1st Central European Conference
for Advanced Therapy
and Immunotherapy

CREATIC

Rare diseases need innovative therapies —
innovative therapies need scientific discoveries

4.–5. NOVEMBER 2024
BRNO

BOOK OF ABSTRACTS

MASARYK
UNIVERSITY
PRESS

Funded by
the European Union

MUNI
MED

MUNI| CREATIC
Central European Advanced
Therapy and Immunotherapy Centre

1st Central European Conference
for Advanced Therapy
and Immunotherapy

CREATIC

Rare diseases need innovative therapies —
innovative therapies need scientific discoveries

4.–5. NOVEMBER 2024
BRNO

Masaryk University Press
Brno 2024

BOOK OF ABSTRACTS

The conference is supported by the Central European Advanced Therapy and Immunotherapy Centre (CREATIC) project HE 101059788

The project National Institute for Cancer Research (Programme EXCELES, ID Project No. LX22NPO5102) – Funded by the European Union – Next Generation EU.

Book of Abstracts edited by:
Markéta Salačová
Lucie Pospíšilová
Hana Vladíková

ISBN 978-80-280-0652-5

TABLE OF CONTENTS

TABLE OF CONTENTS

DEAR COLLEAGUES AND DISTINGUISHED GUESTS,

We are thrilled to welcome you to the 1st CREATIC Conference – the 1st Central European Conference for Advanced Therapy and Immunotherapy. This gathering brings together leading minds from academia, clinical sites, and research institutions across the Central European region to address shared challenges in the fields of rare diseases and advanced therapies. Your presence here is a testament to our collective commitment to advancing healthcare and improving the lives of patients who are often overlooked. The European Union estimates that between 6,000 and 8,000 rare diseases affect approximately 30 million people across the region, representing around 6-8% of the population. These conditions are often chronic, progressive, and life-threatening, significantly impacting patients' quality of life. On a local level, over half a million people in the Czech Republic alone are affected by rare diseases. Despite these numbers, many patients are still waiting for an accurate diagnosis. The number of newly identified rare diseases continues to rise, alongside well-known challenges such as delays in diagnosis. Due to their rarity, many of these conditions are difficult to diagnose, often taking years to reach the correct diagnosis or, in some cases, remaining undiagnosed. Additionally, the small patient populations for each disease can make it less financially viable for pharmaceutical companies to invest in research and drug development, leading to limited funding and fewer available therapies.

Even when treatments are developed, they can be prohibitively expensive, and access varies greatly across EU countries, with some treatments being entirely unavailable. The challenges and progress in managing rare diseases differ significantly among EU countries due to variations in healthcare infrastructure, funding, and policies.

The purpose of the CREATIC Conference is, among other things, to foster collaboration among academic and clinical sites in the geographically close Central European region. It aims to address these gaps and disparities, as well as to explore current trends and future directions, including advances in genetic testing and ATMP development, and the importance of research collaborations. We hope you find the program engaging and that this event fosters meaningful discussions and collaborations that will drive progress in diagnostics, therapies, and research.

Enjoy your time in Brno!

Regina Demlová, on behalf of the CREATIC CoE Team

CREATING PATHWAYS TO AVAILABLE CELL AND GENE THERAPY FOR RARE DISEASES

The Central European Advanced Therapy and Immunotherapy Centre (CREATIC) is a center of excellence at the Faculty of Medicine of Masaryk University. It is dedicated to the research, development, and production of advanced therapy medicinal products for selected rare diseases. The CREATIC Centre will seek innovative ways to provide very expensive advanced therapy medicinal products to patients in need at an affordable price.

As a public research center, it addresses the need for non-commercial development and production of technologies to treat individuals or very small groups of patients suffering from rare or undiagnosed diseases.

By collaborating with leading scientific centers, CREATIC strengthens the existing achievements of the Masaryk University Faculty of Medicine in the development and production of cell and gene therapies. Our partners in the project include the Fraunhofer Institute for Cell Therapy and Immunology IZI, Leipzig University, and the University of Copenhagen.

The CREATIC Centre combines academic, research, and clinical spheres at a strategically accessible location for the entire Central European region.

MUNI | CREATIC

Central European Advanced
Therapy and Immunotherapy Centre

WHAT PROBLEM ARE WE FACING?

The essential role of the medical technology industry is to develop medicines suitable for common diseases, helping to treat the conditions that affect the majority of the population. The level of interest in developing technologies to treat individuals or very small groups of patients is less relevant to the commercial sector; it is considered risky and may be cost-prohibitive for society.

WHY ARE WE HERE?

As a public research center, we develop and address the need for non-commercial development and production of technologies to treat individuals or very small groups of patients at a cost that makes treatment accessible to all those in need.

HOW DO WE WORK?

We are building on unique know-how with a proven track record in the development of advanced therapies, which we are strengthening by collaborating with key European scientific centers focused on the research and development of advanced therapies.

We are constructing technologically advanced production laboratories on the premises of the Faculty of Medicine of Masaryk University, which will serve as excellent facilities for international researchers involved in the development and production of cell and gene therapies. Our team also includes experts in intellectual property, financing, and regulatory affairs.

WHAT IS OUR MISSION?

CREATIC aims to provide advanced therapy medicinal products to treat rare and undiagnosed diseases in a sustainable manner. Shared know-how across Europe, transparent funding, and an agile approach to drug approval will benefit hundreds of thousands of patients in the EU.

RARE DISEASES NEED INNOVATIVE THERAPIES –

- INNOVATIVE THERAPIES NEED SCIENTIFIC DISCOVERIES

LIST OF SPEAKERS

SESSION I

Ana Hidalgo-Simon

Linda Aagaard Thomsen

Ulrike Köhl

Dalibor Valík

Regina Demlová

Nina Worel

SESSION II

Jakob Wested

Radoslav Hajgajda

Renske ten Ham

Jacques Demotes-Mainard

SESSION III

Aleš Hampl

Ondřej Slabý

David Morrow

Pavlína Danhofer

Jaroslav Štěrba

SESSION IV

Pavel Otáhal

Maik Friedrich

Lenka Zdražilová Dubská

Heiko Von der Leyen

Justyna Drukala

PROGRAMME

PROGRAMME
04.11.2024

FOREWORDS: 13:00-13:30

Welcome speech by Jakub Dvořáček (Deputy Minister of Ministry of Health), Martin Bareš (Rector of Masaryk University), and Martin Repko (Dean of the Faculty of Medicine, Masaryk University)

SESSION I: 13:30-15:30
BRIDGING THE GAP: HOW TO OVERCOME BARRIERS IN THE TRANSLATION OF ATMPS TO CLINICAL PRACTICE

13:30–13:50	Orphans lead the way: ATMPs journey from idea to clinical reality (Ana Hidalgo–Simon)
13:50–14:10	Manufacturing of CAR effector cells: Pushing the boundaries in cancer treatment and beyond (Ulrike Köhl)
14:10–14:30	How Denmark addresses regulatory and reimbursement challenges for ATMPs (Linda Aagaard Thomsen)
14:30–14:50	The current CREATIC CoE research strategy (Dalibor Valík)
14:50–15:30	Panel discussion: Ana Hidalgo-Simon, Linda Aagaard Thomsen, Ulrike Köhl, Tomáš Boráň, Dalibor Valík, Regina Demlová (moderator)

COFFEE BREAK: 15:30-16:00

SESSION II: 16:00-17:50
INNOVATIVE PATHWAYS IN RARE DISEASE TREATMENT: FROM CLINICAL TRIALS TO ACCESSIBLE THERAPIES

16:00–16:20	FAIR medicine - A framework for Responsible innovation of ATMPs (Jakob Wested)
16:20–16:40	Association of Gene Therapy: Role of patients in research on rare diseases (Radoslav Hajgajda)
16:40–17:00	Challenges in health technology assessment and reimbursement of ATMPs (Renske ten Ham)
17:00–17:20	The importance of multinational academic clinical trials for ECRIN (Jacques Demotes-Mainard)
17:20–17:50	Panel discussion: Renske ten Ham, Jacques Demotes, Radoslav Hajgajda, Jiří Samek, Jakub Dvořáček, Jakob Wested (moderator)

THE CONFERENCE DINNER: 19:00-23:00

Dress code: Business Casual

The programme is subject to change.

PROGRAMME
05.11.2024

SESSION III: 9:00-10:30
EVOLVING RARE DISEASE TREATMENT: FROM PRECLINICAL DEVELOPMENT TO CLINICAL IMPLEMENTATION

09:00–09:15	Precision medicine in oncology and ultra-rare diseases as a basis for CREATIC patient-centric approach: experiences from University Hospital Brno (Ondřej Slabý)
09:15–09:30	3D organoids – principle and promise to biomedicine (Aleš Hampl)
09:30–09:45	Building an effective Ecosystem for ATMP development for rare diseases - The role of EATRIS (David Morrow)
09:45–10:00	Practical examples of clinical implementation of precision medicine in paediatric neurological patients (Pavlína Danhofer)
10:00–10:15	Personalized/precision pediatric oncology – cons and pros (Jaroslav Štěrba)
10:15–10:30	Discussion

COFFEE BREAK: 10:30-11:00

SESSION IV: 11:00-12:15
ADVANCES OF ATMPS: FROM CUTTING-EDGE RESEARCH TO SCALABLE MANUFACTURING

11:00–11:15	Novel manufacturing platform utilizing linear DNA transposon for the point-of-care manufacturing of therapeutical GMP-grade CAR-T cells (Pavel Otáhal)
11:15–11:30	Advancing ATiMPs for rare diseases: Development and manufacturing of cell-based therapies for investigator-initiated early clinical trials (Lenka Zdražilová Dubská)
11:30–11:45	Decentralised Manufacturing: New Pokare Strategies for ATMPs (Heiko von der Leyen)
11:45–12:00	Manufacturing of ATMP Products for Skin Regeneration - Clinical Experience (Justyna Drukala)
12:00–12:15	Discussion

LUNCH: 12:15-13:15

The programme is subject to change.

BIOGHRAPHIES

ANA HIDALGO-SIMON

LEIDEN UMC

Ana Hidalgo-Simon, MD, Ph.D., is an experienced scientist and regulator, currently working as an Associate Professor and reNEW Translational Ambassador at Leiden University Medical Center (LUMC). Her current mission is to increase the translation of academic research on Advanced Therapies into clinical practice in a sustainable and fair manner.

For the past 20 years, she has worked at the European Medicines Agency (EMA), holding various key scientific and managerial positions, including establishing and leading the office for Advanced Therapies. Previous roles at EMA include Head of the Specialised Scientific Disciplines Department, Head of Signal Detection, and Head of Risk Management. She holds a degree in Medicine and Surgery from the University of the Basque Country, Spain, and a Ph.D. from the University of London, UK. Additional qualifications include Health Economics (University of York) and Computing (University of Westminster). As Ana Hidalgo-Simon states, her mission is to enhance the translation of academic research on Advanced Therapies into clinical practice in a sustainable and fair manner.

LINDA AAGAARD THOMSEN

DANISH MEDICAL COUNCIL

Linda Aagaard Thomsen has a strong background in health services research. She has a background as a pharmacist and a Ph.D. in pharmacoepidemiology and health economics from the school of pharmaceutical sciences, University of Copenhagen.

Linda Aagaard Thomsen began her research career at the Danish College of Pharmacy Practice and later continued at the Danish Cancer Society Research Center. Her core research competencies lie in the design and evaluation of complex healthcare interventions, implementation science, and health technology assessment. After 20 years in research, she left academia to become Head of the Department for Medicines for Rare Diseases at the Danish Medicines Council, the Danish health technology assessment organization for medicines.

She represents the Danish Medicines Council in the Danish working group on ATMP, a group established to bring together all relevant authorities, payers, and researchers across the Danish healthcare sector to create a seamless collaborative model for introducing commercial and academic ATMP into patient care in Denmark. She is also a member of the coordination group on health technology assessment, established by the EU Commission. The key tasks of the coordination group are to coordinate and adopt the joint health technology assessment work starting in January 2025 within the scope of the EU HTA regulation, adopt methodological and procedural guidance documents for joint work, and ensure cooperation between relevant European Union bodies. The group also ensures the appropriate involvement of stakeholder organizations and experts in its work.

ULRIKE KÖHL

FRAUNHOFER IZI

Prof. Dr. Dr. Ulrike Köhl is a renowned expert in the field of Immuno-oncology. Her extensive expertise, leadership, and contributions in this field have made a significant impact on the development and advancement of cell-based therapies and immunology research.

She has extensive experience in managing academic research groups and has led various EU consortia and graduate schools. In addition to her academic and research responsibilities, Prof. Köhl is a member of numerous national and international societies and serves as a reviewer for various authorities as well as for several journals and foundations.

Prof. Köhl obtained her Ph.D. degree in Pharmacology in 1995 and received her habilitation and venia legendi for Experimental Medicine in 2008 at the Goethe University Frankfurt, Germany. From 1999 to 2012, Prof. Köhl headed the Laboratory for Stem Cell Transplantation and Immune Therapy at the Department of Pediatric Hematology, Oncology and Hemostaseology at the University Hospital Frankfurt (Main), where she additionally managed the Emergency Laboratory for Hematology and coagulation in the period from 2008 to 2010. From 2012 to 2023, Prof. Köhl was director of the Institute for Cell Therapeutics at the Hannover Medical School (MHH). Since 2017, she has been the director and a full professor (W3 level) at the Institute of Clinical Immunology at the University of Leipzig and the Head of the Fraunhofer Institute for Cell Therapy and Immunology (Fraunhofer IZI) with over 600 employees in Leipzig, Germany. In 2023, Prof. Köhl was further appointed as a member of the Saxon Academy of Sciences and Humanities in Leipzig.

REGINA DEMLOVÁ

MASARYK UNIVERSITY

Head of Dept. of Pharmacology, Director of the Centrum of Excellence CREATIC, Head of CZECRIN, Masaryk University, Faculty of Medicine.

Regina Demlova, MD, Ph.D., Assoc. Prof., is a graduate of the Faculty of Medicine at Masaryk University. She began her career as a medical doctor in the internal department of the hospital in Frýdek Místek, but later shifted her focus to oncology.

Since 1997, she has worked at the Masaryk Memorial Cancer Institute (MMCI) in Brno, Czech Republic, where she serves as the Head of the Clinical Trial Unit. After completing Board I in Internal Medicine and Board II in Clinical Pharmacology, she specialized in clinical pharmacology with a focus on clinical trial methodology and design. In 2001, she completed a four-month internship at the Clinical Research Unit of Karolinska Hospital in Stockholm. She earned her Ph.D. in Clinical Oncology in 2009, with a thesis titled "Interindividual Variability of Metabolizing Enzymes – A Pharmacogenetic Perspective in Anti-Cancer Therapy." Since 2011, she has also served as the Head of the Department of Pharmacology at the Faculty of Medicine, Masaryk University, where she focuses on pre- and postgraduate education, as well as research, development, and regulation of medicinal products, including advanced therapy medicinal products (ATMPs). She is the principal investigator of the CZECRIN clinical research infrastructure, which supports non-commercial clinical trials. Between 2010 and 2013, she represented the Czech Republic as a member of the Committee for Orphan Medicinal Products (COMP) at the European Medicines Agency (EMA). Since 2024, she has been the director of the newly established Center of Excellence CREATIC for Research, Development, and GMP Production of Cell and Gene Therapies at the Faculty of Medicine, Masaryk University.

DALIBOR VALÍK

MASARYK UNIVERSITY

Prof., M.D, Ph.D, DABCC, Scientific Director at Creatic CoE, Masaryk University.

Dalibor Valik graduated from medical school in 1985 and subsequently specialized in pediatrics and clinical biochemistry. From 1994 until 1996, he worked at the Department of Clinical Chemistry and Immunology at Mayo Clinic, Rochester, USA. His professional interest was in metabolic disorders and biochemical genetics.

In 1997, he was appointed Head of the Department of Laboratory Medicine at Masaryk Memorial Cancer Institute (MMCI) in Brno, CZ, before becoming an associate professor in oncology in 2009.

The year after, he was appointed both Executive Director of the newly established Regional Centre of Applied Molecular Oncology MMCI (RECAMO) and served as National Coordinator of BBMRI.cz for ten years. As National Node Coordinator, he was responsible for constructing and designing the national network of research biobanks for cancer research. In 2011, he became Head of the Advanced Cell Immunotherapy Unit at the Department of Pharmacology, Masaryk University. In 2017, he was elected Chairman of the BBMRI-ERIC Financial Committee. Dalibor Valik is a member of the Dean's College at the Faculty of Medicine, serving on several committees including the Branch Committee on Experimental Oncology and Tumor Biology, Pharmaceutical Medicine, the Professional Council of Paediatrics, and the Working Group for Infrastructure at the Faculty of Medicine. He also serves on the Program Board for Laboratory Diagnostics in Healthcare (bachelor's study). Currently, he is the Deputy Head at the Institute of Laboratory Medicine and the Head of the Department of Clinical Biochemistry at Brno University Hospital. He also serves as a Czech Delegate in the ECRIN-ERIC Assembly of Members and as the acting Scientific Director of the CREATIC Centre of Excellence at Masaryk University, Brno.

JAKOB WESTED

UNIVERSITY OF COPENHAGEN

Associate Professor, University of Copenhagen, Center for Advanced Studies in Bioscience Law (CeBIL)

Dr. Jakob Wested's research focuses on the regulatory framework for Advanced Therapy Medicinal Products (ATMPs). This includes the regulation of clinical trials, marketing, health technology assessment, as well as intellectual property (IP) policy.

He has extensive experience in interdisciplinary projects, including collaborations with the Danish Health Authority, the Ethical Council of Denmark, and the Danish Medicines Agency, where he completed a three-year industrial postdoc on neglected populations in clinical trials.

In his research on ATMPs, Dr. Wested draws on his in-depth knowledge of European pharmaceutical legislation, including clinical trial and orphan drug regulation, precision medicine, and biotech patents. He wrote his Ph.D. dissertation on the patenting of CRISPR genome editing technology.

Dr. Wested is also the Managing Editor of the European Health & Pharmaceutical Law Review (EHPL), contributing to discussions on pharmaceutical policy and law across Europe.

RADOSLAV HAJGAJDA

ASGENT

Radoslav Hajgajda is a co-founder of the non-profit organization Gene Therapy Association, z.s. He recognizes the importance of genetic disease research and initiated basic research into rare genetic disorders. His greatest motivation is his son, Oliver, who was diagnosed with the rare genetic condition Angelman syndrome.

The Gene Therapy Association has been active for over three years, during which Radoslav has worked purely on a voluntary basis, dedicating his free time to the cause. Asgent is the first non-profit patient organization in the Czech Republic to support research into the treatment of rare diseases. We are part of the technology-knowledge platform "Alliance for Research and Therapy of Rare Diseases," connecting the worlds of science, medicine, and patients.
Currently, our primary focus is on supporting the development of the first drug for Angelman syndrome. We have registered over 80 patients with the condition in the Czech Republic and around 500,000 worldwide. Our efforts have already yielded significant results: the scientific team has made progress in testing and improving methods to influence the expression of UBE3A on the paternal allele in developed mouse models. They have also begun verifying the effectiveness of alternative delivery mechanisms and methods being explored by other research teams abroad.

RENSKE TEN HAM

UMC UTRECHT

Renske ten Ham is an assistant professor at the University Medical Center Utrecht's Julius Centre in the Netherlands, specializing in health economics and health technology assessment (HTA) of regenerative medicines, including gene- and cell-based therapies. Trained as a pharmacist with an MSc in HTA, she holds a Ph.D. in Drug Innovation titled “Development, Market Authorization and Market Access of Gene- and Cell-Based Therapies.”

Over the years, Renske has conducted research at the University of California, San Francisco (UCSF), and spent time at the Dutch Medicines Evaluation Board (CBG-MEB) and the Dutch National Health Care Institute (Zorginstituut Nederland). She is the recipient of the Greiner Award for Best Ph.D. Thesis, the University of York Centre for Health Economics Fellowship, and an NWO VENI Laureate.

At the UMC Utrecht Julius Center, Renske leads the Regenerative Medicines (RM) group within the Department of Epidemiology & Health Economics. She strives to enhance the translation of regenerative medicines and (academic) gene- and cell-based therapies into healthcare services. Her research focuses on payment models, development costs, early economic evaluations, and funding/business models. She aims to contribute to a better understanding of how innovative therapies fit within existing development frameworks, which is not only relevant for regenerative medicines but also for future biomedical innovations.

JACQUES DEMOTES-MAINARD

ECRIN-ERIC

Jacques Demotes-Mainard is a neurologist and professor of Cell Biology, with an extensive background in mathematics and computer science (BA), molecular biology and neuroscience (Master's degree), medicine (MD, Neurologist), a Ph.D. in Neuroscience, and an international MBA.

After 15 years as a clinical neurologist and basic neuroscientist, focusing on signal transduction, neuro--immunological models of Parkinson's disease, mood disorders, and brain tumors, he became chair of a clinical research center at Bordeaux University Hospital. Since 2004, he has coordinated four FP6 and FP7 ECRIN projects, and he currently serves as Director-General of ECRIN-ERIC, a research infrastructure on the ESFRI-roadmap supporting multinational clinical trials in Europe, based in Paris. He has also served as an advisor to the Biology and Health Research Department of the French Ministry of Higher Education and Research since 2005, and he chaired the working group that drafted the OECD Council Recommendation on the governance of clinical trials.

ONDŘEJ SLABÝ

MASARYK UNIVERSITY

Ondřej Slabý, Professor, RNDr., Ph.D., is a Czech molecular biologist, geneticist, professor, and the author of numerous publications. He is the head of the Department of Biology at the Faculty of Medicine, Masaryk University in Brno. He also leads a research group at the Central European Institute of Technology (CEITEC) at Masaryk University and the Center for Precision Medicine at University Hospital Brno.

Ondřej Slabý is the Scientific Director of the National Institute for Cancer Research and the Scientific Secretary of the Masaryk Memorial Cancer Institute in Brno. Board-certified in Clinical Genetics, he is a pioneer in precision oncology and precision medicine, co-founding the molecular tumor board at University Hospital Brno. His team was the first in the Czech Republic to conduct comprehensive genomic profiling for individualized oncology treatment. He actively contributes to educational projects and is a member of the AACR, FRSB, Czech Oncological Society, and others. He co-founded the Czech Neuro-Oncology Society and has chaired the Czech-Slovak Biological Society since 2018. In 2023, he became Chairman of the Czech Health Research Council, previously serving as the Government Commissioner for Health Science and Research. He is now Science and Research Advisor to the Minister of Health and Vice-Chairman of the Scientific Council of the Minister of Health, also serving on the Scientific Council at Masaryk University and the Masaryk Memorial Cancer Institute.

ALEŠ HAMPL

MASARYK UNIVERSITY

Aleš Hampl, D.V.M., CSc., is an Associate Professor specializing in Animal Genetics. He heads the Department of Molecular Embryology at the Institute of Experimental Medicine in the Czech Republic. Research in the department focuses on studying cells with pluripotent properties, including the development of gametes and cells of embryonal origin—specifically, embryonal carcinoma cells and embryonic stem cells.

The department is the first and only laboratory in the Czech Republic where embryonic stem cell lines (ESCs) were established from human blastocyst-stage embryos in 2003. Dr. Hampl's research primarily explores the role of cell cycle regulators in the development of oocytes and embryonic cells. His significant work includes the derivation, propagation, and differentiation of embryonic stem cells, particularly human stem cells. On May 18, 2023, Rector of Masaryk University, Prof. MD Martin Bareš, Ph.D., recognized outstanding achievements in science and research for 2022. Among the laureates of the Rector's Prize was Associate Professor Aleš Hampl, D.V.M., CSc.

Aleš Hampl is an internationally recognized expert on stem cells and their applications in biomedicine. He received the MU Rector's Award for long-term excellence in research in the fields of natural sciences and medicine. In addition to his role as head of the Department of Histology and Embryology at the Faculty of Medicine of Masaryk University, he also leads the ICRC Cell and Tissue Regeneration team. His research focuses on understanding and targeting the biological properties of various types of human stem cells, aiming for their safe application in biomedicine.

DAVID MORROW

EATRIS-ERIC

Dr. David Morrow is a Senior Scientific Programme Manager at EATRIS, coordinating the ATMP (Advanced Therapy Medicinal Products) and Vaccine and Immune Monitoring Platforms, which involve 51 institutions across 15 countries and 31 institutions across 15 countries, respectively. David received a BSc (Hons) in Molecular Biology from University College Dublin in 2001 and a Ph.D in Vascular Biology from Dublin City University in 2006.

Following this, he completed an American Heart Association Postdoctoral Fellowship at the University of Rochester Medical Center, NY, from 2006 to 2008, which resulted in an American Heart Association Young Investigator Award in 2008. From 2009 to 2015, he was an NIH/American Heart-funded Principal Investigator, heading multiple projects in cardiovascular disease and cancer as a faculty member at the University of Rochester Medical Center. At EATRIS, David coordinates the scientific activities of the Advanced Therapies and Vaccines and Immune Monitoring Platforms, including developing proposals to address bottlenecks in the translation of ATMPs to the clinic. He also leads the EATRIS COVID-19 Research Forum and coordinates the scientific output of the EATRIS training course in Advanced Therapies, known as ADVANCE. Additionally, David holds an MBA in Health Science Management and has worked as a consultant and in technology transfer within the life sciences sector.

EATRIS aims to provide the CREATIC project with advice and support to create an effective platform that connects this regional initiative for ATMP development to relevant regional hubs across Europe. This collaboration seeks to address shared areas and challenges of interest, ultimately facilitating the rapid and cost-effective development of ATMPs that could represent a cure for patients where none currently exists.

PAVLÍNA DANHOFER

MASARYK UNIVERSITY

Pavlína Danhofer, Associate Professor, MD, Ph.D., is a pediatric neurologist and university teacher. Since 2007, she has been working at the Department of Pediatric Neurology at the University Hospital Brno, where she has held the position of Head of the Department since 2023.

The Department of Pediatric Neurology at University Hospital Brno and the MU Faculty of Medicine (KDN) is a modern medical facility that offers care for children and adolescent patients with the entire spectrum of neurological diseases. KDN is part of ERN-EpiCARE and ERN-NMD. We are a highly specialized workplace primarily for the comprehensive diagnosis and therapy of epilepsy, extrapyramidal disorders, neuromuscular diseases, and neurodevelopmental disorders, especially ASD (Autism Spectrum Disorders). Pavlína Danhofer specializes in pediatric epileptology and extrapyramidal disorders. She is the Head of the Center for the Diagnostics and Research of Neurodevelopmental Disorders and the Head of the Center for Functional Neurological Disorders (FND) in children. She is a member of the Coordination Panel on FND of the European Academy of Neurology (EAN) and the Committee for Membership and Liaison of the FND Society (FNDS).
In 2011, she obtained certification in neurology and, in 2015, in pediatric neurology. She completed her doctoral studies at the Faculty of Medicine of Masaryk University. She is a member of the Special Education Council. In 2022, she was accepted as a member of the Czech League Against Epilepsy ČLS JEP. She is also a member of the Society of Pediatric Neurology, where she holds the position of Scientific Secretary.

JAROSLAV ŠTĚRBA

MASARYK UNIVERSITY

The professional journey of prof. MUDr. Jaroslav Štěrba, Ph.D., began as a resident in the Department of Pediatrics at University Hospital Ostrava in 1987. He then completed a pediatric oncology fellowship at the same hospital from 1990 to 1993, before becoming the Head of the Pediatric Oncology Unit from 1993 to 1995.

From 1995 to 1997, Jaroslav Štěrba worked as a pediatric oncologist at the Kuwait Cancer Control Center. Since 1997, he has progressed from senior lecturer to professor at Masaryk University in Brno. He also served as the head of the Pediatric Oncology Department at University Children's Hospital Brno since 1998 and as the Vice-Dean of the School of Medicine at Masaryk University since 2010. From 2020 to 2022, he was the CEO/Director of University Hospital Brno.

Jaroslav Štěrba has held visiting positions at Great Ormond Street Hospital in London (multiple visits), the University of California, San Francisco (1993), Johns Hopkins Hospital in Baltimore (1997), Montreal Children's Hospital (2000), and the Fiona Elsey Cancer Research Institute in Australia (2019).

He is a member of the Children's Oncology Group as an International Associate Member, the European Bone and Marrow Transplant Group, and the International Society of Pediatric Oncology (SIOP).

His main research interests focus on metronomic and precision therapy in pediatric solid tumors and lymphomas. He is proficient in English, Czech, Polish, and Russian.

PAVEL OTÁHAL

ÚHKT

Doc. MUDr. Pavel Otáhal, Ph.D., is an experienced clinical hematologist and researcher focusing on developing novel cellular therapies for hematological malignancies.

At the beginning of his career, he gained experience in basic research, particularly in cancer immunotherapy, and completed his postdoctoral fellowship at Pennsylvania State University, USA. After returning home, he received clinical experience as a hematologist at Charles University Faculty of Medicine and the General University Hospital in Prague. During this time, he began focusing his research on chimeric antigen receptor (CAR) therapies for hematological malignancies and started a research group at the Institute of Hematology and Blood Transfusion (UHKT) in Prague. The work of his team resulted in the development of non-viral CAR-T cells that are currently produced at UHKT and tested in clinical trials. These CAR-T therapies include CD19-specific CAR-T for the treatment of B-cell malignancies and CD123-specific CAR-T cells for acute myeloid leukemia.

He is currently focused on developing multi-gene modified CAR-T cells with enhanced antitumor functions and novel CAR-T manufacturing techniques utilizing non-viral transposon systems.

LENKA ZDRAŽILOVÁ DUBSKÁ

MASARYK UNIVERSITY

Lenka Zdražilová Dubská, prof. RNDr. Ph.D. was born in Nové Město na Moravě, Czech Republic. In 2005, she graduated from the Faculty of Science of Masaryk University in Brno with a Ph.D. degree in Cellular and Molecular Biology.

In 2006, she passed the specialization examination in Laboratory Methods in Clinical Hematology. In 2008, she obtained the RNDr. degree in Microbiology, and the following year, she passed the specialization examination in Medical Immunology. In 2017, she completed her habilitation at the MU Faculty of Medicine in Medical Immunology. From 2004 to 2020, she worked at the Department of Laboratory Medicine at the Masaryk Memorial Cancer Institute. Since 2012, she has been Head of Quality Control at the Advanced Cell Immunotherapy Unit of the Department of Pharmacology at MU. In 2020, she became Head of the Department of Clinical Microbiology and Immunology at University Hospital Brno. In 2023, she was promoted to Head of the Department of Laboratory Medicine at University Hospital Brno, covering Clinical Chemistry, Microbiology, and Immunology. In 2024, Lenka Zdražilová Dubska was promoted to full Professor of Medical Immunology and Microbiology at Charles University. She is also the leader of the Innovative ATMP for Rare Diseases Research Group within the CREATIC Centre of Excellence at the Faculty of Medicine MU. Under her leadership, the CREATIC program focuses on the research and development of promising ATMPs (Advanced Therapy Medicinal Products) emphasizing cell-based immunotherapy, MSC-based therapy, CAR natural killer (NK) cells, and CAR macrophages (Mφ). Her innovative approaches and tireless work are bringing new perspectives to medicinal product development and hope to patients while advancing the careers of young researchers and students in the ATMP field.

HEIKO VON DER LEYEN

ORGENESIS

Prof. Heiko von der Leyen, MD, was trained in Pharmacology, Internal Medicine, and Cardiology at University of Hamburg and Hannover Medical School.

After three years of research at Stanford's Falk Cardiovascular Research Center focusing on cardiovascular gene therapy, he was appointed as a junior faculty member at the Division of Cardiovascular Medicine at Stanford University from 1995 to 1996. From 1998 to 2005, Prof. von der Leyen held several top management positions in the biotechnology industry, focusing on the clinical development of advanced therapy medicinal products (tissue engineering, gene therapy, DNA medicine). In 2005, he became the managing director of Hannover Clinical Trial Center GmbH (HCTC), an academic research organization specializing in clinical trial management services and early product development support, now incorporated into Hannover Medical School. In 2020, Prof. von der Leyen became the Medical Director of Orgenesis, Inc., a biotech company focusing on cell and gene therapy. He was a member of the Network Committee of ECRIN-ERIC, a pan-European clinical trials infrastructure organization, from 2014 to 2022. He is also a member of the Scientific Advisory Board of F-CRIN, the academic network for clinical research in France.

JUSTYNA DRUKAŁA

JAGIELLONIAN UNIVERSITY
IN KRAKOW

Prof. Justyna Drukala, Head of Cell Bank with Advanced Therapy Medicinal Products Facility, Department of Cell Biology, Jagiellonian University in Krakow

Justyna Drukała is a Professor of Medical Sciences and Health Sciences at the Jagiellonian University, Kraków, Poland. As a pioneer in the field of tissue engineering, she holds the distinction of being the first researcher in Poland to establish a clinical skin cell culture facility that produced cells for routine skin transplantations aimed at wound treatment. Her research is focused on the regenerative potential of skin cells, and she is currently conducting studies on a new generation of pharmaceuticals, including tissue-engineered products, and their potential applications in regenerative medicine. She is an active scientist and academic teacher mentoring students, post-doctoral fellows, and young faculty members interested in tissue engineering. Author of over 70 experimental and review publications. She collaborates closely with medical professionals and actively participates in the development of new strategies for the implementation of advanced therapy medicinal products especially tissue engineering products. She cooperates with companies implementing new solutions in the ATMP area as a consultant providing validation of the manufacturing process in GMP standard, appropriate consents/authorisations for manufacturing of the product, and coordinating application of the developed product in humans in medicinal experiments.
She is a member of the Commission of Experts of the Polish Society for the Treatment of Burns and the Polish National Transplants Council.

ABSTRACTS

ORPHANS LEAD THE WAY: ATMPS JOURNEY FROM IDEA TO CLINICAL REALITY

ANA HIDALGO-SIMON

The promise of ATMPs moving along the regulatory pathway to the market is now a reality, although at a much slower pace than anticipated. Many are in the pipeline, with a healthy landscape of clinical trials (CTs) at a global level, and a smaller picture at the EU level. Out of 27 approved ATMPs in the EU, 10 are orphan drugs, and orphan medicines are playing a key role in this transition.
Within this new landscape, new challenges are emerging: high prices, high uncertainty, and high risk are slowing down access. Even within the orphan disease communities, the reach of the medicines to patients is sometimes restricted, delayed, and difficult. Expectations from patients and society, on the other hand, are unwavering, and the increasingly well-organized orphan disease community is putting pressure on decision-makers to make access a reality.

HOW DENMARK ADDRESSES REGULATORY AND REIMBURSEMENT CHALLENGES FOR ATMPS

LINDA AAGAARD THOMSEN

The regulatory framework for ATMPs differs from that of traditional medicinal products, and the trajectory of ATMPs from bench to bedside involves many stakeholders in the healthcare system. At the same time, commercial ATMPs come with sparse evidence and exceptionally high prices, which challenge reimbursement. This presentation will outline the HTA considerations concerning the reimbursement of commercial ATMPs and the coming changes with the implementation of the EU-HTA regulation in 2025. The challenges concerning the introduction of commercial and academic ATMPs in the Danish healthcare system were addressed by the Danish National Working Group on ATMPs to optimize cooperation between national stakeholders and create a smooth and seamless trajectory for the introduction of commercial and academic ATMPs to patients in the Danish healthcare system. The working group identified all relevant stakeholders involved in the development and implementation of ATMPs, mapped organizational, administrative, environmental, or legal barriers to implementing ATMPs, and outlined possible solutions.

MANUFACTURING OF CAR EFFECTOR CELLS: PUSHING THE BOUNDARIES IN CANCER TREATMENT AND BEYOND

ULRIKE KÖHL

Chimeric antigen receptor (CAR) T cell therapy has transformed the treatment landscape for relapsed/refractory hematological diseases, providing a promising option for patients with solid tumors and autoimmune diseases. Starting with a short overview of ongoing CAR T cell trials, the reproducible manufacture of high-quality clinical-grade CAR T cells will be discussed next. With the increasing number of patients, this is becoming an ever-greater challenge. New processing techniques, quality-control mechanisms, and logistical developments are required to meet both medical needs and regulatory restrictions. Still, personalized manufacturing is time-consuming and expensive. Results from automated manufacturing present opportunities for improvement in both centralized and decentralized manufacturing units. However, a modular, open, and transferable system with AI-mediated robotics and digital control, as well as the automated documentation of all in-process parameters, is still missing to address the needs of 100-fold more patients. In addition, there are no harmonized rules for patient selection regarding the leukapheresis starting material, and surrogate markers are nearly nonexistent to predict production failure. In several cases, manufacturing failures occur because patients are heavily pre-treated, which can substantially influence the fitness of the cells. Allogeneic CAR effector cells, such as mature or iPS-derived CAR NK cells, play an increasing role in overcoming the limitations of autologous CAR T cell manufacturing. Moreover, the switch from lentiviral to AAV or non-viral gene transfer has opened a platform for improved safety and decreased manufacturing costs. In summary, both improvements in manufacturing and quality control are necessary, as well as concepts to use allogeneic effector cells as an “off-the-shelf product” to overcome current limitations.

THE CURRENT CREATIC COE RESEARCH STRATEGY

DALIBOR VALÍK, REGINA DEMLOVÁ

Successful translation of research outputs into clinically useful medicinal products requires a “drug discovery pipeline” that must be strictly followed at each stage, from discovery to clinical practice translation. The general discovery pipeline identifies major technological and organizational drawbacks that make the translation from discovery to bringing a new medicinal or diagnostic product to market an overtly difficult endeavor. The pipeline phase where most activities fail or are discontinued for some reason is appropriately designated “the Valley of Death.” Therefore, the main focus shall be on the cost-intensive translational research needed to establish and use good manufacturing practice (GMP) conforming production of ATMPs with the respective clinical phase I/IIa trial. The Centre of Excellence CREATIC was established at the Faculty of Medicine, Masaryk University, in collaboration with international partners at Fraunhofer IZI, University of Leipzig, and University of Copenhagen to foster patient-centered academic medical research focused predominantly on Advanced Therapy Medicinal Products (ATMPs) and their effective translation to clinical practice. Clinical investigators and researchers at CREATIC have demonstrated long-term practical experience in translating biomedical research and advanced medicinal therapeutics product development and manufacturing research via clinical trials.

FAIR MEDICINE - A FRAMEWORK FOR RESPONSIBLE INNOVATION OF ATMPS

JAKOB WESTED

How do we get new innovative treatments to patients as expediently, safely, and affordably as possible? This simple question has complex answers addressed under the headline of Fair Medicine.

Background

Advanced therapy medicinal products (ATMPs) introduce new modalities of treatment, pushing the boundaries of treatment targets and effects. Advanced technology platforms, such as CRISPR genome editing technology and CAR-T cells, enable the creation of ATMPs customized for individual patients and can target rare, deadly, or seriously debilitating diseases that have often lacked effective treatment options.

The lack of treatments for the majority of rare diseases can be attributed to a combination of factors, including a lack of scientific understanding of their molecular basis, inadequate regulatory and economic incentives, and the predominance of market-driven business models in the pharmaceutical domain. These multifaceted challenges in translating new treatment modalities from the lab to the large but fragmented rare disease patient populations are crucial to explore in order to realize the potential of ATMPs.

A framework for Fair Medicine

The development of new medicinal products and treatments is often illustrated as a pipeline of discrete steps, spanning research & development, clinical development, marketing, and post-marketing stages. For each step, policies oriented toward future values, practices informing day-to-day activities, and experiences drawing on the past have a formative impact on choices and possibilities in the entire ATMP ecosystem and pipeline. These two dimensions provide a framework for visualizing and structuring fair medicine in the ATMP domain. This presentation will introduce and elaborate on this framework for fair medicine, present examples, and provide some methodological considerations.

ASSOCIATION OF GENE THERAPY: ROLE OF PATIENTS IN RESEARCH ON RARE DISEASES

RADOSLAV HAJGAJDA

Rare genetic diseases affect more people than cancer and AIDS combined, yet they are often overlooked. Patients face limited treatment options and a lack of research focused on their specific needs. However, gene therapy offers hope for a major breakthrough in the treatment of these conditions. The Association of Gene Therapy (Asgent) aims to support the research and development of new therapeutic approaches that could transform the lives of patients.

In this presentation, supported research will be discussed, and the role of Asgent as a linking partner among diverse parties involved will be explained. The flagship project focuses on developing a treatment for Angelman syndrome, a severe neurological disorder that affects motor and cognitive functions.

Activities in fundraising, collaboration with the scientific community, and raising public awareness will be presented. Asgent's goal is not only to foster studies but also to facilitate patient access to innovative treatments that can change their future for the better.

THE IMPORTANCE OF MULTINATIONAL ACADEMIC CLINICAL TRIALS FOR ECRIN

JACQUES DEMOTES-MAINARD

A digital revolution in clinical research was driven by the generation of big data through -omics technology, multimodal data management tools, the development of data standards, and the capacity to analyze large data sets through artificial intelligence. On the other hand, the secondary use of electronic health records is seen as a promising solution to contain the costs of trials by reusing material collected in the healthcare system, thus avoiding duplication of data collection. Additionally, methodological innovation in clinical research has enabled the development of complex trials using master protocols and trials nested in cohorts. However, the problems raised by clinical research on rare diseases and the development of advanced therapy medicinal products remain poorly addressed. Methods to reduce the number of patients recruited in trials, including Bayesian models, enrichment approaches, historical or synthetic control arms, and other virtual approaches, face limitations that are reflected in the regulatory oversight of the trials, while reproducibility in the manufacturing of cell therapy products continues to hamper their development.

Multinational patient recruitment is needed to address both rare diseases and ATMP development.
As the European infrastructure supporting multinational trials in Europe, ECRIN is involved in various initiatives to facilitate biotherapy and rare diseases clinical studies in Europe. Supported by a major ECRIN partner, the CREATIC project is viewed as a key opportunity to develop and disseminate best practices, establish cooperative networks, and share expertise at a pan-European level.

PRECISION MEDICINE IN ONCOLOGY AND ULTRA-RARE DISEASES AS A BASIS FOR CREATIC PATIENT-CENTRIC APPROACH: EXPERIENCES FROM UNIVERSITY HOSPITAL BRNO

ONDŘEJ SLABÝ

University Hospital Brno is recognized as a pioneer in various fields of precision medicine in the Czech Republic. Starting with precision oncology in pediatric patients, the Department of Pediatric Oncology became the first in the Czech Republic and the entire CEE region to implement comprehensive genomic profiling into practice a decade ago. This was followed by the establishment of the first outpatient clinic for undiagnosed pediatric patients in the Czech Republic at the Department of Pediatrics of the University Hospital Brno in September 2023.

The continuously increasing extent of the implementation of precision medicine into clinical practice has led to the establishment of the Center for Precision Medicine of the University Hospital Brno. This center brings together experts from various fields of precision medicine, consolidating their clinical and research activities into one joint interdisciplinary center (http://www.fnbrno.cz/cpm/en). The Center aims for coordinated and efficient development in this field, which will also enable the rapid implementation of new technologies and approaches of precision medicine into clinical practice, thus ensuring the availability of the most advanced diagnostic and therapeutic solutions for patients at the University Hospital Brno. The successful introduction of precision medicine into clinical practice at the University Hospital Brno has resulted in hundreds of successfully treated cancer patients, children who, after many years of diagnostic odyssey, received their genetic diagnosis, and their siblings who were born healthy. The Center for Precision Medicine serves as a strategic clinical partner of the CREATIC Center, participating in most of its scientific programs. The content of the lecture will include examples of the activities of the Center for Precision Medicine, where active cooperation with CREATIC is ongoing.

3D ORGANOIDS – PRINCIPLE AND PROMISE TO BIOMEDICINE

ALEŠ HAMPL, DÁŠA BOHAČIAKOVÁ, TOMÁŠ BÁRTA

In the last two decades, remarkable progress has been made in understanding how stem cells operate to build multicellular organisms and maintain the integrity and function of tissues and organs throughout the lifespan. Although stem cells exist in various forms, ranging from pluripotent stem cells to organ progenitors, they all possess two defining properties: unlimited proliferative capacity and the ability to differentiate into a spectrum of somatic cell phenotypes. Importantly, the differentiative potential of stem cells is retained even in vitro, providing opportunities for the ex vivo production of various somatic cell types by applying external signals that recapitulate developmental cues. Furthermore, since the seminal work of Dr. Clevers (Sato et al., 2013), it has become evident that stem cells and organ progenitors can give rise in vitro to 3D structures that, in many aspects, resemble the complex morphologies typical of normal organs. Such artificially created mini organs, commonly referred to as organoids, have recently witnessed tremendous interest, as they appear to overcome the limitations of standard 2D cell cultures. The biological foundations of organoid technologies will be provided, along with a summary of their envisioned applications in understanding the pathophysiology of diseases, drug development, and personalized medicine. Examples will be presented illustrating how human brain organoids can be used to address Alzheimer's disease and how human retinal organoids can provide information on anomalies affecting the eye.

BUILDING AN EFFECTIVE ECOSYSTEM FOR ATMP DEVELOPMENT FOR RARE DISEASES - THE ROLE OF EATRIS

DAVID MORROW

Over the past few years, Advanced Therapy Medicinal Products (ATMPs), particularly cell and gene therapies, have brought about a remarkable transformation in the field of therapeutics. ATMPs possess the potential to be tailored to individual patients based on their distinct molecular characteristics, making them a crucial aspect of personalized medicine (PM) strategies. Unlocking the full potential of ATMPs is essential for their development as the treatments of the future. Despite their immense promise, significant complexity hinders their success, as evidenced by various systemic bottlenecks in the realms of science, clinical implementation, and regulation. Currently, ATMPs face challenges such as limited understanding and predictability of in vivo cell fate specific to each patient, regulatory issues arising from rapid technological advancements, inadequate standardization in data acquisition, limited reproducibility during preclinical development, and insufficient knowledge exchange among key stakeholders. Addressing these aspects is vital to fully harness the benefits of ATMPs in healthcare. EATRIS, the European Research Infrastructure for Translational Medicine, is actively enhancing its capabilities in the field of ATMPs through a series of key initiatives. These efforts aim to support ATMP development and are focused on delivering novel and innovative scientific tools for the scientific community. As the future unfolds, the ultimate goal is to create the right ecosystem for more effective ATMP development in Europe by connecting successful regional infrastructures and better serving academia and industry in the translation of ATMPs for patient benefit.

PRACTICAL EXAMPLES OF CLINICAL IMPLEMENTATION OF PRECISION MEDICINE IN PAEDIATRIC NEUROLOGICAL PATIENTS

PAVLÍNA DANHOFER

Paediatric neurology as a field has already entered the genetic era and a number of diseases that were previously classified only on the basis of clinical manifestation and syndromological classification such as epilepsy, cerebral palsy or myopathic syndrome acquire much more precise contours on the basis of genetic diagnosis and identification of pathogenic sequence variants underlying the cause of the disease. This is a crucial moment, as it opens up the possibility not only to diagnose children and to use the findings in genetic counselling in preimplantation and prenatal diagnosis, but also to target research on gene therapy, which opens the door to individualised precision medicine. Then we are no longer just addressing individual symptoms, but also the cause of the disease, which is crucial for the patient. This presentation will focus on practical examples of the use of precision diagnostics and its implementation in the treatment process for paediatric neurological patients.

PERSONALIZED/PRECISION PEDIATRIC ONCOLOGY – – CONS AND PROS

JAROSLAV ŠTĚRBA

Individualization of treatment, necessitated by the reality that no two tumors are alike, no two patients are alike, no clinical courses are identical, and tumor–host interactions are highly individual, is increasingly adopted in contemporary pediatric oncology despite regulatory and reimbursement obstacles. Significant gaps and limitations of classical clinical trial schemas exist in areas such as identifying the appropriate dose of biological anticancer agents and the impracticality of randomized trials for the growing number of rare and ultra-rare cancer subtypes, particularly for small population subgroups like children with cancer. Additional obstacles include a limited understanding of the biology of such rare cancers and a lack of interest from the pharmaceutical industry in developing and registering products for children with cancer.

There exists a high unmet medical need for academic institutions, parents/patients' organizations, regulators, and health insurances to expand their perspectives and support new types of clinical studies and individualized precision oncology initiatives aimed at "offering the right drug for the right patient at the right time." Such efforts are intended to improve health-related quality of life (HRQoL), reduce toxicity, tailor treatments to specific patient and disease characteristics, and potentially lower costs. The focus should also encompass Real World Data (RWD) and Real World Evidence (RWE), as RWD holds significant potential, as do N-of-1 cancer trials. Both approaches differ fundamentally from classical randomized controlled trials (RCTs) in that they are patient-centered, fitting drugs to patients rather than fitting patients to drug trials. Trials should be offered to patients, rather than patients being recruited for drug-centric single-agent trials primarily driven by regulatory filing intentions.

NOVEL MANUFACTURING PLATFORM UTILIZING LINEAR DNA TRANSPOSON FOR THE POINT-OF-CARE MANUFACTURING OF THERAPEUTICAL GMP-GRADE CAR-T CELLS

PAVEL OTÁHAL

Chimeric antigen receptor-modified T cells are highly efficient therapeutic products based on gene-engineered T cells. Despite the clinical success achieved with this novel therapy in patients with refractory hematological malignancies, a major limitation to its further development and global availability is its high cost, primarily resulting from the manufacturing process that utilizes lentiviral or retroviral vectors. The main objective of this research was to develop a fully synthetic pipeline for the rapid and cost-effective production of clinical-grade CAR-T at an unparalleled level compared to currently available solutions.

This process utilized polymerase-chain-reaction (PCR)-produced transposon linear DNA and in-vitro transcribed (IVT) transposase mRNA. CD123-specific Chimeric Antigen Receptor-T Cells (CAR123) were produced and clinical testing was initiated in patients with refractory AML. The use of plasmid DNA as a transposon delivery vehicle creates issues, such as the presence of bacterial DNA in the plasmid backbone and the complicated GMP production process of plasmids produced in E. coli. To overcome these caveats, large-scale PCR using high-fidelity polymerase was employed to produce linear transposon DNA of approximately 5kb. The template for PCR amplification was a piggyBac transposon plasmid containing a CD123 CAR (with a 4-1BB-zeta intracellular signaling domain) joined via a T2A self-cleaving motif with CD20 protein. The transposase mRNA was synthesized from a plasmid template using T7 RNA polymerase via large-scale IVT.

CAR123 T cells were produced by electroporating PBMCs obtained from healthy donors or patients undergoing chemotherapy with linear DNA and mRNA. The transfected T cells were then polyclonally activated with anti-CD3/CD28 antibodies and expanded in vitro in a G-Rex bioreactor. Produced CAR123 T cells were thoroughly analyzed by i) multiparametric flow cytometry to determine their immunophenotype and identify cellular subsets, ii) digital PCR (ddPCR) to determine the vector copy number, iii) in vitro cytotoxic tests against cell lines and primary AML cells to evaluate biological activity, and iv) in NSG mice transplanted with AML cells to further prove in vivo antileukemic potency and demonstrate basic safety.

It was verified that linear DNA and mRNA production were feasible, with no issues regarding identity and purity noted. The production of CAR123 T cells was highly effective, as 1 µg of linear DNA yielded approximately 100-150 million CAR-T cells per electroporation of 10 million PBMCs from healthy donors (n=5). The produced CAR123 cells displayed efficient cytotoxicity in vitro against target AML cell lines and in the NSG mice model. The linear DNA transposon platform enables straightforward GMP certification and is especially suitable for the rapid and cost-effective production of novel experimental gene-engineered T-cell therapeutics. The described CAR123 product was approved by the regulatory agency to be tested in a clinical trial (Safety and efficacy of anti-CD123 chimeric antigen receptor-modified autologous T cells (CART123) in patients with relapsed/refractory CD123+ hematologic malignancies: A dose escalation, open-label, phase I study).

ADVANCING ATIMPS FOR RARE DISEASES: DEVELOPMENT AND MANUFACTURING OF CELL-BASED THERAPIES FOR INVESTIGATOR-INITIATED EARLY CLINICAL TRIALS AT THE FACULTY OF MEDICINE, MASARYK UNIVERSITY

LENKA ZDRAŽILOVÁ DUBSKÁ

At the Faculty of Medicine, Masaryk University, cell-based ATiMPs have been developed and manufactured for academic investigator-initiated clinical trials. The focus is placed on translating cutting-edge research into therapeutic solutions that address unmet medical needs, particularly for patients with rare diseases. Currently, a dendritic cell-based cancer immunotherapy for pediatric cancer patients (EudraCT No. 2014-003388-39) and an allogeneic adipose tissue-derived MSC-based IMP for epidermolysis bullosa patients (EudraCT No. 2020-002936-55) are in early-phase investigator-initiated clinical trials.

DC-based immunotherapy for pediatric cancer patients involves the production of personalized dendritic cell (DC) vaccines. This therapy aims to enhance the immune system's recognition and destruction of pediatric cancer cells, offering a promising treatment option for young patients with refractory or high-risk cancers.

Mesenchymal stromal/stem cell therapy for patients with epidermolysis bullosa (EB) is derived from allogeneic adipose tissue. Epidermolysis bullosa (EB) is a rare genetic disorder characterized by extremely fragile skin that blisters easily. By administering MSCs intradermally to EB patients, the aim is to promote wound healing.

Through close collaboration with academic institutions and clinical investigators, a commitment is made to bring innovative, life-changing therapies to patients in need, while advancing the field of cell-based medicine through rigorous research and clinical evaluation. Support is provided by CREATIC and NUVR.

DECENTRALIZED MANUFACTURING: NEW POCARE STRATEGIES FOR ATMPS

HEIKO VON DER LEYEN

Disruptive manufacturing technologies are designed to harmonize and optimize decentralized manufacturing. These technologies encompass both the manufacturing environment, which requires the highest quality standards, and the efficiency and scalability of the manufacturing process itself. Availability, affordability, and accessibility are the cornerstones of realizing such cost-effective cell treatment:

- Availability: developing and optimizing cell processing for cell and gene therapy that are designed to be produced in closed, automated technology systems, reducing the need for high grade cleanroom environments.
- Affordability: Decentralized manufacturing in closed systems eliminates complicated logistics and reduces manufacturing failure risk and the high cost of manual processing. Standardization and harmonization of automated closed systems that are customized for each therapy and available as a total manufacturing solution that ensures consistent quality and supply.
- Accessibility: Mobile manufacturing environment solutions available for rapid on-site deployment without the need for expensive infrastructure. A global collaborative PoCare Centers Network can serve local leading hospitals and medical centers applying cell and gene therapy; the required automation provides an inherited distribution channel for existing and future therapies.

Orgenesis has designed and developed a production framework according to applicable international quality standards. It has transformed the traditional fixed (“brick and mortar”) production room into a mobile, harmonized unit: the Orgenesis Mobile Processing Unit and Lab that can easily be deployed throughout a PoCare Network. These Units are designed to enable parallel processing of CGT products in a safe, reliable, and cost-effective manner at the point of care. CGT products manufactured in such units may be used in validation studies, clinical trials, or, after approval, for marketed clinical therapies.

MANUFACTURING OF ATMP PRODUCTS FOR SKIN REGENERATION - CLINICAL EXPERIENCE

JUSTYNA DRUKAŁA

Tissue engineering and its products represent a new generation of drugs used in regenerative medicine for several decades. One of the first cellular products applied clinically was keratinocytes—epidermal cells successfully used to treat burns in children. Based on these published facts from the 1980s, keratinocytes have since been used clinically for wound treatment.

Our laboratory utilizes cultured keratinocytes obtained from skin biopsies to provide permanent wound coverage for extensive burn treatment. The protocol employs a suspension of cultured epithelial autografts (CEA) in fibrin glue, which is transplanted onto the wound bed. The ability of CEA to ensure wound healing with minimal hypertrophy makes it an attractive alternative to split-thickness skin grafts. We manufacture HE-ATMPs under GMP standards based on the consent of the Chief Pharmaceutical Inspector. The product is produced upon the physician's order and produced under their responsibility, based on the positive opinion from the bioethics committee regarding the therapeutic experiment. The starting material—autologous skin—is accepted by our tissue and cell bank, which is authorized by the Minister of Health for subsequent use in the manufacturing of HE-ATMP.

Our product as a HE-ATMP is manufactured for patients with severe, life-threatening burns for whom conventional treatment methods, are insufficient or impossible to apply. This method does have certain limitations related to the depth of wounds and can be used for second and third degree burns, as well as for mosaic burns. Over the past 10 years, we have prepared products for 54 severely and extremely burned patients. The procedures are funded under the Polish National Transplant Program financed by the Minister of Health.

EXPERTISE

About CZECRIN

CZECRIN is a large research infrastructure, established by a decision of the Ministry of Education, Youth and Sports (MEYS), which is also financed from the earmarked support of large research infrastructures. The decision to establish the research infrastructure was signed on 21 March 2014, on the basis of cooperation between Masaryk University (MU; host institution) and the University Hospital of St. Anny v Brně (FNUSA; partner institution) with the aim of creating a nationwide scientific network of partners for conducting non-commercial clinical research and clinical studies at the national and international level. For the years 2020 – 2022, a financial subsidy from the Ministry of Education, Youth and Sports (LM2018128) was provided for the solution of a large research infrastructure project.

Similarly to other clinical research infrastructures within ECRIN-ERIC, LRI CZECRIN does not have a legal entity's status. Masaryk University (MU) as one of the leading Central European scientific institutions is the legal entity and the host institution of CZECRIN. Research infrastructures operated by MU are an important pillar of research and innovation systems in the Czech Republic. Their importance is emphasized by participation in 16 research infrastructures listed in the Czech National Roadmap for Large RDI Infrastructures. Nine of these projects are also part of research infrastructures of pan-European interest included in the European Strategy Forum for Research Infrastructures (ESFRI). Eight research infrastructures are in the field of health and nutrition.

www.CZECRIN.cz

"...towards patient oriented medicine"

MINISTRY OF EDUCATION, YOUTH AND SPORTS

MUNI MED

ST. ANNE'S UNIVERSITY HOSPITAL BRNO

10th CZECRIN ANNIVERSARY

MUNI
FACULTY
OF MEDICINE

The mission of the Faculty of Medicine Masaryk University is to educate new generations of doctors and healthcare professionals, to share their best knowledge and skills and to participate in the development of research and scientific knowledge actively. The pillar of university values lies in respect for people in their diversity and a commitment to provide medical care regardless of their social status, health status or religious beliefs. The main goal is to facilitate the continuous improvement of the quality of life and the conditions for human existence.

The Faculty of Medicine is active in international networks in education, science and public administration. It has a long history of creating and promoting themes in healthcare, education and prevention, influencing these themes in regional, national and international policies.

Quality facilities, a stimulating environment, and a transparent personnel policy are being developed to attract both junior researchers and established scientists and clinicians. Human resource management is viewed as key to the dynamic development of the faculty.

The objective is to establish the Faculty of Medicine at Masaryk University as a successful and internationally recognized institution with excellent research, a clearly defined strong social role, and a deeply rooted academic culture. It aims to become an attractive place for careers, study, and life, while continuing to be a sought-after partner for collaboration with the academic, healthcare, industrial, and public sectors.

WWW.MUNI.CZ
WWW.MED.MUNI.CZ

The entire vision of CREATIC is not only to deliver ambitious research – we are going beyond – to deliver the results of the research to patients. It means the innovation strategy needs to contain as well as the new conceptual way of translating the results to clinical practice, including the new innovative models for reimbursement strategies. The excellent research in biomedicine has to undergo an extremely dangerous way - extreme price growth rates followed with problematic accessibility to new treatments and lack of proper reimbursement schemes. The sustainable fair pricing of the products is quite an urgent and painful area, where CREATIC will be providing new scientific data and models in the area of health technology assessment and pharmacoeconomics. CREATIC as well will focus on the IP law and the proper use of IP for the benefit of society. By adopting and integrating the principles of Responsible Research and Innovation (RRI), the Centre of Excellence (CoE) will be able to offer patients and society a safe, unique, and financially sustainable treatment, hereinafter referred to as Fair Medicine.

ADVANCED THERAPY MEDICINAL PRODUCTS

Today's science and biotechnology make it possible to enhance the healing properties of various cells of the human body. This is what is studied and performed in ACIU-CREATIC laboratories. The medicinal products developed and manufactured at ACIU-CREATIC belong to the so-called advanced therapy medicinal products (ATMP). We focus on cell or gene therapy products suitable for the treatment of rare diseases.

Gene therapy aims to introduce a normal “healthy” gene into some somatic cells of the patient. This could be a gene that helps immune cells to better recognize a tumor or virus-infected cell. A gene can also be introduced into a malfunctioning mutated cell, ensuring that, for example, damaged nerve cells can transmit impulses and thus maintain functional muscles, or ensuring the replacement of a missing enzyme needed for the brain to function properly. These introduced genes remain only in the recipient's body and do not have the ability to spread to the patient’s offspring. Our medicinal products aim to support cancer treatment.

Cell therapy uses the patient's own cells or those of a healthy donor, which have been promoted in the laboratory to increase their therapeutic abilities. It is currently used, for example, for some complications of Crohn's disease. Our medicinal products aim to promote wound healing and support cancer treatment. Issue-engineered medicinal products use the patient's own modified cells or those of a healthy donor to replace the damaged or dead cells of the recipient. They are currently used to treat severe corneal injuries or damage to articular cartilage.

RARE DISEASES

There are currently around 8,000 known rare diseases – medical conditions that occur very rarely in the human population (at most 1 in 2 000) but often threaten the lives of patients or significantly affect their health and daily functioning.

Some of these diseases are already well known to the general public and the professional community – for example, cystic fibrosis, butterfly wing disease, muscular dystrophy and some cancer diseases that occur in childhood. However, many other diseases pass unnoticed and remain known only to the families of patients and the healthcare staff and social workers who care for them.
Rare diseases arise from a variety of causes and have very different manifestations. Patients thus have a variety of difficulties and needs. For most rare diseases, there is no cure yet, but appropriate health care can prolong and improve patients' lives and make care more manageable for their families.

Health care for patients with rare diseases is complicated by:

- Insufficient scientific knowledge and the slow development of new treatment options,
- Lack of physicians-specialists,
- Long path to the final diagnosis and the difficulty of accessing optimal healthcare

UNDIAGNOSED PATIENTS

Despite the efforts of treating physicians, some patients can be undiagnosed for a long time. In most cases, these are paediatric patients whose diseases can be genetic.
These patients can receive the best care only in specialised centres. Physicians there can perform the necessary genetic tests and consult with colleagues abroad, which facilitates the identification of the causes of the disease, treatment options both in the Czech Republic and abroad, and collecting and analysing data that can help future patients.

FAIR MEDICINE
by CREATIC

prof. RNDr. Ondřej Slabý, Ph.D.

CREATIC implements a patient-centric approach consisting of human genome analyses by using high-throughput technologies and Next- and Third Generation Sequencing methods. By incorporating the principles of RRI in the R&I&D of precision genomics to enable deep gene structure characterisation and stratification of patients, future ATMP treatment strategies have a greater likelihood of being offered to patients as Fair Medicine.

doc. MVDr. Aleš Hampl, CSc.

To verify and prove ATMPs, our researchers will implement functional studies, including ex vivo organoid testing to enhance translational approaches into clinical practice. The organoid research group will be oriented to patient-derived organoids. In vitro amplification of patient organoids from disease-site biopsies can deliver sufficient material for deep sequencing to reveal causal mutations, or for in-depth phenotypic profiling to facilitate more tailored ATMP treatment regimes.

doc. RNDr. Lenka Zdražilová Dubská, Ph.D.

To create and invent prospective ATMPs we are focusing primarily on somatic and mesenchymal stem cells, antigen-specific T cells, CAR T cells, CAR Natural Killer (NK) cells and CAR macrophages (Mφ), mainly for paediatric and adult patients with high-risk tumours; and gene therapies for currently undiagnosed rare diseases, where high-throughput technologies for human genome analyses will help precisely characterise the rare disease. The excellent research will address and experimentally cover several topics like insertion of both vectorbased vs non-viral transposon approach, source of effector immune cells, insertion of genetic material or achievement of tissue-specific and regulated expression of transferred genes.

doc. MUDr. Regina Demlová, Ph.D.

By integration of SSH disciplines (law, RRI, pharmaco-economics, ethics) throughout the R&I process, CREATIC will focus on national and EU regulations on GMP manufacturing and ATMPs authorisation requirements, as well as national and EU requirements for clinical trials (including GMP, import restrictions, and ethical requirements). We also focus on the issue of sustainable and fair pricing of products and services, with legally supported and holistic proposals on dealing with the enormous expense currently associated with ATMP treatments. CREATIC will provide new scientific data and models in health technology assessment and pharmaco-economic studies for ATMPs, as well as leveraging intellectual property rights (IP) to ensure science can be transformed into market-ready innovations for the benefit of the EU citizens.

Mgr. Jakub Jamárik

To monitor and analyse both the efficacy and safety of ATMPs, longitudinal monitoring of the patients in clinical trials and medical practice will be desirable to accompany the clinical staging. We will establish e.g. standardised flow cytometry assays suitable to characterise immune cell subpopulations or individually formulated genomic assays to monitor for minimal residual disease. Our research will also cover data science, bioinformatics, biomedical ethics, and computational biology aiming at advanced strategies for therapy response prediction. We will use machine- and statistical learning to explore bioinformatics analysis of complex transcriptomic and genomic data and to develop prototypes for in vitro diagnostics and point-of-care platforms.

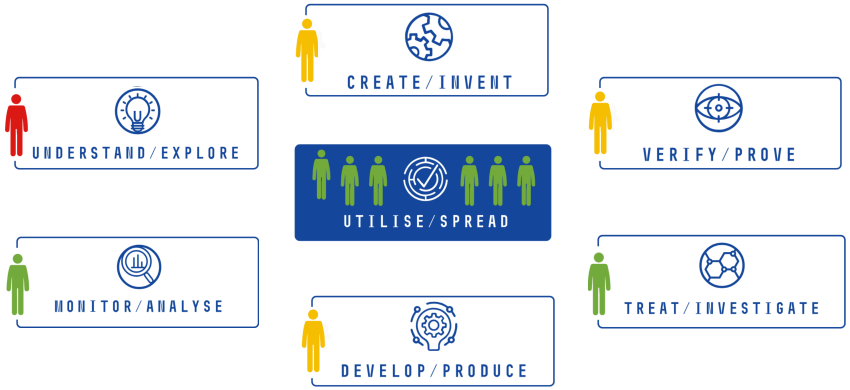
prof. MUDr. Jaroslav Štěrba, Ph.D.

To deliver the research results to patients is a significant element of CREATIC's overall strategy. It means to integrate knowledge and methodologies and to translate them to a testable environment of investigator-initiated clinical trials using ATMPs in the appropriate modes – either as single-agent therapies for monogenic disorders and/or – assumingly much more often – into combination therapies in those rare diseases requiring comprehensive medical care at the tertiary academic medical centre within CREATIC surrounding areas.

prof. MUDr. Dalibor Valík, Ph.D., DABCC

ATMPs in GMP conditions, the RG will be responsible for transferring manufacturing processes from the lab into a clinical setting. GMP-compliant processes will be developed or adapted from existing processes and optimised to obtain official manufacturing licenses to produce clinical test samples. The development of GMP-compliant manufacturing protocols will be a part of this RG, closely associated with the definition of respective quality controls.

7 RESEARCH PROGRAMMES COMBINING STM AND SSH DISCIPLINES



PARTNERSHIPS

FRAUNHOFER IZI

Fraunhofer Institute for Cell Therapy and Immunology IZI is a strategic partner of CREATIC in particular for the research and development of cell and gene therapies paired with expert training and exchange.

The Fraunhofer IZI investigates and develops solutions to specific problems at the interfaces of medicine, life sciences and engineering. One of the institute's main tasks is to conduct contract research for companies, hospitals, diagnostic laboratories and research institutes operating in the field of biotechnology, pharmaceuticals and medical engineering.
The Fraunhofer IZI develops, optimizes and validates methods, materials and products within the business fields of cell and gene therapy, drugs and vaccines, molecular diagnostics and immunodiagnostics, as well as extracorporeal therapies. Its areas of competence lie in cell biology, immunology, drug biochemistry, bioanalytics and bioproduction as well as process development and automation.
Research in these areas is centered around the developments in immuno-oncology and infectious disease pathology. The on-site S3 safety laboratories allow to conduct research and development activities and to investigate highly pathogenic agents under biosafety level 3 conditions.
The institute works in close cooperation with hospital institutions and performs quality tests besides manufacturing investigational medicinal products in line with GMP requirements. Furthermore, it supports partners in developing processes for the pharmaceutical production of ATMPs and biologicals, for example by helping them to obtain manufacturing licenses.

RESEARCH & DEVELOPMENT

- Cell and gene therapy design
- Experience with various effector cell types (T cells, NK cells, and macrophages)
- Experience with viral and non-viral gene modification methods

PRECLINICAL DEVELOPMENT

- In vitro and in vivo testing (efficacy and safety) of drugs as well as ATMPs according to GLP
- Cell analysis, assay development and diagnostics
- Modern animal testing facility, numerous models established, development of customized disease models

GMP PROCESS DEVELOPMENT AND UP-SCALING

- GMP process design, optimization and automation
- Implementation and development of quality controls
- Testing and optimizing new devices, products and processes in compliance with GMP regulations

GMP MANUFACTURING OF CELL AND GENE THERAPEUTICS AND BIOPHARMACEUTICALS

- More than 17 years of experience in GMP manufacturing of cell-based therapeutics
- 3,500 released products for clinical applications (incl. ~500 CAR T-cell products)
- Modern clean room infrastructure and well-trained staff

GMP TRAINING

- Specialized trainers with hands-on experience in GMP manufacturing of cell and gene therapies (e.g., CAR T-cell therapies)
- GMP basic training, courses for good documentation and sterile work in the laboratory
- Customized training courses on the basics of GMP production of cell and gene therapies

Fraunhofer IZI

LEIPZIG UNIVERSITY

Leipzig University is a key partner in the CREATIC project, contributing its expertise in cutting-edge research, education, and innovation. With a long-standing tradition dating back to 1409, Leipzig University is one of the oldest universities in Germany and has a strong focus on interdisciplinary research across a wide range of scientific fields, including life sciences, medicine, and engineering.

The university's contribution to CREATIC is particularly centered on the development and optimization of advanced therapies, as well as fostering the next generation of scientists through targeted training programs. As part of the Faculty of Medicine, leading researchers at the Institute of Clinical Immunology are driving forward research in cell and gene therapy.

Research efforts at the University of Leipzig are characterized by a close integration of fundamental science and clinical application. By collaborating with university hospitals and research centers, the university excels in translating scientific discoveries into tangible therapeutic solutions. In addition, its state-of-the-art laboratories and research infrastructure provide the ideal environment for conducting studies under stringent quality and safety standards.

RESEARCH & DEVELOPMENT

- Expertise in the development and validation of innovative therapeutic approaches, particularly in the fields of cell and gene therapies
- Comprehensive experience in molecular diagnostics and the integration of bioinformatics for precision medicine
- Research focus on translational medicine bridging basic research and clinical application

PRECLINICAL AND CLINICAL EXPERTISE

- Access to specialized clinical trial units, supporting early-phase trials and the development of Advanced Therapy Medicinal Products (ATMPs)
- Strong track record in conducting ethically and scientifically robust clinical studies, ensuring patient safety and regulatory compliance

TRAINING AND CAPACITY BUILDING

- Extensive experience in academic teaching and training programs, particularly in life sciences and medicine
- Development of customized training modules in cell and gene therapy, combining theoretical knowledge with practical hands-on experience

Through this collaboration, Leipzig University not only brings its academic excellence and research capabilities to CREATIC but also ensures that the project is supported by a holistic approach combining scientific discovery, clinical application, and the training of future experts in the field.

UNIVERSITÄT LEIPZIG

UNIVERSITY OF COPENHAGEN

In the CREATIC project, the University of Copenhagen brings expertise in social sciences and humanities, biomedical law, ethics, and data protection. UCPH also coordinates an international ecosystem of collaborating institutions, organises stakeholder engagement and knowledge valorisation as well as establishes a legally supported responsible research innovation (RRI) framework.

Driven by intellectual creativity and critical thinking since 1479, researchers and students at the University of Copenhagen have expanded horizons and contributed to moving the world forward. With its 5,000 researchers and 37,500 students, the University boasts an international research and study environment and is highly ranked on the leading ranking lists of the world's best universities.

The University offers researchers and students the opportunity to develop their talent and launches ambitious interdisciplinary initiatives to support its strong academic communities. Through research-based teaching – and by involving them in research – students are equipped to address society's challenges and needs.

The University of Copenhagen is working towards becoming one of the world's greenest campus areas, leaving as little environmental and climate footprint as possible. The University facilitates cross-organisation collaboration, liaises with the business community and helps students find relevant programmes and projects in the field of sustainability. The University also focuses on gender equality and sees diversity as a strength.

UNIVERSITY OF COPENHAGEN

1st Central European Conference for Advanced Therapy and Immunotherapy.
Book of Abstracts

Markéta Salačová, Lucie Pospíšilová, Hana Vladíková (eds.)

Published by Masaryk University Press,
Žerotínovo nám. 617/9,
601 77 Brno,
Czech Republic

First electronic edition, 2024
ISBN 978-80-280-0652-5

BOOK OF ABSTRACTS

WWW.CREATIC.MUNI.CZ

MASARYK
UNIVERSITY
PRESS