, education, and social development. As a marketing specialist by profession she has developed and led numerous projects and campaigns to improve awareness and services related to cancer care, autism, mental health and the welfare of vulnerable populations in Malta, amongst others.

Global Recognition: Michelle's work has been acknowledged by various international organizations. Her leadership in advocating for rare disease policies has made her a key figure in global healthcare conversations including patron of EURORDIS for 11 consecutive years, representing Malta at Rare Diseases International and on the ECOSOC Committee on Rare Diseases at the United Nations, encouraging other nations to prioritize rare disease management.

Her work has not only reshaped Malta's healthcare landscape but also garnered international recognition and partnerships for her dedication to promoting inclusivity and support for marginalized communities.

MICHELLE MUSCAT REMAINS A VITAL FIGURE FOR STAKEHOLDERS IN THE HEALTHCARE AND SUSTAINABILITY SECTORS INITIATIVES.

DR JAMES CLARK

Dr James Clark is a Physician and Gastroenterologist by training, and pursued studies in Quality and Safety in Healthcare at Imperial College, London. Dr Clark is Mater Dei Hospital's representative for all the twenty-four European Reference Networks (ERNs).

DR ANTONIO GONZALEZ MENESES LOPEZ

Dr Antonio González-Meneses López is a Spanish Paediatrician working in Metabolic diseases (mainly Lysosomal Storage Diseases) and Rare Genetic diseases in children in the Dysmorphology and Metabolic Paediatric Unit of Virgen del Rocío Children Hospital (Seville, Spain), part of the MetabERN (Metabolic European Reference Centre). He is also Professor of Paediatrics in the Medical Scholl of the University of Sevilla, Spain.

DR PETER SCHIELEN

Since September 2019 Peter Schielen is the manager of the Office of the International Society for Neonatal screening, he has been a member of the ISNS-scientific committee for many years and he is the Editor in Chief of International Journal of Neonatal Screening. His current interest is neonatal screening on the European continent and innovation in neonatal screening (especially molecular testing in NBS). He is involved in the Screen4Rare initiative, a stakeholder network with ISNS as one of its co-founders, to stimulate collaboration between European partners and states concerning neonatal screening. He was a co-organizer of the world congresses of the ISNS in The Hague, Netherlands (2016), Hangzhou, China (2020) Luxembourg-virtual (2021) and Luxembourg live-2025. Peter Schielen has an MSc in Biology and a PhD in Immunotoxicology, both at Utrecht University, The Netherlands. He worked as a toxicologist at the Dutch Institute of Public Health and the Environment (RIVM) until 1999, when he became project leader Down syndrome screening at the reference laboratory for pre-and neonatal screening (RIVM). Since 2013 he was the head of the reference laboratory for neonatal screening (RIVM) where he contributed to expanding the neonatal screening panel. Since October 2020 he is assisting a team at RIVM to implement breast cancer-, colon cancer- and cervical cancer-screening programs on the Caribbean part of the Dutch Kingdom at the Centre for Population Screening-RIVM. Since 2023, he is also an assistant professor at the Utrecht University Medical Centre-Julius Centre, department of Global Public Health and Bio-ethics. Since 2015 he is technical assessor for the Dutch Accreditation Council (ISO15189-Medical Laboratory Guideline). He has been a member of the Dutch Health Council (commission Pregnancy and Birth) between 2017-2020.

DR KIRSTEN JOHNSON, FRSA

Kirsten Johnson is a pianist, composer and recording artist of international acclaim. She has recorded 26 discs of solo piano music with Centaur, Nimbus, Delos and Guild. This includes the complete piano music of Benjamin Carr, Arthur Foote, James Hewitt and Amy Beach, and world premiere recordings of Albanian piano music and Dmitri Kabalevsky's op. 1. Her release of two discs of piano pieces by Florence Price included 34 world-premiere CD recordings.

Johnson's latest release is Pieces for String Orchestra by Kirsten Johnson on Centaur Records (2025, CRC 4169). The second disc of her own piano pieces, Journeys (2025, CRC 4133) follows the 2024 release of Expressions: Piano Music by Kirsten Johnson (CRC 4095).

Performances of Johnson's works include: the London Contemporary Chamber Orchestra; Festival Osmose, Brussels; Vent Nouveau, NYC; the Boston New Music Initiative; and Fifteen Minutes of Fame, NYC.

In 2025, November Wind was premiered in NYC by pianist Max Lifchitz; The Four Elements, a chamber piece, premiered in Italy by Ear to the Earth Ensemble; I heard a baby, for soprano, premiered in Hong Kong; Prayer, for organ, at the Historical Organ Society National Convention, USA; and Do you bloom?, for baritone, in NYC. Johnson was the 2025 Sara Pennypacker Composer Fellow at the Virginia Center for the Creative Arts. Kirsten Johnson is a Fellow of the Royal Society of Arts and a Fellow of the Incorporated Society of Musicians.

MR IAN BRINCAT

Ian Brincat began his career as a Medical Laboratory Scientist in clinical chemistry in 1997, initially working in the immunoassay laboratory before moving into paediatric laboratory medicine. During his time in paediatric services, he played a key role in strengthening the newborn screening programme through the introduction of blood spot collection, which supported the addition of phenylketonuria (PKU) screening in 2020.

In addition to his clinical work, Ian is a Visiting Senior Lecturer in the Department of Applied Biomedical Science within the Faculty of Health Sciences, where he contributes to teaching and research in biomedical science. His career reflects a strong commitment to improving laboratory practice, advancing newborn screening services, and supporting the education of future biomedical scientists.

DR MIRIAM AZZOPARDI

Dr Miriam Azzopardi graduated as a Doctor of Medicine and Surgery (UOM, 1993). She further specialised in Family Medicine, obtained a Masters in Public Health Medicine (UOM, 2004) and subsequently also obtained a specialisation in Public Health Medicine. She occupied the post of Director, Health Care Standards between 2010-2013 where she had a special interest in the regulation of Blood, Tissues and Cells. She was appointed Consultant in Public Health in 2014 and currently is the head of the Malta National Cancer Register and the Malta Rare Disease Register.

DR CHRISTOPHER BARBARA

Dr. Christopher Barbara is a Consultant Microbiologist and Head of Pathology in Malta with extensive expertise in clinical microbiology, infectious diseases, and public health surveillance. As Clinical Chairman of the Pathology Department at Mater Dei Hospitals and has played a pivotal role in strengthening Malta's laboratory services, establishing molecular diagnostics, and leading national influenza and infectious disease surveillance programmes.

Dr. Barbara has contributed extensively to European and global public health initiatives through collaborations with the WHO, ECDC, and international surveillance networks. He is a published researcher with numerous peer-reviewed articles in leading international journals, focusing on antimicrobial resistance, influenza, emerging infections, and COVID-19. He is a founder member of the Malta College of Pathologists and a Member of the Order of Merit of the Republic of Malta.

DR ANTHONY GATT

Dr Anthony Gatt is a Consultant in Public Health Medicine within the Department Policy in Health within the Office of the Chief Medical Officer at the Ministry for Health and Active Ageing. He joined Public Health in 2005 in the field of infectious diseases surveillance and control, and subsequently joined the Office of the Chief Medical Officer in 2014 working in Policy in Health. Since the inception of the Cross-border Healthcare Regulations of 2013 in Malta he has been in charge of implementing this regulation in Malta and is the National Contact Point.

MS ISABELLE ZAHRA PULIS

Isabelle Zahra Pulis is a Pharmacist with extensive experience across Malta's National health system, furthering her studies in Health Management and Pharmacoeconomics. Her multidisciplinary background spans across community, retail, and hospital pharmacy settings, laying a strong foundation for her later specialization in pharmaceutical policy.

Over the course of her career, she has become a national expert in pharmaceutical policy, pricing, and reimbursement. She has held key management and headship roles within the public health sector, contributing to the development, governance, and sustainability of Malta's medicines framework. She has represented Malta in numerous EU fora, networks, and working groups focusing on medicines access, strategy, and policy harmonisation.

Isabelle's current role centres on ensuring equitable and evidence based access to medicines. She plays a pivotal role in the introduction of new therapies onto the Government Formulary List and serves as Chairperson of the Exceptional Medicines Treatment Committee, which evaluates requests for treatments for rare and complex diseases. Through her leadership, she continues to advocate for patients with unmet clinical needs while safeguarding the principles of quality, value, and system-wide equity.

DR GERTRUDE A. BUTTIGIEG

Dr. Gertrude A. Buttigieg is a licensed Speech Language Pathologist. She holds a master's degree in health management from the University of Malta, as well as a second Master's in International Patient Advocacy Management from the Universita Cattolica del Sacro Cuore, Rome.

Currently, Dr. Buttigieg works full-time at the Office of the Commissioner for the Rights of Persons with Mental Disorders. In addition to her professional role, she volunteers as Chairperson of the Malta Health Network (MHN), an umbrella organization representing over 40 health-related entities. Dr. Buttigieg has spoken at numerous conferences both in Malta and internationally. She has served on the Malta Council for the Voluntary Sector since 2013 and has been Chairperson since March 2023.

MS DANIELA GRIMA BEZZINA

Daniela Grima Bezzina is an experienced educator, inclusion specialist, and lecturer with over twenty years of dedicated service to learners and the wider educational community. She holds a degree in Psychology, a postgraduate qualification in Personal and Social Development, and a master's degree in Early Childhood Education from the University of Sheffield, specialising in developmental and challenging behaviour.

Daniela has worked extensively in home based intervention, supporting children and adolescents in developing core skills in literacy, numeracy, and effective study strategies. Her leadership experience includes a decade as an Inclusion Coordinator in a church school and eight years as an Inclusion Director in a private school, roles through which she championed inclusive practices and empowered educators to respond to diverse learning needs.

Currently, Daniela serves as an Education Officer for Inclusion within the Inclusive Education Support Services at the Ministry for Education, Sport, Youth, Research and Innovation (MEYR). In this role, she contributes to the design and implementation of inclusive policies, advocating for equitable and accessible learning environments at a national level.
Alongside her professional role, Daniela lectures at the University of Malta, MCAST, and Future Focus Malta, where she teaches across programmes in Early Years Education, Inclusive Education, and Applied Sciences. Her work continues to be driven by a strong commitment to building compassionate, inclusive, and supportive educational systems.

MR OLIVER SCICLUNA

Mr Oliver Scicluna, CEO of Aġenzija Sapport is a graduate in informatics, youth studies and public administration. He has led a number of voluntary organisations including Breaking Limits. He served as Commissioner for the Rights of Persons with Disability and served on various Boards within different entities including Transport Malta, Valletta18, NCPE, Jobs+, Malta Community Chest Fund, FITA and Public Broadcasting Services. Oliver was also co-opted in Maltese Parliament and served as MP between 2021 to 2022, during which time he contributed to the advancement of several legislative initiatives. He has also presided over the Parliament International and European Affairs Committee.

Over the years, Mr Scicluna has played a pivotal role in the development of key policies and legislation concerning disability rights in Malta. This includes his involvement in crafting the first national policy for the rights of persons with disabilities, shaping the national strategy for the rights of persons with disabilities (2021-2030), amending the Equal Opportunities Act, enacting the Blue Badge legislation, passing the Maltese Sign Language Act, implementing the Autism (Empowerment) Act, establishing Access for All standards in the built environment, founding the Malta Business Disability Forum, and most recently, spearheading the Personal Budget and Personal Assistant reform.

MS ALLISON ZAMMIT

Allison serves as Manager (Research and Policy) of the Research and Monitoring Unit at the Commission for the Rights of Persons with Disability (CRPD) which is Malta's national equality body responsible for safeguarding and promoting the rights of persons with disabilities. The unit is tasked with conducting research on disability-related issues and monitoring Malta's implementation of the United Nations Convention on the Rights of Persons with Disabilities (UNCRPD).

In this role, Allison works on research and initiatives to advance inclusion, accessibility, and equal opportunities for persons with disabilities. Allison is deeply committed to advocating for change that empowers persons with disabilities to participate fully in society. Her work has included research on employment, auditing services to enhance inclusivity, and studies on deinstitutionalisation to support community-based living.

Beyond her professional role, Allison is active in the voluntary sector, contributing to NGOs that promote social inclusion.

DR JOANNA VELLA

Joanna was awarded the prestigious Reach High II scholarship and is a full-time Post-Doctoral researcher in the Department of Applied Biomedical Science, Faculty of Health Sciences at the University of Malta (UM). She is researching mitochondrial diseases, sudden cardiac deaths and the genetics of the Maltese under the mentorship of Professor Joseph Borg and the late Professor Alex Felice. She holds a Bachelor Honours degree in Pharmacy from UM and a Master's degree in Forensic Science from King's College London. She completed her doctoral degree at UM researching the genetic landscape of the Maltese population and mitochondrial diseases. Joanna setup and managed the University of Malta Biobank between 2010-2019 and managed several EU funded projects at UM including RD-Connect (FP7) and ADOPT-ERIC (H2020). She was also seconded to the largest EU Health Research Infrastructure Biobanking and BioMolecular Research Infrastructure (BBMRI-ERIC) as Quality Manager responsible for managing the quality tasks of the H2020 teaming project 'CY-Biobank' together with the project team at the University of Cyprus. Joanna is the current administrator for EuroBioBank (the first Rare Disease network of biobanks in Europe). Joanna was awarded the Joint Research Council (JRC) Malta Young Scientist Award in 2017 for biobank-led research in rare disease and another award by the National Alliance for Rare Diseases Support – Malta.

PROF. JOSE SEGOVIA SANZ

Jose-Carlos Segovia, Research Professor, PhD from Universidad Autónoma de Madrid works on the study of hematopoietic stem cells (HSC) and on HSC gene transfer, to develop gene therapy protocols for the treatment of hematopoietic genetic diseases. Currently, he is Head of the Cell Technology Division (CTD) and of the Flow Cytometry and Cell Separation Laboratory (LACISEP), at the Center for Energy, Environmental and Technological Research (CIEMAT), Centro de Investigación Biomédica en Red de Enfermedades Raras (CIBERER) e Instituto de Investigación Sanitaria Fundación Jimenez Díaz (IIS-FJD), Madrid, Spain. He has developed lentiviral gene therapy for Pyruvate Kinase Deficiency and contributed to Fanconi Anemia one, nowadays in successful clinical trials. He is a scientific founder of DanausGT Biotechnology, with the aim to drive gene editing to patients. He has been secretary of the Spanish Society of Gene and Cell Therapy, vice-president of the Iberian Society of Cytometry and nowadays, consultant of the Spanish Agency for Medicine and Sanitary Products.

DR MARK ABELA

Dr Mark Abela is a Cardiology registrar practicing at Mater Dei Hospital in Malta. He has undergone a fellowship in Sports Cardiology and Inherited Cardiac Conditions at St George's Hospital in London. His main academic and clinical interests are athletic cardiac adaptation, cardiac screening and inherited cardiac conditions. He read for an MSc (with distinction) in Sports Cardiology (St George's University, London). He has been appointed as a fellow of the European Society of Cardiology (FESC) and the American College of Cardiology (FACC).

He is the sports cardiology clinic lead at Mater Dei Hospital. He also helped establish cardiac screening protocols for the Armed Forces of Malta, Malta Olympic Committee and the Malta Football Association. He is the lead cardiologist for these associations and is a member of their respective medical committees.

He also plays a very active role on an international level within the European Society of Cardiology. On an academic level, he has presented at several local and international conferences, and has also published in several high impact. He is also an editorial board members on several journals. As part of his PhD, he is the principal investigator for BEAT-IT, a national cardiac screening program in Maltese adolescents. This has helped raise awareness about cardiac screening and inherited cardiac conditions on this Maltese islands, paving the way for new screening initiatives in sport clubs and other well established non-sport related entities.

DR GABRIELLA GUO SCIRIHA

Gabriella Guo Sciriha is a specialist ophthalmic surgeon at Mater Dei Hospital, Malta, with particular interest in rare genetic ophthalmic conditions and glaucoma. Gabriella graduated in Medicine and Surgery from the University of Malta in 2005 and went on to obtain both the Diploma and Membership of the Royal College of Ophthalmologists (UK) in 2013. In 2014, she was awarded Fellowship of the European Board of Ophthalmology. Dr. Guo Sciriha subsequently pursued doctoral studies in the field of molecular genetics, focusing on ophthalmic conditions associated with mutations in the Transforming Growth Factor Beta Induced (TGFBI) gene. She was awarded the Dean's Grant from the Department of Medicine and Surgery of the University of Malta for the duration of her doctoral work. Gabriella completed her PhD on Maltese corneal dystrophy genetic variants and TGFBI knockdown as a potential future therapeutic approach in 2025, making her the first female ophthalmologist in Malta to obtain a PhD. Her research resulted in high-impact publications in Taylor & Francis and Springer Nature journals

PROF. NEVILLE VASSALLO

Neville Vassallo is a Full Professor within the Dept. of Physiology & Biochemistry, Faculty of Medicine and Surgery, University of Malta. Prof. Vassallo obtained his M.D. at the University of Malta Medical School, and carried out doctoral training for his Ph.D. studies in the fields of neurobiology and protein misfolding at the Zentrum für Neuropathologie of the Ludwig-Maximilians-University of Munich (LMU), Germany. Since 2008 he has lead a research group at the University of Malta dedicated to understanding the fundamental role of amyloid protein aggregation in diseases like Alzheimer's dementia, Parkinson's disease, and type-2 diabetes. He has published extensively in the field of protein science; in particular, his published work has contributed to establishing the importance of mitochondrial damage through nanopore formation as a unifying toxic mechanism shared by multiple amyloid proteins. Prof. Vassallo has been appointed as Editorial Board member and reviewer by numerous peer-reviewed academic journals and grant societies, including the Medical Research Council (UK), the German Research Foundation (DFG), the Swiss National Science Foundation and the Natural Sciences & Engineering Research Council of Canada. Prof. Vassallo has also been elected Fellow of the Royal Society of Biology (FRSB) and Fellow of the Royal Society of Chemistry (FRSC).

MS FRANCESCA GRECH

Francesca Grech is a researcher at the University of Malta's Motor Neuron Disease Laboratory. She studies amyotrophic lateral sclerosis (ALS) using fruit flies as model organisms, with the goal of understanding the biological mechanisms behind the disease and supporting the development of future treatments.

PROF. JENS HABERMANN

Professor Jens K. Habermann, M.D., PH.D., is Director General of BBMRI-ERIC (Biobanking and Biomolecular Resources Research Infrastructure – European Research Infrastructure Consortium) since September 2020 and a Professor at the University of Lübeck. Prof. Habermann obtained his M.D. training at the Medical University of Lübeck (Lübeck, Germany), received his Ph.D. at the Cancer Center Karolinska, Karolinska Institute (Stockholm, Sweden) and a Postdoctoral Fellowship at the National Cancer Institute, NIH (Bethesda, USA). As board certified specialist in human genetics, Prof. Habermann combines clinics, biobanking, and translational (cancer) research to optimize precision medicine. Prof. Habermann was actively involved in the Molecular Tumor Board as part of the precision medicine program in Lübeck. Prof. Habermann was President of ESBB (European, Middle Eastern & African Society for Biopreservation & Biobanking; esbb.org) from 2018 to 2020 and board member of GBN/GBA (German Biobank Node and German Biobank Alliance; bbmri.de). Prof. Habermann received more than 15 scientific awards, holds about 10 patents and patent applications, is reviewer and editorial board member of more than 25 scientific journals and member of numerous scientific societies. He has a translational cancer research and biobanking related publication track record and was principal investigator and co-PI in more than 21 national and European grant projects.

MS JANA PAVLIČ-ZUPANC

Jana Pavlič-Zupanc is the Head of Public Affairs at BBMRI-ERIC (Biobanking and Biomolecular Resources Research Infrastructure – European Research Infrastructure Consortium) since September 2021, where she leads relations with Member States, the EU, other Research Infrastructures and key stakeholders, including patient organizations. Ms Pavlič-Zupanc has been the proxy to the Director General since November 2024 and since 2025 serving as the Acting Head of the Ethical, Legal and Societal Issues Department. Since 2011 to 2020 Ms Pavlič-Zupanc worked in international relations for the European Molecular Biology Laboratory (EMBL), since 2017 as the Head of Government and EU Relations. Previously Ms Pavlič-Zupanc held different roles for the European Commission and for the Slovenian government. Ms Pavlič-Zupanc obtained her master's degree in European Affairs at the College of Europe in Bruges, Belgium, in 2005, and completed her university studies in International Relations - Political Science at the University of Ljubljana, Slovenia, in 2004.

PROF. EDITH SAID

Prof Edith Said is a consultant medical geneticist at Mater Dei Hospital and has worked in clinical genetics and cytogenetics. As a clinical geneticist she is responsible for the clinical assessment as well as the organization and interpretation of genomic testing on patients with rare diseases. She specializes in intellectual disabilities, congenital anomalies, chromosomal syndromes, reproductive genetics, growth disorders, epilepsy and neurological conditions.

Prof Said is also an associate professor in the Faculty of Medicine & Surgery at the University of Malta. Her research interests include intellectual disabilities, epilepsy, reproductive and renal genetics.

MS STEPHANIE MAGRI

Stephanie Magri is a Biomedical Scientist who embarked on a journey in the field of healthcare in 2015. Graduating with a Bachelor's degree in Biomedical Science in 2019, she started on a fulfilling career in the Pathology Department. For the past six years, she has been an integral part of the Haematology Laboratory, where her passion for Haemato-Oncology began to flourish.

In January 2022, she took a significant step forward in her career by joining the Flow Cytometry Team. Here, she undertook specialised training at the Institute of Cancer Research in Salamanca, Spain, solidifying her expertise in Leukaemia and Lymphoma immunophenotyping. This invaluable experience has allowed her to contribute to the diagnosis and monitoring of these complex conditions. In 2025, she graduated with a Master's Degree in Pathology at the University of Malta. Her research study, titled 'Investigation of the Stem cell compartment in patients with chronic cytopenias and low-risk MDS' reflects her commitment to advancing our understanding of Haematological malignancies and contributing to their effective management. The study aimed to explore the role of investigating the stem cell compartment in patients with unexplained, persistent chronic cytopenias and provide insights into the clinical behaviour of these conditions, aiding in better clinical management.

PROF. ROSIENNE FARRUGIA

Rosienne Farrugia obtained her BSc and MPhil degrees from the University of Malta and her PhD from the University of Cambridge, UK. She is currently an Associate Professor within the Department of Applied Biomedical Science and an Associate Member of the Centre for Molecular Medicine and Biobanking at the University of Malta where her research interests encompass the genomics of rare diseases with a particular focus on infertility due to idiopathic hypogonadotropic hypogonadism. Over the past years she has contributed to the setting up of genomics and bioinformatics as research fields at the University of Matla through an EU TWINNING grant with the University of Cambridge and the Katholieke Universiteit, Leuven and an ERA-Chair EU grant to develop Bioinformatics in Malta.

MR CLÉMENT MOREAU

Clément holds a Master's degree in European and International Project Management from the University of Nantes (France). After an initial internship in project management and European affairs at the Jean Monnet Association in 2019, he worked for two years at Université Côte d'Azur (UCA, Nice, France), where he managed Erasmus+ Capacity Building projects (ERASMUS+, KA2).

He joined the European Joint Programme on Rare Diseases (EJP RD) in August 2021 as Project Manager for Pillar 3 – Training and Empowerment, while also coordinating activities related to strategy development and national alignment within the programme.

He is currently Project Manager for National Alignment within ERDERA, the partnership succeeding EJP RD. In this role, he is responsible for the development and coordination of National Mirror Groups, and is also involved in sustainability planning and monitoring activities, contributing to the long-term impact and strategic orientation of the partnership.

MS MARICHELA SCHEMBRI

Marichela Schembri is a medical laboratory scientist by profession and has been working at the National Blood Transfusion Services (NBTS) for the past six years. She obtained her MSc in Applied Biomedical Sciences from the University of Malta in 2022 and currently holds a position as a Research Support Officer II within the Department of Applied Biomedical Science at the University of Malta. Her research interests focus on the genetics of osteoporosis, aiming to improve understanding of the molecular factors that influence bone health.

PROF. JOSEPH BORG

Joseph Borg is a Full Professor of Genetics and Experimental Haematology at the University of Malta and Founder of Spaceomix Ltd. His research focuses on globin gene regulation, foetal haemoglobin reactivation, and rare blood disorders. He leads pioneering space-biomedicine missions with NASA and SpaceX, translating space science into therapies for patients on Earth.

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ABSTRACTS

TOWARDS HEMATOPOIETIC STEM CELL KNOCK IN GENE EDITING TRANSFER TO THE CLINIC

Jose Bonafont1*, Luis-Javier Serrano1*, Isabel Ojeda-Perez[2,3], Carmen Contreras[2,3], Sridhar Selvaraj[4], Andrés Bustos[5], Min Lu[1], Daniel Lei[1], Shan Chen[1], Omaira Alberquilla-Fernandez[2,3], Aida Garcia-Torralba[2,3], Raul Torres-Ruiz[2,3,6], Sandra Rodriguez-Perales[6], Cesar Trigueros[6], Rafael Mayo-Garcia[4], Rebeca Sánchez-Dominguez[2,3], Oscar Quintana-Bustamante[2,3], Michael Tadros[1], Michael Wang[1], Matthew Porteus[4], Qiang Chen[1], Jose-Carlos Segovia[2,3]

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The use of allogeneic hematopoietic stem and progenitor cells (HSPCs) for the treatment of genetic blood cell disorders represents a potentially curative approach, but its application is limited by donor availability, graft-related complications and immune-mediated toxicity. The emergence of lentiviral gene therapy and gene editing strategies has enabled a shift from allogeneic to autologous therapeutic approaches, overcoming many of these limitations and expanding treatment accessibility. In this context, we have developed a knock-in gene editing strategy based on the combination of CRISPR/Cas9 technology and recombinant adeno-associated viral vector (rAAV6)–mediated donor delivery in HSPCs intended for autologous transplantation.

Optimization of the gene editing protocol resulted in a targeted integration efficiency of up to 60% in HSPCs, without detectable adverse effects on colony-forming capacity or clonal diversity, as assessed using a therapeutic DNA barcode donor. In addition, gene-edited HSPCs demonstrated robust engraftment in immunodeficient mouse models, giving rise to a polyclonal human hematopoietic compartment in vivo, thereby supporting the functional integrity and long-term repopulating potential of the edited cells. These preclinical data supported the successful Orphan Drug Designation of this therapeutic strategy by both the European Medicines Agency (EMA) and the U.S. Food and Drug Administration (FDA).

Subsequently, the optimized gene editing protocol was scaled up using mobilized peripheral blood HSPCs (mPB-HSPCs) from five independent donors. Two of these manufacturing runs were conducted under Good Manufacturing Practice (GMP) conditions in distinct facilities located in Europe and Asia, demonstrating the robustness and transferability of the process. All drug products met predefined quality specifications, including cell viability above 80% and preserved capacity to generate committed progenitors, with consistent knock-in efficiencies exceeding 40% across donor samples.

Altogether, these results enabled the initiation of a first-in-human investigational clinical trial for the treatment of Pyruvate Kinase Deficiency, a chronic inherited hemolytic disorder of the hematopoietic system, with the aim of demonstrating the clinical feasibility and efficacy of this autologous gene editing–based therapeutic approach.

CARDIOMYOPATHY AND CHANNELOPATHY RESEARCH IN MALTA

Dr Mark Abela
Department of Medicine, Faculty of Medicine & Surgery, University of Malta

Inherited cardiomyopathies and primary electrical disorders are important causes of cardiac morbidity and sudden death worldwide. Research in this area helps us better understand their presentation, detection, and management within the Maltese context. Our programme integrates clinical screening, advanced cardiac imaging, genetic testing, and longitudinal follow-up to characterise the burden, phenotypic spectrum, and familial patterns of inherited cardiac disease in the Maltese islands. Through dedicated Sports Cardiology and Inherited Cardiac Disorders services, we combine population-level initiatives—such as adolescent ECG screening—with targeted evaluation of high-risk families to improve early detection and refine risk stratification. This work has established Malta as a model for small-nation precision cardiology, generating high-quality epidemiological data, uncovering population-specific genetic variants, and informing evidence-based pathways for athlete safety, prevention, and personalised care.

MALTESE CORNEAL DYSTROPHY GENE VARIANTS AND TGFBI KNOCKDOWN AS A POTENTIAL THERAPEUTIC STRATEGY

Dr Gabriella Guo Sciriha
Department of Surgery, Faculty of Medicine & Surgery, University of Malta

This work investigates the Maltese CD genetic landscape. Population-level genetic analysis compared single nucleotide polymorphisms (SNPs) in CD-related genes from a large Maltese cohort, with worldwide populations, using fixation index (FST) values to evaluate population differentiation. Substantial genetic differentiation was observed between the Maltese and African cohorts and the least differentiation was seen between the Maltese and Puerto Rican, Mexican, and Colombian cohorts.

We then investigated the functional role of TGFBI through transcriptome analysis and explored the possibility of gene therapy as a treatment modality for the visually debilitating TGFBI Corneal Dystrophies (CDs). TGFBI knockdown was achieved in human corneal epithelial cells using shRNA lentiviral vectors, resulting in an effective 70.5% reduction in expression. These findings demonstrate the feasibility of TGFBI silencing and provide insight into the molecular consequences of TGFBI dysfunction. Together, this population-genetic and functional approach informs future diagnostic strategies and supports further exploration of TGFBI-targeted gene therapy for corneal dystrophies.

THE A30P ALPHA SYNUCLEIN MUTATION AS A RARE CAUSE OF PARKINSON'S DISEASE

Prof. Neville Vassallo

Department of Physiology & Biochemistry, Faculty of Medicine & Surgery, University of Malta

Parkinson's disease (PD) in a clinically important neurodegenerative condition, and a single point mutation in the SCNA gene which codes for the α-synuclein protein (known as the A30P mutation) is linked to a rare inherited form of the disease. Familial PD caused by mutant A30P is usually characterised by an earlier age of onset of motor symptoms (often in the 40s or 50s) and a rapid progression of symptoms, including cognitive decline. In our molecular and cellular studies at the Dept. of Physiology & Biochemistry of the University of Malta, we have uncovered a toxic mechanism involving the A30P α-synuclein protein and mitochondria, the latter being the energy powerhouses of a neuronal cell. Our findings point to potential therapeutic interventions that preserve mitochondrial function and therefore prevent a bioenergetic collapse of the neuronal cell.

MALTA ALS MND RESEARCH PROGRAMME: GENES TO THERAPEUTIC INSIGHTS

Ms Francesca Grech

Department of Physiology & Biochemistry, Faculty of Medicine & Surgery, University of Malta

Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disease in which the motor neurons that control muscle movement gradually degenerate, leading to increasing muscle weakness and, ultimately, the loss of everyday functions such as walking, speaking, and eating. Genetic factors play a significant role in disease causation and risk, which is often elevated in genetically isolated populations like the Maltese population. Given Malta's genetic distinctiveness from other European populations, investigating the genetic basis of ALS within this population is particularly important. This talk will provide an overview of ALS, followed by a focused discussion of the disease in Malta. It will highlight the use of the well-established fruit fly model system to characterise newly identified ALS-associated genes. By uncovering disease mechanisms linked to population-specific genetic variation, this work contributes to the development of precision medicine approaches, with potential benefits for both local and global ALS patients.

BBMRI ERIC'S ROLE IN ADDRESSING RARE DISEASES AS A PRIORITY OF THE EUROPEAN RESEARCH AREA

Ms Jana Pavlič-Zupanc and Prof. Jens Habermann,
Biobanking and BioMolecular resources Research Infrastructure (BBMRI-ERIC)

Rare diseases have been identified as one of key priorities of the EU Research and Innovation efforts. This requires coordinated access to high-quality samples, data and expertise across borders. As the European Research Infrastructure for biobanking and biomolecular resources, BBMRI-ERIC advances health and life sciences research across 25 Member and Observer countries and IARC/WHO, covering roughly 500 biobanks. Through its GDPR-compliant federated access and analysis platform, BBMRI-ERIC provides a unique framework for responsible access to high-quality biological samples and associated data from over 7 million individuals across 32 countries, resources relevant to rare diseases from clinical and population-based biobanks. By contributing to initiatives such as the European Partnership ERDERA and the Rare Disease Moonshot, and through collaboration with EuroBioBank, BBMRI-ERIC strengthens the integration and visibility of rare disease resources, accelerating research, diagnosis and innovation across Europe.

RARE EPLIEPSY SYNDORMES IN MALTA

Prof. Edith Said
Department of Anatomy, Faculty of Medicine & Surgery, University of Malta

Epilepsy syndromes (ES)are defined as epilepsy of a specific type and associated with specific changes on EEG. ES are also categorized by the age at which they present and the vast majority of ES present in childhood or adolescence. The diagnosis is dependent on the type of epilepsy as well as the gene affected. Some of the ES are also associated with developmental delay and epileptic encephalopathy (DEE) which some others are seen in childhood and improve or resolve in adolescence. Some ES arise de novo in the patient while others maybe inherited in an autosomal dominant, autosomal recessive, X-linked dominant and X-linked recessive mode. The spectrum of ES in Malta includes a number of known ES presenting in childhood but also specific autosomal recessive conditions presenting with epileptic encephalopathy and progressive myoclonic epilepsy which are commoner in Malta. Achieving a precise genetic diagnosis of the ES is important to direct specific treatment and management of the individual patient.

INVESTIGATION OF THE STEM CELL COMPARTMENT IN PATIENTS WITH CHRONIC CYTOPENIAS AND LOW RISK MDS

Ms Stephanie Magri

Department of Pathology, Faculty of Medicine & Surgery, University of Malta

Myelodysplastic syndromes (MDS) are defined by the WHO as a group of clonal haematopoietic stem cell (HSC) disorders which are characterised by cytopenias, ineffective haematopoiesis and dysplasia, the presence of blasts and molecular aberrations (WHO, 2022). Patients with MDS have an increased risk of developing Acute Myeloid Leukaemia (AML) with an evolution from low-risk to high-risk MDS which can transform to AML (Mitchell and Steidl, 2019). Patients with persistent cytopenias are relatively frequent encounters in routine Haematology screening and the clinical management of these patients can be challenging due to unpredictable clinical course. This study aims to explore the role of investigating the stem cell compartment in patients with persistent, unexplained cytopenias, and provide insights into the clinical behaviour of these conditions, aiding in better clinical management.

In this study, the stem cell compartment of 53 patients was investigated in two separate cohorts: Cohort A (n=30) included patients with persistent cytopenias (potential pre-MDS conditions, or low-risk MDS) and Cohort B (n=23) patients with high-risk MDS and AML, as a control group. A one-tube flow cytometric assay was used for the detection of leukaemic stem cells (LSCs) using a combination of 13 different monoclonal antibodies, to identify immunophenotypic aberrancies. Molecular studies by next-generation sequencing (NGS) were carried out using a targeted myeloid NGS panel to detect any molecular aberrations. Immunophenotypic findings were then correlated with the molecular findings to confirm or otherwise the clonal nature of cytopenias.

LSCs were found in 60% of patients from Cohort A and 91% of patients from Cohort B with the most common LSC markers being CD45RA and Combi markers. LSCs were detected at higher percentages in Cohort B. Various molecular aberrations which are commonly associated with MDS and AML were also detected in both Cohorts. There was high agreement between Immunophenotyping and Molecular results in Cohort A (56.6%) and Cohort B (91.3%). Cohort A was further sub-classified into low-risk MDS (50%), ICUS (33%), CCUS (7%) and 'Other' (10%) based on cytopenias, dysplasia and the presence of molecular aberrations. The presence of LSCs in 80% of LR-MDS patients, is an important adjunct finding that may prompt clinicians to monitor these patients more closely, with early therapeutic interventions in certain cases.

In conclusion, patients with persistent cytopenias together with the presence of LSCs and molecular aberrations might have an increased risk of leukaemic progression and should be monitored more closely. The LSC assay provides valuable information on the stem cell compartment, better guiding clinicians on the course of action for patients with persistent cytopenias. Detection of LSCs is also important in view of the development of therapeutic targets such as immunotherapy targeted towards aberrant markers including CD33, CD123, TIM-3 and CLL-1 leading to more specific and personalised treatments (Hansen et al., 2022). Molecular analysis is also very important for patient stratification, prognosis and targeted therapy. The strong concordance between immunophenotyping and molecular results shows the importance of using a holistic approach when investigating patients with persistent cytopenia and suspected MDS.

GENOMICS OF RARE DISEASE: HOW RESEARCH CAN INFORM DIAGNOSTICS

Prof. Rosienne Farrugia
Department of Applied Biomedical Science, Faculty of Health Sciences, University of Malta

High throughput sequencing (HTS) has revolutionised genetics research and is finding widespread application in clinical diagnostics of Mendelian disorders greatly improving on the diagnostic sensitivity of traditional approaches. Through the Genomics of Rare Diseases project, we have studied a number of rare diseases, identifying local variants and carried out extensive functional characterisation. Using DNA extracted from blood or saliva, selected gene panels, whole exome and whole genome sequencing were used to generate HTS data. Raw data was mapped to GrCh37 as paired-end libraries. An in-house data analysis pipeline was set-up to shortlist potentially causative variants which were filtered against an in-house database of more than 1000 HTS datasets. A number of variants which can be classified as pathogenic, likely pathogenic or which influence the risk for the development of disease have been identified and characterised. Some of these variants are novel, possibly unique to the Maltese population. A number of founder effects have also been identified, highlighting conditions which are much more common locally than elsewhere and which can shape local diagnostic and screening programmes. This highlights the importance of studying the local population as many of our causative variants differ from the more commonly published northern European variants. These findings enable the design of cheap, targeted diagnostic tests enabling the timely diagnosis and treatment of rare diseases.

UPDATES FROM THE EUROPEAN RARE DISEASE RESEARCH ALLIANCE (ERDERA)

Mr Clément Moreau
Project Manager for National Alignment, ERDERA

The European Rare Diseases Research Alliance (ERDERA) aims to improve the health and well-being of the 30 million people living with a rare disease in Europe, by making Europe a world leader in Rare Disease (RD) research and innovation, to support concrete health benefits to rare disease patients, through better prevention, diagnosis and treatment. This Partnership will deliver a RD ecosystem that builds on the successes of previous programmes by supporting robust patient need-led research, developing new diagnostic methods and pathways, spearheading the digital transformational change connecting the dots between care, patient data and research, while ensuring strong alignment of strategies in RD research across countries and regions. Structuring goal-oriented public-private collaborations targeted at interventions all along the R&D value chain will ensure that the journey from knowledge to patient impact is expedited, thereby optimising EU innovation potential in RD. To support its ambition and missions ERDERA has been designed as a comprehensive and integrated ecosystem of which structure can be compared to an institute encompassing three main parts: (i) funding, (ii) internal (in house) Clinical Research Network that implements research activities targeting clinical trial readiness of RDs and accelerating diagnosis and translation of research discovery into improved patient care, and (iii) related supporting services (Data, Expertise, Education and Training) as well as an acceleration hub that serve external and internal RD community, all supported by all-embracing coordination and strategy and foundational (inter)national alignment.

EARLY-ONSET OSTEOPOROSIS: GENOMICS AND FUNCTIONAL MODELLING

Ms Marichela Schembri
Department of Applied Biomedical Science, Faculty of Health Sciences, University of Malta

Osteoporosis is a major health concern among the elderly population, resulting in decreased bone mass, increased risk of fractures and reduced quality of life. However, in rare cases, bone loss with fragility fractures can occur much earlier in life and present in childhood or early adulthood. Early-onset osteoporosis (EOOP) may be secondary to nutritional deficiencies, prolonged medication use or chronic illnesses. In the absence of an identifiable secondary cause, EOOP is regarded as primary and may then be related to rare variants in genes playing a key role in bone signaling pathways. A 3-generation Maltese family with EOOP was recruited and genetic testing in the form of whole genome sequencing was performed on the most phenotypically informative relatives. A novel variant in the STAT4 gene (c.1309C>T; p.Leu437Pro) predicted to be deleterious by several in silico tools was identified in the affected relatives and absent in both local and European population studies. STAT4 promotes osteoblast differentiation and bone formation. Since the nucleotide and affected amino acid are conserved in zebrafish, genome editing using the Clustered Regularly Interspaced Short Palindromic Repeats/CRISPR-associated protein 9 (CRISPR/Cas9) technique was applied to determine whether a similar phenotype is observed in stat4 mutant fish. Whole-body bone staining resulted in reduced mineral deposition in the vertebrae of stat4 knockout fish compared to the wild-type zebrafish matched for age, indicating that loss of STAT4 impairs normal skeletal mineralisation during early development. Further testing of deleterious variants in STAT4 in larger study collections and sequencing efforts (GRIT: R&I2023-007L; DETERMINE: REP-2024-027; TESS Scholarship 1100/2024/6) could potentially lead to a better understanding of the gene's association with osteoporosis.

LESSONS FROM SPACEFLIGHT: GLOBIN GENE CONTROL AND THERAPEUTIC PATHWAYS FOR RARE ANEMIAS

Prof. Joseph Borg
Department of Applied Biomedical Science, Faculty of Health Sciences, University of Malta

Thalassaemia is an inherited rare blood disorder caused by defects in the genes responsible for producing haemoglobin, the oxygen-carrying protein in red blood cells. When haemoglobin production is impaired, patients develop chronic anaemia and often require lifelong medical care. Our research focuses on understanding how haemoglobin production is regulated at the genetic level. Humans naturally switch from producing foetal haemoglobin (HbF) before birth to adult haemoglobin after birth.

Interestingly, foetal haemoglobin can compensate for defective adult haemoglobin and significantly reduce disease severity in patients with thalassaemia. By studying the molecular mechanisms that control this haemoglobin "switch," we aim to identify ways to safely reactivate foetal haemoglobin in adults as a therapeutic strategy. This involves advanced genetic and molecular approaches to understand how key regulatory genes influence red blood cell development.

Research in extreme environments, including spaceflight, has also provided unique insights into how blood responds to physiological stress, helping us better understand haemoglobin regulation under challenging conditions. Our ultimate goal is to translate fundamental discoveries in blood genetics into innovative treatments that improve outcomes for individuals living with rare inherited blood disorders.