TRANSLATIONAL MEDICINE '17
Enhancing Predictivity

PROGRAMME

ENHANCING PREDICTIVITY IN MEDICINES DEVELOPMENT

powered by

eatris

September 24-26, 2017
Corinthia Hotel, Prague, Czech Republic

TRANSLATIONALMEDICINE2017.EU

WELCOME

Welcome to Translational Medicine 2017, the third biennial conference hosted by EATRIS ERIC European Infrastructure for Translational Medicine. We are proud to present this year's programme, centred around the theme 'Enhancing Predictivity in Medicines Development.' The goal of this year's conference is to explore the frontiers of translational medicine by bringing together all relevant sectors, including academic and industry researchers, policymakers, patients and the regulator. Improving our ability to innovate from the creative realms of academia, reducing late stage failures by developing promising tools and technologies, and enhancing regulatory dialogue and interaction are key areas of discussion.

Please contribute actively and help make each session interactive, lively and challenging!
A new feature this year is the educational programme on Sunday 24th, with six workshops focused on the latest developments in a range of operational and technical areas, organised with key partners and faculty from around the world. And don't forget to take the opportunity to meet with key opinion leaders from the EATRIS platforms, industry and policy circles throughout the conference period.

With many thanks to and on behalf of the conference team, platform chairs committee and all our partners, we hope you have a memorable TransMed '17!

Giovanni Migliaccio
Scientific Director, EATRIS

Anton Ussi
Operations & Finance Director, EATRIS

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FAST TRACK TO CLINICAL PROOF OF CONCEPT

ABOUT EATRIS

EATRIS helps you de-risk and add value to your drug, vaccine or diagnostic development programme. We do this by providing fast, tailored access to cutting-edge enabling technologies in translational research.

Infrastructure

Via our central hub, you can access the vast array of clinical expertise and high-end facilities that are available within the 80+ top-tier academic centres across Europe.

Product Platforms

EATRIS focuses on preclinical and early clinical development of drugs, vaccines and diagnostics.

Solutions are provided in the fields of advanced therapy medicinal products, biomarkers, imaging and tracing, small molecules and vaccines. The wide-ranging services portfolio focuses on supporting early decision-making and de-risking of projects.

Examples include validation and development of in vitro and in vivo biomarkers for patient stratification, molecular imaging tracers for drug development programmes, GMP manufacturing of cellular therapy products, patient-derived xenograft models, and many more highly specialised capabilities.

See **eatris.eu** for more information.

PROGRAMME

SEPTEMBER 24 - SEPTEMBER 26

INTRODUCTION

This year's conference programme is split into three plenary sessions, each with a different focus and all with more technical content than in previous years. We will hear from high level speakers from Europe, North America and Japan, for a truly global view.

The first session looks at the issues and emerging innovations in policy, regulation and funding that will have a lasting impact on the drug development process. A panel comprising representatives from multiple sectors will close the session, debating the subject of cross-sector collaboration in translational medicine.

The second and third sessions look at the drug development pipeline itself, with a focus on showcasing novel tools to improve drug and diagnostics development pipeline productivity, with session two on clinical development, and session three on preclinical development.

All sessions will be lively and interactive, with audience members offered the opportunity to question the speakers directly or via our audience interaction application.

SUNDAY, SEPTEMBER 24

PRE-CONFERENCE WORKSHOPS

12:30 - 13:30	**Registration**
13:30 - 19:00	**Educational Workshops** Two workshop sessions: 13:30 - 16:00 and 16:30 - 19:00
13:30 - 16:00	**Workshop A** Translating biomarkers into in-vitro diagnostics (IVD)
13:30 - 16:00	**Workshop B** Challenges and best practices in academic drug development
13:30 - 16:00	**Workshop C** Designing your research for maximum impact: building a data package fit for investment
16:00 - 16:30	**Coffee break**
16:30 - 19:30	**Workshop D** Potency assays in advanced therapies and vaccines
16:30 - 19:00	**Workshop E** Molecular imaging supporting CNS drug development
16:30 - 19:00	**Workshop F** Designing your research for maximum impact: how to assess and maximise the potential impact of your research plan
19:00 - 20:00	**Networking Drink** Business Lounge, 24th floor

MONDAY, SEPTEMBER 25

SUITE II (3RD FLOOR)

08:30 - 09:30	**Registration & posters presentation**
09:30 - 09:45	**Welcome Words** Robert Plaga, Deputy Minister for Research and Higher Education, Czech Ministry of Education, Youth and Sport Giovanni Migliaccio, Scientific Director, EATRIS
09:45 - 10:00	**Setting the scene** Exclusive video-recorded interview with Dr. Elias Zerhouni, President, Global R&D, Sanofi

PLENARY SESSION 1:

THE FUNDER, DEVELOPER AND REGULATOR AS PARTNERS IN INNOVATION
MODERATOR: Anton Ussi, Operations & Finance Director, EATRIS

10:00 - 10:10	**Launch of "Translation Together"** Joint announcement by NIH-NCATS (USA), TIA (AU), LifeArc (UK), CDRD (CA) and EATRIS
10:10 - 10:30	**Personalised medicine activities at EU level** Elmar Nimmesgern, Deputy Head of Unit Innovative and Personalised Medicine, DG Research & Innovation, European Commission KEYNOTE SPEAKER
10:30 - 10:50	**From gatekeeper to enabler: a new role for regulators?** Isabelle Moulon, Senior Advisor on Stakeholders Engagement, European Medicines Agency KEYNOTE SPEAKER
10:50 - 11:20	**Coffee break & posters presentation**
11:20 - 11:40	**"The Tale of Two Worlds" – Can finance rescue lives?** Clayton Heijman, Director, Privium Fund Management, The Netherlands KEYNOTE SPEAKER
11:40 - 12:00	**Multi-disciplinary, multi-sector collaboration as a key enabler of biomedical innovation** Anton Ussi, Operations & Finance Director, EATRIS KEYNOTE SPEAKER

12:00 - 12:45 **Panel session**
Increasing efficiency of medicines development by bringing funder, researcher and regulator closer together

12:45 - 14:00 **Lunch & posters presentation**

PLENARY SESSION 2:

NOVEL APPROACHES IN CLINICAL DEVELOPMENT
MODERATOR: Kjetil Tasken, EATRIS National Director, University of Oslo, Norway

14:00 - 14:05 **Setting the scene**
Exclusive video-recorded interview with Dr. Elias Zerhouni, President, Global R&D, Sanofi

14:05 - 14:35 **Enabling innovation through external networks: experiences from clinical imaging for pharmaceutical R&D**
Philip Murphy, Head Experimental Medicine Imaging, GSK, United Kingdom
KEYNOTE SPEAKER

14:35 - 15:05 **From an idea to a medicinal product - a success history**
Ragnhild Marie Loeberg, Head of Quality and Regulatory Affairs, Bayer AS, Norway
KEYNOTE SPEAKER

15:05 - 15:35 **Application of PET imaging for clinical development of treatments for neuropsychiatric disorders: trials and tribulations**
Mark Schmidt, Senior Director R&D, Janssen, Belgium
KEYNOTE SPEAKER

15:35 - 16:00 **Coffee break & posters presentation**

16:00 - 16:20 **Translating clinical proteomics into clinical practice**
Marian Hajdúch, Director, Institute of Molecular and Translational Medicine, Czech Republic
KEYNOTE SPEAKER

16:20 - 16:40 **Pitfalls in study design - and how to avoid them**
Matejka Rebolj, Senior Epidemiologist, Queen Mary University of London, United Kingdom
GUEST SPEAKER

16:40 - 16:55 **Immunomonitoring of MSC-treated GVHD patients reveals no obvious markers for therapy response or safety concerns**
Johanna Nystedt, Development Director, Cell Therapy Services, Finnish Red Cross Blood Service, Finland
ABSTRACT SPEAKER

16:55 - 17:10 **Metabolomic profiling approach to improve patient's selection and prediction of outcome for cancer treatment**
Susan Costantini, Researcher, IRCCS-National Cancer Institute of Naples "G. Pascale Foundation", Italy
ABSTRACT SPEAKER

17:10 - 17:25 **miRNAs as accurate and useful biomarkers of acute kidney injury in cardiac surgery patients**
María Laura García Bermejo, Head of the Biomarkers and Therapeutic Targets Research Group, Institute Ramón y Cajal for Health Research (IRYCIS), Spain
ABSTRACT SPEAKER

17:25 - 17:40 **18F-FAZA-PET/CT hypoxia imaging in lung cancer and high grade glioma**
Maria Picchio, Researcher, IRCCS-San Raffaele Scientific Institute, Italy
ABSTRACT SPEAKER

17:40 - 17:55 **A new path for accelerating therapies for rare diseases to patients**
James McArthur, President of R&D, Cydan, United States
ABSTRACT SPEAKER

17:55 - 18:00 **Closing**

18:00 - 20:00 **Networking cocktail**
Bellevue Hall, 24th floor

TUESDAY, SEPTEMBER 26

PLENARY SESSION 3:

DEVELOPING MORE PREDICTIVE PRECLINICAL TOOLS TO BETTER REACH PROOF OF CONCEPT
MODERATOR: Ulrika Bäckman, EATRIS National coordinator, Uppsala University, Sweden

09:00 - 09:10
Summary of discussions & Setting the scene, exclusive video-recorded interview
Dr. Elias Zerhouni, President, Global R&D, Sanofi

09:10 - 09:35
Catalysing translational innovation on a global stage
Christopher Austin, Director, National Institutes of Health-National Center for Advancing Translational Sciences, United States
KEYNOTE SPEAKER

09:35 - 10:00
The translational safety challenge from the perspective of Innovative Medicines Initiative (IMI)
Jacques Richard, Scientific Advisor, Sanofi & Scientific Coordinator of the IMI Translational Safety Strategic Governing Group, France
KEYNOTE SPEAKER

10:00 - 10:25
Increasing predictability and developability of academic drug discovery & development projects
Per Arvidsson, Executive Director Drug Discovery & Development, SciLifeLab Karolinska Institutet, Sweden
KEYNOTE SPEAKER

10:25 - 11:00
Coffee break & posters presentation

11:00 - 11:25
Novel enveloping mechanism of action in Alzheimer's disease
Petr Kocis, Vice President Preclinical Development, Alzheon, United States
KEYNOTE SPEAKER

11:25 - 11:40
Embryonic regulation of the mouse hematopoietic niche and implications for haematotherapy
Daisuke Sugiyama, Deputy Director, Centre for Clinical and Translational Research, Kyushu University, Japan
ABSTRACT SPEAKER

11:40 - 11:55
A 3D Microfluidic model for evaluating immune parameters associated to the efficacy of antitumor therapies
Lucia Gabriele, Group Leader, Department of Oncology and Molecular Medicine, Istituto Superiore di Sanita (ISS), Italy
ABSTRACT SPEAKER

11:55 - 12:10
In vivo imaging and theranostics: a lesson from preclinical studies
Paolo Bigini, Head of Nanobiology Unit, Mario Negri Institute, Italy
ABSTRACT SPEAKER

12:10 - 12:25
Network-guided modelling allows prediction of sensitivity to all-trans retinoic acid in several tumor types
Maddalena Fratelli, Head of Pharmacogenomics Unit, Mario Negri Institute, Italy
ABSTRACT SPEAKER

12:25 - 12:40
Human midbrain-specific organoids as a novel approach for in vitro disease modeling
Kathrin Hemmer, Research Associate, Luxembourg Centre for Systems Biomedicine (LCSB), University of Luxembourg
ABSTRACT SPEAKER

12:40 - 12:45
Closing of the conference

12:45 - 14:00
Lunch

EDUCATIONAL AFTERNOON

SUNDAY, SEPTEMBER 24

PRE-CONFERENCE WORKSHOPS

The educational programme on Sunday 24th is an exciting new feature of the Translational Medicine Conference format. Divided in two parallel streams, this year comprises six workshops, with a blend of technical and non-technical themes.

Each session was chosen on the basis of its relevance and currency in translational medicine. Each workshop has been designed to be small, highly interactive and will enjoy the insights of international key opinion leaders. All sessions have been developed in partnership with leading organisations in their fields, such as Hologic, IgenBiotech, Cydan, UCB, the European Society for Molecular Imaging and our Translation Together partners:

PART 1

13:30 - 16:00

WORKSHOP A

TRANSLATING BIOMARKERS INTO IN-VITRO DIAGNOSTICS (IVD)

This workshop will provide an overview of all the steps starting from biomarker(s) discovery to product marketing and reimbursement.

Using real life case studies, the participants will experience potential roadblocks researchers need to tackle together with the various development phases to successfully launch an IVD on the market.

MODERATOR:

Florence Bietrix, Operations Manager, EATRIS

SPEAKERS:

- **Tim Moser,** Industry Partnering Specialist, EATRIS
- **Alain van Gool**, Chair EATRIS Biomarker Platform, Radboudumc, The Netherlands
- **Paul Docherty**, Regional Sales Manager, Hologic, United Kingdom
- **Kim Pettersson**, Professor, Turku University, Finland
- **Monica Marchese,** Biomarker Validation Scientist, Integrated Biobank of Luxembourg
- **Jiri Drabek**, Associate Professor, Institute for Molecular and Translational Medicine, Czech Republic
- **Leticia Lopez,** Project Manager, IgenBiotech, Spain

In partnership with IgenBiotech and Hologic.

WORKSHOP B

CHALLENGES AND BEST PRACTICES IN ACADEMIC DRUG DEVELOPMENT

During this workshop you will gain an understanding of the do's and don'ts in academic drug research. Based on real life case studies we will zoom in on key components for success, root causes of failure, and main struggles for ongoing projects. Participants will be encouraged to share their own experiences, with an emphasis on novel approaches and emerging technologies.

MODERATOR:

Kees de Ruig, Business Development Manager, EATRIS

SPEAKERS:

- **Marian Hajdúch**, Director, Institute for Molecular and Translational Medicine, Czech Republic
- **Maurizio D'Incalci**, Chief Department of Oncology, Mario Negri Institute, Italy
- **Marko Anderluh**, Professor of Medicinal Chemistry, University of Ljubljana, Slovenia
- **Michele Caraglia**, Associate Professor of Biochemistry, University of Campania, Italy
- **Marcela Krecmerova**, Head of Research Team, Charles University, Czech Republic
- **Luca Cardone**, Principal Investigator, Istituto Regina Elena, Italy

WORKSHOP C

DESIGNING YOUR RESEARCH FOR MAXIMUM IMPACT: BUILDING A DATA PACKAGE FIT FOR INVESTMENT

In this workshop, you will learn what types and level of research data you will need to secure interest from the investors and shared risk collaborators that finance early development projects, so you can structure (or assess, if you are a funder) your research for maximum future potential. On the basis of examples and use cases, learn about the most common pitfalls and the recipes for successful further funding of your positive results.

MODERATOR:

Anton Ussi, Operations & Finance Director, EATRIS

SPEAKERS:

- **Justin Bryans**, Executive Director of Drug Discovery, LifeArc, United Kingdom
- **Mike Dalrymple**, Executive Director, Diagnostics & Science Foresight, LifeArc, United Kingdom
- **James McArthur,** President, Cydan Development Inc., United States

This workshop is offered in partnering with Cydan and as part of the "Translation Together" initiative. Translation Together is a joint initiative involving EATRIS, National Institutes of Health-National Center for Advancing Translational Sciences (USA), Center for Drug Research and Development (Canada), Therapeutic Innovation Australia and LifeArc (UK).

PART 2

16:30 - 19:00

WORKSHOP D

POTENCY ASSAYS IN ADVANCED THERAPIES AND VACCINES

This workshop will address the issue of the Potency Assay, highlighting the strategy, pitfalls and regulatory pathway for the development of ATMPs and Vaccines. Chaired by Maria Cristina Galli and Lucia Gabriele (Istituto Superiore di Sanità, Italy)

MODERATOR:

David Morrow, Scientific Programme Manager, EATRIS

SPEAKERS:

- **Koen Brusselmans**, Quality Assessor, Scientific Institute of Public Health, Belgium
- **Marcus Timon**, Head of Advanced Therapies and Biotechnology, Biological Products and Biotechnology Division, Spanish Agency of Medicinal Products
- **Ivana Haunerova,** Quality Assessor, State Institute for Drug Control, Czech Republic
- **Graziella Pellegrini,** Head of Cell Therapy Programme, Unimore, Italy

WORKSHOP E

MOLECULAR IMAGING SUPPORTING CNS DRUG DEVELOPMENT

The development of novel therapies faces challenges due to the extremely high failure rates in development of (e.g. against neurodegenerative disease). Using several neuroimaging case studies, we will discuss the challenges, opportunities and lessons learned for how molecular imaging can support the development of novel CNS drugs.

MODERATOR:

Martin de Kort, Scientific Programme Manager, EATRIS

SPEAKERS:

- **Bert Windhorst**, Chair EATRIS Imaging Platform, VUmc, The Netherlands
- **Tony Gee,** Professor of PET and Radiochemistry, King's College London, United Kingdom
- **Mark Schmidt,** Senior Director, Janssen, Belgium
- **Joel Mercier,** Associate Director Medicinal Chemistry, UCB Pharma, Belgium
- **Xin Yu,** Research Group Leader, Max Planck Institute for Biological Cybernetics, Germany

With the support of the European Society for Molecular Imaging (ESMI) and in joint collaboration with the EANM Drug Development Committee.

WORKSHOP F

DESIGNING YOUR RESEARCH FOR MAXIMUM IMPACT: HOW TO ASSESS AND MAXIMISE THE POTENTIAL IMPACT OF YOUR TRANSLATIONAL RESEARCH PLAN

This session will provide an overview of the main components of the development pipeline that affect the feasibility of translational research. By being aware of the major issues, including definition of the end-product and regulatory classification, target patient population, intellectual property, you will have more confidence in designing or selecting your projects for maximum potential impact.

MODERATOR:

Anton Ussi, Operations & Finance Director, EATRIS

SPEAKERS:

- **Matejka Rebolj,** Senior Epidemiologist, Queen Mary University of London, United Kingdom
- **Giovanni Migliaccio**, Scientific Director, EATRIS
- **Bernd Eisele**, CEO-CSO, Vakzine Project Management GmbH, Germany
- **Monica Ensini**, National Expert, European Medicines Agency, United Kingdom

WELCOME WORDS

MONDAY, SEPTEMBER 25

Robert Plaga

Deputy Minister for Research and Higher Education, Ministry of Education, Youth and Sport, Czech Republic

Robert Plaga, Ph.D., has held the position of Deputy minister for the Higher Education, Science and Research section of the Ministry of Education, Youth and Sports since 2015. Previously, he held the position of director of the Centre of Technology Transfer of the Mendel University in Brno. Besides being among the founding members, Mr. Plaga specialised in the protection and use of intellectual property and its commercial potential, the knowledge potential of scientific discovery and communication with industry officials and other stakeholders. He also worked as an academic specialising in the fields of finance, public affairs and regional development in the context of European integration. Mr. Plaga was also previously a lecturer, consultant and a financial and project manager.

Giovanni Migliaccio

Scientific Director, EATRIS

Giovanni Migliaccio has been EATRIS Scientific Director since 2011. He obtained a PhD in Biological science in 1977 at the University of Naples (Italy). His area of scientific expertise is in experimental haematology and stem cell proliferation and differentiation mechanisms. He spent two years as Post Doc at the University of Washington (Seattle, WA) and 5 years as Associate Scientist at the New York Blood Center (New York, NY). He continued his studies at the Istituto Superiore di Sanità (ISS) in Rome resulting in more over 190 scientific publications over the years.

He is currently the sitting member for Advanced Therapies Medicinal Products in the committees delegated to the authorisation of clinical trials in Italy. As such he was proposed to the European Medicines Agency (EMA) as an expert and participated in the drafting of guidelines for the Cell Therapy working group from 1997 to 2011. He was the Italian National Delegate to the Committee for Advanced Therapies at EMA from 2009 to 2011.

SESSION 1

MONDAY, SEPTEMBER 25

THE FUNDER, DEVELOPER AND REGULATOR AS PARTNERS IN INNOVATION

In this session, we will hear about the latest developments in the research, funding and regulatory science areas that will directly impact academia's ability to drive biomedical innovation. Centered around the need to facilitate true collaboration across all sectors, the panel session will discuss the remaining challenges and future prospects for translational science field.

Anton Ussi

Operations & Finance Director, EATRIS

Moderator

Anton Ussi is Operations & Finance Director of EATRIS ERIC. Anton Ussi has a background in engineering, technology transfer and SME administration. He is a specialist in the establishment and execution of strategic public-private and public- public collaborations based on the deployment of high value translational research infrastructure for medicine. Anton has been co-responsible for the development of several public private partnerships in medical imaging, and supported the formation of spin-out companies in the biotech, pharma and services sectors. He has been active in EATRIS since 2011 and is member of the Executive Board and legal representative since 2015.

Elmar Nimmesgern

Deputy Head of Unit Innovative and Personalised Medicine, DG Research & Innovation, European Commission

10:10 - 10:30

Personalised medicine activities at EU level

The European Union is developing policies to move towards personalised medicine. This is underpinned by a sustained and significant investment in research funding.

Biography
Elmar Nimmesgern has been in charge of different aspects of health research at the European Commission since 2000. He has been Deputy Head of Unit since 2013, initially in the strategy unit of the Health Directorate and since 2014 in the Innovative and Personalised Medicine unit. Before joining the European Commission, he worked for 5 years at Vertex Pharmaceuticals in Cambridge (USA), first as research scientist in the department of biophysical chemistry, then from 1997 to 2000 as project head of preclinical programme for IMPDH research. Elmar Nimmesgern is a biochemist by training; he performed cell biology research at the University of Munich and at Memorial-Sloan-Kettering Cancer Center in New York.

Isabelle Moulon

Senior Advisor on Stakeholders Engagement, European Medicines Agency

10:30 - 10:50

From gatekeeper to enabler: a new role for regulators?

Beyond safeguards of public health by ensuring safety and efficacy of medicines, regulators have expanded their contribution by facilitating and supporting innovation. The network of EU regulators recognises the need to potentiate collaboration with academia to support the translation of innovation (of which academia is a major driver) into effective and safe medicinal products.

Biography
Isabell Moulon is a qualified medical doctor from the University de Grenoble (France), who specialised in endocrinology and metabolic diseases. She worked as a clinical endocrinologist in hospital until 1987 and then joined the Directorate of Pharmacy at the French Ministry of Health. She worked for the pharmaceutical industry from 1992 to 1995 before joining the European Medicines Agency (EMA) in 1995.

She was responsible for Scientific Advice until December 2000 and was appointed Head of Sector for Safety and Efficacy of Medicines in January 2001. From 2004 and 2016, she developed the interaction with patients, healthcare professionals and academia and co-chaired the EMA patients and healthcare professionals working parties. In 2016, she became Senior Advisor on Stakeholders Engagement.

Clayton Heijman

Director, Privium Fund Management, The Netherlands

11:20 - 11:40

"The Tale of Two Worlds" – Can finance rescue lives?

Although they seem to live in different worlds two different sides of our society can work better together if we want to make it happen for the search for new and better medicines.

Biography
Clayton Heijman is a Director of Privium Fund Management. He obtained a degree as Master in Business Administration from Webster University in Leiden, with an emphasis in marketing and management. After working for Kas-Bank and merchant bank MeesPierson he joined Goldman Sachs as an executive director in the Equity Finance & Prime Brokerage division from 1994. In 1998 he joined Fortis as a Managing Director to set up the Prime Fund Solutions activities. After leaving in 2006 he joined Credit Agricole-Calyon as a Managing Director. In 2008, he founded Privium Fund Management and Darwin Platform, a firm that provides start up support to new investment management initiatives and offers COO support. These activities are now provided for over 30 clients, from 5 different locations with an overall asset size of more than $ 1.4 Bn.

Anton Ussi

Operations & Finance Director, EATRIS

11:40 - 12:00

Multi-disciplinary, multi-sector collaboration as a key enabler of biomedical innovation

Translating novel biological discoveries into effective medical interventions is a complex undertaking requiring a truly multi-disciplinary, team science approach. By accessing advanced analytical technologies, together with the biological and clinical expertise needed to probe the mechanisms of disease and test a therapeutic hypothesis, it is possible to advance a promising concept towards the clinic. In this presentation we will hear the latest developments in translational research from the perspective of the EATRIS European Infrastructure for Translational Medicine.

Biography
Anton Ussi is Operations & Finance Director of EATRIS ERIC. Anton Ussi has a background in engineering, technology transfer and SME administration. He is a specialist in the establishment and execution of strategic public-private and public- public collaborations based on the deployment of high value translational research infrastructure for medicine. Anton has been co-responsible for the development of several public private partnerships in medical imaging, and supported the formation of spin-out companies in the biotech, pharma and services sectors. He has been active in EATRIS since 2011 and is member of the Executive Board and legal representative since 2015.

SESSION 2

MONDAY, SEPTEMBER 25

NOVEL APPROACHES IN CLINICAL DEVELOPMENT

This session is focused on technical and operational developments to improve clinical success rates. On the basis of success and failure stories we will hear from industry, academia and patient advocates on a subject of crucial importance to drug development.

Kjetil Taskén

EATRIS National Director, University of Oslo, Norway

Moderator

Prof. Kjetil Taskén is Director of the Centre for Molecular Medicine Norway (NCMM), Nordic EMBL Partnership and Director of the Biotechnology Centre of Oslo (BiO), both at UiO. He is also the national Director for Norway of the ESFRI infrastructures EATRIS (translational medicine) and EU-OPENSCREEN (academic chemical biology and screening) and in charge of the corresponding national infrastructures. He has co-founded two small biotech companies and has been on the Board of a number of other SMEs in the biotech sector. Dr. Taskén received the King Olav V's Prize for Cancer Research 2016 (national life-achievement award by the Norwegian Cancer Society, June 2016). He was elected to the Norwegian Academy of Science and Letters in 2005 and to the ScanBalt Academy in 2008. He is author of more than 250 scientific publications and inventor of 17 patents.

Philip Murphy

Head Experimental Medicine Imaging,
GSK, United Kingdom

14:05 - 14:35

Enabling innovation through external networks: experiences from clinical imaging for pharmaceutical R&D

Drug development requires a flow of innovative technologies to characterise drug candidates early. Needs across R&D are broad, as too are the array of rapidly developing technologies able to underpin drug development. Matching R&D needs with technology solutions can only be achieved through robust, long-term external partnerships to access the best expertise and infrastructure to solve drug development challenges. Successes, challenges and an outlook for improved models will be shared with examples.

Biography
Phil heads clinical imaging for GSK supporting imaging for small, information rich experimental medicine studies through to standard endpoints for regulatory filing. Our group partners extensively with academic and industrial collaborators to identify new imaging technologies, develop methods towards clinical application and then deploy within clinical trials. Phil has been applying clinical imaging in industry for over 15 years at Pfizer and GSK). Phil's academic background is in magnetic resonance with a Ph.D. from the Institute of Cancer Research, University of London in MR Spectroscopy of brain tumours.

Ragnhild Marie Loeberg

Head of Quality and Regulatory Affairs,
Bayer AS, Norway

14:35 - 15:05

From an idea to a medicinal product - a success history

A product idea was conceived in an academic environment, with no experience in product development, no knowledge of the rules of the game in the highly regulated pharmaceutical industry, and in an environment without big money. After approx. 15 years, the medicinal product was approved by the US FDA and EMA. From the idea to the marketing authorisation, a lot of hard work was put in: to develop and document the product, build a company and also to understand the rules of the industry and act compliants with the regulations.

Biography
Ragnhild M. Løberg is currently Head of Quality and Regulatory Affairs in Bayer AS, Norway, after Algeta ASA was acquired by Bayer in 2014. She started in Algeta i 2002, and as Senior VP Quality and Regulatory Affairs, she had a central role in development and documentation of the medicinal product Xofigo, including the regulatory processes resulting in NDA and MAA approval, as well as the FDA approval of Algeta's manufacturing facility. Løberg has approx. 30 years' experience from pharmaceutical R&D mainly in start-up biotech companies, in challenging positions at the intersection of the well-defined documentation and quality requirements given by the medicines agencies, and the real life situation with lack of time and resources.

Mark Schmidt

Senior Director R&D, Janssen,
Belgium

15:05 - 15:35

Application of PET imaging for clinical development of treatments for neuropsychiatric disorders: trials and tribulations

The value of PET imaging with site specific radioligands for confirming target engagement and modelling exposure/occupancy relationships is well known. Timely development of novel PET tracers requires at risk investment in ligand discovery that can be significantly enhanced by collaboration with academic radiopharmacy labs. More recently, the discovery of PET radioligands for misfolded protein aggregates has transformed clinical testing of treatments for Alzheimer's disease.

Biography
Dr. Schmidt is a Senior Director in Experimental Medicine for Janssen Pharmaceutica, N.V. in Beerse, Belgium. He received his medical degree from the University of Chicago in 1983 and entered postgraduate training in psychiatry and clinical service in the US Navy. Following Naval service, Dr. Schmidt was a research fellow in the National Institute of Mental Health (NIMH) intramural program where he focused on the use of functional imaging as a pharmacodynamic marker. Following fellowship, he worked at Lilly Research Laboratories, Novartis, and now Janssen. He has been responsible for clinical testing of NMEs for psychiatric indications through proof of concept, provided guidance to micro PET and MRI studies of Alzheimer's transgenic mouse studies, and has led a preclinical imaging group for development of site specific PET tracers and then qualifying them in human. He supervised multisite [11C] PiB amyloid PET substudies for the Phase 3 trials of bapineuzumab and co-leads the advanced disease modeling work package in AMYPAD.

Marian Hajdúch

Director, Institute for Molecular and
Translational Medicine, Czech Republic

16:00 - 16:20

Translating clinical proteomics into clinical practice

Major advances in mass-spectrometry based techniques of protein identification and quantification recently enabled multiplexed analyses of biomarkers in clinically relevant situations. The presentation will focus on innovative approaches for identification, validation and clinical use of protein based biomarkers for diagnosing, prognosing and prediction of therapeutic response in human cancers and inflammatory lung diseases.

Biography
Marian Hajdúch is Director of the Institute of Molecular and Translational Medicine, Palacky University and one of leading experts in the research of treatments and molecular oncology in the Czech Republic. He has long-term experience in project management; R&D and technology transfer activities, including the construction and management of large research infrastructures. He has been involved as principal investigator, investigator or clinical site manager in 12 clinical trials. He actively participated in the research and/or management of more than 40 national and international projects and established a major cancer research foundation in the country. He published over 200 scientific papers and holds several patents in the area of basic and applied biomedical research. He is also the chairman of the Board of National Directors and Czech National Director for the European Infrastructure for Translational Medicine (EATRIS).

Immunomonitoring of MSC-treated GVHD patients reveals no obvious markers for therapy response or safety concerns

Matejka Rebolj

Senior Epidemiologist, Queen Mary University of London, United Kingdom

GUEST SPEAKER

16:20 - 16:40

Pitfalls in study design - and how to avoid them

Medical research is not only expensive but also affects human lives. To avoid waste and even harm, it is worthwhile to have study designs and the overall research plans discussed as early as possible and include experts with experience in various methodological aspects. Such expertise is, unfortunately, not always available locally. In the field of early detection of cancer, for example, researchers, policy makers and funders can since recently ask for advice from ECaDE, a multidisciplinary network of European experts who provide independent advice on a voluntary basis.

Biography

Matejka Rebolj, PhD, is senior epidemiologist at Wolfson Institute of Preventive Medicine's Centre for Cancer Prevention at Queen Mary University of London, UK (2016-). She previously worked as scientific researcher at Department of Public Health of Erasmus Medical Centre in Rotterdam, The Netherlands (2002-2008), as postdoctoral researcher and associate professor at Centre for Epidemiology and Screening at University of Copenhagen in Denmark (2008-2014), and as senior researcher at Department of Pathology, Copenhagen University Hospital Hvidovre in Denmark (2014-2015).

Matejka's research has focused on evaluation of cancer screening and aetiology using various administrative register and clinical trial data. Her methodological work has been dedicated to providing accurate and transparent evidence for health care. She has international research experience in multidisciplinary and multinational teams and has been a management board member for multiple screening studies, expert advisor to various policy making bodies, and is a member of international cancer screening networks. She is associate editor for BMC Cancer (2010-).

Johanna Nystedt

Development Director, Cell Therapy Services, Finnish Red Cross Blood Service

Johanna Nystedt has been actively pursuing research in novel cell therapies during the last 10 years, especially surrounding mesenchymal stromal cells. Johanna Nystedt, PhD, Adj Prof, is the department head of the FRCBS Advanced Cell Therapy Centre in Helsinki, Finland, with GMP facilities and quality control labs for the development and manufacturing of novel cell therapy products. She is the head of ATMP production and is experienced in clinical cell therapy manufacturing, ATMP legislation and preclinical and translational cell therapy research.

Johanna has pursued active research in the cell therapy field during the last 10 years and has thus far published around 30 scientific articles in this area, mostly about mesenchymal stromal cells (MSCs). Johanna defended her Ph.D. thesis in cell biology in 2004 and received the title of adjunct professor in cell therapy in 2013.

Abstract

Mesenchymal stromal cells (MSC) are immunosuppressive cells used as salvage therapy to treat acute graft-versus-host disease (aGvHD). To study aGvHD patients' immunological response to allogeneic bone marrow-derived MSCs, we collected patient blood samples immediately before and up to one month after MSC treatment. Lymphocyte differential counting indicated that compared to healthy control individuals, the numbers of T cells (CD3+), B cells (CD19+) and NK cells (CD3- CD16+ CD56+) were reduced in aGvHD patients as expected. The correlation of lymphocyte profiles with the day 28 response of MSC treatment showed that there were no obvious differences in the lymphocyte profiles between MSC responders and non-responders.

The number of CD4+ T helper cells remained at a particularly low level throughout the follow-up period. The relative proportion of type 1 T helper cells (Th1) decreased after MSC therapy, while the proportion of regulatory T cells (Treg) remained unaltered. Very few Th2 and Th17 cells could be measured in these patients. We also assessed the value of Reg3α (regenerating islet-derived protein 3-alpha), CK-18F (cytokeratin-18 fragment) and elafin in the prediction of MSC therapy response. These proposed aGvHD serum markers differentiated aGvHD patient samples from healthy controls and exhibited some degree of tissue specificity, but showed no prognostic value in MSC therapy response. In conclusion, these results revealed no obvious markers for MSC therapy response in this patient cohort, but showed that non-HLA-matched allogeneic MSCs do not provoke an evident T cell mediated immune activation in aGvHD patients, advocating for the safety of MSC therapy.

1) Joni Keto, Tanja Kaartinen, Jukka Partanen, Matti Korhonen, Kaarina Lähteenmäki, Johanna Nystedt
2) Urpu Salmenniemi, Maija Itälä-Remes
3) Arno Hänninen

1) Finnish Red Cross Blood Service, Helsinki, Finland,
2) Stem Cell Transplant Unit, Clinical Hematology, Turku University Hospital, Turku, Finland,
3) Department of Medical Microbiology and Immunology, University of Turku, Turku, Finland

Metabolomic profiling approach to improve patient's selection and prediction of outcome for cancer treatment

Susan Costantini

Researcher, Istituto Nazionale Tumori "Fondazione G. Pascale", Italy

Dr. Susan Costantini has a degree in Chemistry, a PhD in Computational Biology and a second Level Master in Environment and Cancer. Dr. Costantini has developed from 2000 to 2007 research activities at University of Naples, University of Campania and National research Council focusing her attention on studies related to the inflammatory process in different systems and on the structure-function relationships of some cytokines. Since 2008 she is Researcher at National Cancer Institute of Naples "Pascale Foundation". She has been studying the cytokinomic and metabolomic profile in various cellular systems, and biological fluids and/or tissues of patients with colorectal, liver and breast cancer, and melanoma. Moreover, her research activities regard also the application of systems biology approaches to integrate "omics" data by computational methods.

Abstract

Aberrant metabolism is an emerging hallmark of cancer. The evaluation of metabolomic profiling in biological fluids recently emerged as powerful, reliable, sustainable tool for the identification of novel biomarkers to improve early diagnosis and prognosis classification, as well as prediction of treatment benefit in cancer patients. Nuclear Magnetic Resonance (NMR) spectroscopy is the only non-destructive technique that can identify and quantify complex mixtures of metabolites using small sample volumes and an easy sample preparation approach. Tacking advantage of a 600-MHz NMR spectrometer with cryoprobe, equipped with an automation system we performed metabolomic profiling on liquid biopsy samples collected in melanoma and colorectal cancer patients at different stages of the disease and/or at different time points before and during treatment. We identified and quantified the metabolites able to distinguish patients with cancer from healthy donors, with cluster separation depending on the stage of the disease in both colorectal and melanoma patients. Plasma metabolomic profiling was also evaluated on metastatic colorectal patients subjected to first line bevacizumab plus chemotherapy and on metastatic melanoma patients subjected to different immunotherapy treatments. We were able to identify a set of metabolites that, either before or during treatments, can discriminate patients with favorable than those with worst outcome. Overall, these data suggest that metabolomic profiling performed on plasma by NMR is a potent and affordable method to improve patient's selection and outcome prediction for cancer treatment. Moreover, potentially this approach could be useful in the early detection and prognosis definition of cancer disease.

1) Angela Sorice, Francesca Capone, Elena Di Gennaro, Carlo Vitagliano, Alfredo Budillon, Susan Costantini
2) Gabriele Madonna, Domenico Mallardo, Paolo A Ascierto
3) Alfonso De Stefano, Paolo Delrio, Francesco Bianco, Antonio Avallone,

1) Experimental Pharmacology Unit, Istituto Nazionale Tumori "Fondazione G. Pascale" - IRCCS,, Napoli, Italy,
2) Melanoma Cancer Immunotherapy and Innovative Therapy Unit, Istituto Nazionale Tumori "Fondazione G. Pascale" - IRCCS, Napoli, Italy,
3) Abdominal Oncology Department, Istituto Nazionale Tumori "Fondazione G. Pascale" - IRCCS,, Napoli, Italy

miRNAs as accurate and useful biomarkers of acute kidney injury in cardiac surgery patients

María Laura García-Bermejo

Head of Biomarkers and Therapeutic Targets Research Group, IRYCIS, Spain

Dr María Laura García Bermejo, PhD in Cell Biology and Genetics, is the Head of the Biomarkers and Therapeutic Targets Research Group and Core Facility at Ramon y Cajal Health Research Institute, at Madrid, Spain. She is also co-chair of Biomarkers Platform at EATRIS. She has wide experience in translational research, working in close collaboration with clinicians, identifying and validating novel and useful tools for clinical practice, in particular, miRNAs as accurate biomarkers for several pathologies as well as new therapeutic targets in diseases, She has published more than 50 papers.

Abstract

Acute Kidney Injury (AKI) is a syndrome involving an abrupt decline in renal function. In the context of cardiac surgery (CS) with cardiopulmonary bypass (CPB), the AKI incidence reach 13% and mortality of CS-CBP rises to 60% when AKI appears. This mortality has not declined in decades. There is no effective strategy for AKI prevention and / or treatment, due to the lack of accurate markers for AKI diagnosis, in contrast to blood creatinine, mostly used, which is altered very late. In the case of CS-CBP would also be desirable that these biomarkers were able to identify patients at risk. In the context of AKI, miRNAs have been proposed, as new biomarkers with diagnostic, being negative regulators of gene expression. Our laboratory has generated and patented results in 100 patients demonstrating that a combination of 5 miRNAs, namely miR-26b, miR-27, miR-93a, miR-127-3p and miR-146a, determined by qRT-PCR in serum are able to: i) identify the population at risk of AKI in patients to undergo CS-CPB; ii) identify the patients will develop AKI, immediately after surgery. The values of area under the ROC curve analysis are greater than the currently available biomarkers including: creatinine, NGAL or Cystatin C. In summary, we identified and validated a combination of miRNAs as appropriated biomarkers for screening of population at AKI risk, determined before surgery and accurate biomarkers for early AKI diagnosis in the post-surgery period. These miRNAs will allow to a better CS-CBP patient management and to develop new therapeutic approaches in this context.

Elisa Conde, M. Edurne Ramos, Elia Aguado-Fraile, Macarena Rodriguez-Serrano, Lorena Crespo, Sara Giménez-Moyano, Laura Martín-Gómez, Fernando Liaño, Javier Miguelena, Angel Candela-Toha, M Laura García-Bermejo

18F-FAZA-PET/CT hypoxia imaging in lung cancer and high grade glioma

Maria Picchio

Researcher, San Raffaele Institute, Italy

Maria Picchio studied Medicine and Surgery at the University of Milan (Italy) and specialised in Nuclear Medicine. She was research fellow at the Klinikum rechts der Isar, Technische Universität Munchen (Germany) where she contributed significantly to translational research approaches focusing on the development and applications of innovative PET tracers for molecular imaging of cancer, as well as studies of the tumor micro-environment. In the last decade, her research in San Raffaele Hospital (Milan, Italy) is mainly focused on molecular imaging in oncology; her general research interest being the set-up of new non-invasive diagnostic imaging methods to be transferred in clinical practice for the optimisation of diagnosis, prognosis and therapy. She is the author of 120 papers published by peer reviewed scientific journals (H-index: 37), 10 book chapters and she received 7 Scientific Awards.

Abstract

Tumour hypoxia has been identified as a major independent prognostic factor influencing response to therapy and overall survival in many malignancies. Aim of the research is to establish the role of 18F-FAZA-PET/CT as a novel tool for characterizing hypoxic tumour heterogeneity and for patient selection and response prediction in two populations of patients: non small cell lung cancer (NSCLC) and glioma.

Methods. In two clinical trials (EudraCT:2011-002647-98 and EudraCT:2015-000679-28), 18F-FAZA-PET/CT have been respectively performed in patients with NSCLC, who underwent to 18F-FDG-PET/CT and 18F-FAZA-PET/CT before surgery and in patients with high grade glioma before stereotactic biopsy or surgery. 18F-FAZA-PET/CT was compared with histopathological biomarkers (including CAIX and HIF1). In addition, in glioma, 18F-FAZA-PET/CT was also compared to morphological MRI parameters, namely contrast enhancement, or advanced MR imaging parameters such as relative cerebral blood volume (rCBV), fractional plasma volume (fVp), contrast transfer coefficient (Ktrans), mean diffusivity (MD) and fractional anisotropy (FA).

Results. In all lung and glioma lesions 18F-FAZA uptake was correlated to immunohistochemical analysis. A coregistration of PET and MR imaging was obtained in glioma patients to identify tumor hypoxic regions to plan stereotactic biopsy and for further radiation treatment planning.

Conclusions. In NSCLC the presence of 18F-FAZA uptake was concordant with staining for hypoxia biomarkers. In glioma patients, hypoxia delineation could be of utmost importance for treatment planning since higher radiation doses might be delivered on the most hypoxic tumour regions.

Acknowledgments. Research supported by the Italian Ministry of Health, Ricerca Finalizzata GR-2009-1575612 and by AIRC, IG-15243

1) Valentino Bettinardi, Elena Incerti, Federico Fallanca, Luigi Gianolli, Maria Picchio
2) Gian Marco Conte, Nicoletta Anzalone
3) Flavia Zerbetto, AniKo Maria Deli, Nadia Di Muzio
4) Michele Bailo, Filippo Gagliardi, Pietro Mortini

1) Nuclear Medicine Department, IRCCS San Raffaele Scientific Institute, Milan, Italy,
2) Neuroradiology Department, IRCCS San Raffaele Scientific Institute, Milan, Italy,
3) Radiotherapy Department, IRCCS San Raffaele Scientific Institute, Milan, Italy,
4) Neurosurgery Department, IRCCS San Raffaele Scientific Institute, Milan, Italy

A new path for accelerating therapies for rare diseases to patients

James McArthur

President of R&D, Cydan Development, United States

James McArthur, PhD has founded four companies including Imara, Vtesse, Cydan, and Synovex (Adheron) and has published and patented extensively in the areas of gene therapy and rare diseases. He currently serves as President of R&D of Cydan, a rare disease accelerator, and as CEO of Imara, developing therapeutics for the treatment of sickle cell disease. James was an Entrepreneur in Residence at HealthCare Ventures, where he started Synovex and was head of research and the Principal Scientist at Cell Genesys Inc, a pioneer in the field of AAV and lentiviral gene therapy. James is a member of the Board of Directors of NightstaRx, a leader in developing AAV gene therapy treatments for rare retinal genetic diseases, and he also works with the Friedreich's Ataxia Research Alliance (FARA) as a member of its Board of Directors and Scientific Advisory Board, advancing the needs of patients with this rare neurologic disease.

Abstract

Traditional sources of funding; government, patient groups, pharmaceutical companies, each have advantages and disadvantages in terms of speed, available funding and stage of development. A flexible model, bringing both substantial resources, and expertise to help bridge the preclinical-research to clinical-research divide might help accelerate drug development in the greater than 7000 identified rare diseases.

In an effort to increase the efficiency of developing new therapies for rare diseases, the orphan drug accelerator, Cydan Development, was created. Pulling together a group of experienced drug hunters and drug developers, and the financing to conduct the essential studies to go from preclinical project to clinical ready program. We now have four years of data on how the experience with this model. Cydan has looked at >700 projects from academia, government, biotech and pharma labs. Fewer that 9% of these then advanced into project-planning where the path to advancing to clinical development was mapped out. From about 50 project plans, 17 projects were advanced into de-risking, where Cydan conducted studies expanding the pharmacology, toxicology and manufacturability of the assets. Of these 17 de-risking projects, 2 have become companies with clinical programs funded with $73M, 2 are in the preclinical de-risking stage and 13 were terminated. The primary reason for project termination was robustness of preclinical pharmacology, followed by toxicology findings, then epidemiology challenges and then manufacturability.

Cydan continues to explore new therapies to improve the lives of individuals and families living with rare diseases and new partners with which to join in this effort.

SESSION 3

TUESDAY, SEPTEMBER 26

DEVELOPING MORE PREDICTIVE PRECLINICAL TOOLS TO BETTER REACH PROOF OF CONCEPT

Predicting efficacy, safety and tolerability in preclinical development remains a stubborn challenge in medicines R&D. In this session we will hear from key opinion leaders and organisations to gain an overview of where we stand and the emerging initiatives and technologies that can improve confidence to reach clinical proof-of-concept.

Ulrika Bäckman

EATRIS National coordinator, Uppsala University, Sweden

Moderator

Ulrika Bäckman, PhD, has a master in Cell and Molecular Biology, followed by a doctoral degree in Medical Cell Biology received at Uppsala University. After the doctoral degree she spent two years at AstraZeneca Transgenic and Comparative Genomics in Gothenburg. For almost ten years she has worked at Karolinska Development in several of the portfolio companies as project manager in the field of oncology, inflammation and diabetes. Since autumn 2015, she has been back at Uppsala university building up the Swedish EATRIS node.

Christopher Austin

Director, National Institutes of Health-National Center for Advancing Translational Sciences, United States

09:10 - 09:35

Catalysing translational innovation on a global stage

Dr. Austin will discuss how each organisation acts as a catalyst to bring together the teams necessary to develop new technologies and paradigms to improve the efficiency and effectiveness of the translational process. Programs in the NCATS portfolio that are proving to be successful models in accelerating the currents in translational science will be highlighted, along with the recently launched new goals for IRDiRC, 2017–2027, which will ambitiously push the limits of what is currently possible in the longer term with an audacious vision for the field—all with rare disease patients' lives in mind.

Biography
Christopher Austin is director of the National Center for Advancing Translational Sciences (NCATS) at the National Institutes of Health (NIH). NCATS' mission is to enhance the development, testing and implementation of diagnostics and therapeutics across a wide range of human diseases and conditions. The Center collaborates with other government agencies, industry, academia and the nonprofit community. Before joining NIH in 2002, Austin directed research and drug development programs at Merck, with a focus on schizophrenia. In 2016, Dr. Austin was elected chair of the International Rare Disease Research Consortium (IRDiRC). He earned his M.D. from Harvard Medical School, and completed clinical training at Massachusetts General Hospital and a research fellowship in genetics at Harvard.

Jacques Richard

Scientific Advisor, Sanofi & Scientific Coordinator of the IMI Translational Safety Strategic Governing Group (SGG), France

09:35 - 10:00

The translational safety challenge from the perspective of Innovative Medicines Initiative (IMI)

Jacques Richard will present the ongoing efforts of IMI for improving the assessment of the safety of pharmaceuticals through predictive and innovative preclinical and clinical evaluations, both presently and in the long-term vision. The technical and scientific hurdles will be summarised. Examples of topics already launched as well as those in the portfolio of projects will be shared.

Biography
Jacques Richard is Senior Toxicologist. He is pharmacist and clinical pathologist by training. He specialised in toxicology through a PhD from the University of Montpellier in France. After several operational positions at Citoxlab, he moved to more project-centered responsibilities in preclinical safety at Pfizer. He is now Scientific Advisor at sanofi Montpellier in France, giving expert positions on various non-clinical safety issues for drugs in Research and Development portfolio. He is also representing sanofi in several consortia or working groups from the pharmaceutical industry, including Innovative Medicines Initiative. Jacques Richard is the scientific coordinator of IMI Translational Safety Strategic Governing Group.

Per Arvidsson

Executive Director Drug Discovery & Development, SciLifeLab, Karolinska Institutet, Sweden

10:00 - 10:25

Increasing predictability and developability of academic drug discovery & development project

SciLifeLab DDD is a newly established national Swedish infrastructure for academic drug discovery, working with academic researchers to build de-risked drug discovery programs that interest international stakeholders and future partners.

Biography
Per I Arvidsson is Director of the national Swedish Drug Discovery & Development Platform at Science for Life Laboratory (SciLifeLab).

Before being recruited by SciLifeLab & Karolinska Institutet in 2013 to build up this academic drug discovery center, Prof. Arvidsson held various roles at the CNS & Pain iMED at AstraZeneca, Södertälje – the last one as Project Director within the neurodegeneration research area.

In parallel to his work at AstraZeneca, Prof. Arvidsson continued to pursue academic research as Adjunct professor in bioorganic chemistry at Uppsala University (2007-2013). Since 2013, he is also affiliated to the College of Health Science, University of KwaZulu Natal, Durban as part-time research professor. Prof. Arvidsson is named inventor on some 15+ patent applications, and co-author of more than 100 publications, two of which have won "most cited papers" awards.

Petr Kocis

Vice President Preclinical Development, Alzheon, United States

11:00 - 11:25

Novel enveloping mechanism of action in Alzheimer's Disease

Soluble beta-amyloid oligomers play a key role in the pathogenesis of Alzheimer's disease (AD). Petr Kocis will report on the discovery and characterisation of a novel enveloping mechanism of action of the small molecule tramiprosate, the active component of an optimised prodrug ALZ-801 entering confirmatory Phase 3 programme in AD.

Biography
Petr Kocis is Vice President, Preclinical Development at Alzheon, Massachusetts, USA. Alzheon develops innovative treatments for Alzheimer's disease and other neurological and psychiatric disorders.

Before joining Alzheon, Dr. Kocis served as Global Head of Enabling Sciences & Technology, Exploratory Chemistry, at AstraZeneca where he spearheaded modern medicinal chemistry capabilities. Prior to was at Selectide, Arizona, the first combinatorial chemistry company where he was instrumental in the development of the concept of chemical libraries and their application in drug discovery. Dr. Kocis was educated at Technical University in Prague and Oxford University with PhD in medicinal chemistry. He is a recipient of R&D Director's Award for Creativity and Innovation, Zeneca Pharmaceuticals, a recipient of Henry Christian Award for Excellence in Research by Merck.

Embryonic regulation of the mouse hematopoietic niche and implications for haematotherapy

Daisuke Sugiyama

Deputy Director, Centre for Clinical and Translational Research, Kyushu University, Japan

Prof. Daisuke Sugiyama graduated from Gunma University in 1996 and worked as a medical doctor in internal medicine from 1996 until 1999. He engaged in basic research of hematopoiesis and stem cell biology in Japan, France and USA until 2006. He then became a principle investigator at Kyushu University collaborating with academic researchers from Europe, North America, Australia and Asia. He has an extensive publication record.

His research has also led to the development of bioactive peptides for novel therapy. During this time, he developed an understanding of intellectual property systems and industrial-university corporation, as well as founding a bio-venture company. He joined the CCTR to obtain experience in clinical research in 2012 and co-developed the new Department of Next Generation Medicine in 2013, and was co-appointed as the head of department of clinical study (Phase 1) in 2014. In addition, he developed international corporation unit of CCTR and spread his basic research network to clinical research internationally with special attention to East Asian countries. One of his representative activities is “Japan Medical Innovation Programme.”

Abstract

Hematopoiesis has been classically described as occurring in two waves: first primitive and then definitive hematopoiesis. In the mouse embryo, definitive hematopoiesis begins in the yolk sac and then shifts to liver, spleen and bone marrow. Fetal liver serves as the primary organ for hematopoie cell expansion and maturation at mid-gestation and its mechanisms have been well investigated with special attention to niche cells expressing cytokines such as SCF, thrombopoietin and IGF-2. Previously, our group reported that DLK-1+ hepatoblasts support fetal liver hematopoiesis, particularly erythropoiesis, through EPO, SCF and matrix secretion. Loss of DLK-1+ hepatoblasts in Map2k4-/- mouse embryos resulted in decreased numbers of hematopoietic cells in fetal liver, suggesting a key role of DLK-1+ hepatoblasts in hematopoiesis. When sorted DLK-1+ hepatoblasts were further analyzed by microarray, several genes encoding proteinases and peptidases were highly expressed in DLK-1+ hepatoblasts.

Based on the hypothesis that high weight proteins are digested into small peptides that possibly regulate hematopoiesis, we screened out peptides, and identified KS-13 (PCT/JP2010/067011). KS-13 has unique properties in regulation of hematopoiesis and cancer. Both KS-13 and modified KS-13 termed as SL-13R proliferate the number of hematopoietic progenitors from human cord blood cells in vitro, suggesting application of regenerative medicine. In addition, KS-13 can be applied for identification of molecular targets in combination with immuno-precipitation and liquid chromatography-mass spectrometry analysis. I hereby present extrinsic regulation of embryonic hematopoiesis with special attention to niche cells, identification of niche-derived peptides, and implications for future haematotherapy.

A 3D Microfluidic model for evaluating immune parameters associated to the efficacy of antitumor therapies

Lucia Gabriele

Group leader, Istituto Superiore di Sanita, Italy

Lucia Gabriele has a long-standing scientific experience in the field of immunology and oncology and, for many years, she has been working on the dissection of IFN signalling, in both mouse and human models of cancer and infectious diseases. Currently, she is co-chair of EATRIS Vaccines Platform.

Abstract

Microfluidic models represent a new frontier for studying the complex interactions occurring within organ microenvironments in pathologic conditions. Organ-on-chips recapitulate in vivo biological microenvironments suitable for studying complex functions, such as cell-cell interactions and dynamic drug stimuli. This tool owns an enormous potential for investigating the effects of drugs on the crosstalk between immune and cancer cells in pathologic conditions such as tumor microenvironment. Thus, we developed a novel microfluidic platform recreating tightly interconnected cancer and immune systems with specific 3D environmental properties, for tracking the behavior of immune cells toward tumor cells under therapy. By combining the microfluidic platform with advanced microscopy and a revised cell tracking analysis algorithm, we were able to calculate major distinctive parameters characterizing the interactions between cancer and immune cells. Overall, this platform offers a valid and manageable alternative to studies in animals for evaluating the efficacy of novel therapeutic treatments while its further implementation may lead to the development of suitable assays for pre-clinical testing.

1) Stefania Parlato, Elena Toschi, Giulia Romagnoli, Alessandra Fragale, Lorenzo Roccazzello, Maria Buoncervello, Irene Canini, Enrico Bentivegna, Mario Falchi, Lucia Gabriele
2) Adele De Ninno, Arianna Mercattini, Martinelli Eugenio, Corrado Di Natale
3) Francesca Bertani, Anna Maria Gerardino, Luca Businaro
4) Rosa Molfetta, Rossella Paolini
5) Debora Salerno,

1) Istituto Superiore di Sanità,, Rome, Italy,
2) University of Rome Tor Vergata, Rome, Italy,
3) Italian National Research Council, Rome, Italy,
4) University of Rome Sapienza, Rome, Italy,
5) Istituto Italiano di Tecnologia, Rome, Italy

In vivo imaging and theranostics: a lesson from preclinical studies

Paolo Bigini

Head of Nanobiology Unit, Mario Negri Institute, Italy

Paolo Bigini graduated in Biology at University of Pisa, Italy. He specialized in Pharmacological Research at the Mario Negri Institute (Milano, Italy) and then attended the PhD course in life science at the Open University (UK) with a thesis focused on the mechanisms of neurodegeneration in models of Amyotrophic Lateral Sclerosis. In following years He mainly worked to optimize protocols for the in vivo imaging in both cell therapy and nanomedicine. PB is currently the Head of Nanobiology Unit at Mario Negri Institute and member of the Internal Ethical Committee for Animal Experimentation.

Abstract

One of the main goal of the pharmacology is the development of predictable and safe ways to monitor the fate of drugs inside the body. The optimization of non invasive instruments of imaging is taking place in different clinical fields. However, a such technical development is not sufficient and preclinical results are still crucial to pave the way for the clinical application. In the last year the use of imaging to combine therapy and diagnostics has been greatly consideration. This strategy, called theranostics, is related to the use of nanocarriers because of their ability to both selectively deliver drugs toward the target and to track their fate through application of contrast agents, fluorophores, radionuclides. Similarly to “ex vivo” pharmacokinetics, theranostics enables to follow important parameters such as , the permanence in the bloodstream, the tropism to the target, the off-target accumulation, and the clearance of nanodrugs together with the evaluation of the therapeutic effectiveness. However, very importantly, this innovative approach does not require the sacrifice of animals making possible the evaluation of these parameters for each single experimental subject in a way very similar to that commonly used in patients. In last years the Mario Negri Institute made a great effort to optimize transferable procedures of theranostics. A “mouse clinic” equipped by modern instruments of screening for rodents (e.g. magnetic resonance imaging, MicroCT, Fluorescent Molecular Tomography) allowed us to get a large series of results. An overview and a critical evaluation about this activity will be elucidated in this presentation.

Authors
Paolo Bigini, Mario Salmona, Mario Negri Institute, Italy

Network-guided modelling allows prediction of sensitivity to all-trans retinoic acid in several tumour types

Maddalena Fratelli

Head of Pharmacogenomics Unit, Mario Negri Institute, Italy

Maddalena Fratelli studied Biology at the University of Pisa and at the Scuola Normale Superiore of Pisa, Italy. She has been Fellow in the Clinical Pharmacology Laboratory at the IRCCS Istituto di Ricerche Farmacologiche “Mario Negri” in Milano, visiting Postdoctoral Research Fellow in the Neurobiology Unit at the Medical Research Council in Cambridge, UK and staff scientist at the IRCCS Istituto di Ricerche Farmacologiche “Mario Negri”. Since 2005 she is Head of the Parmacogenomics Unit in the same Intitute. The major focus of her group is the use of genomic and transcriptomic systems for the study of drug action and pharmacoresistance.

Abstract

All-trans retinoic acid (ATRA) is a differentiating agent used in the treatment of acute-promyelocytic-leukemia (APL) and it is under-exploited in other malignancies despite its low systemic toxicity.

Using machine learning methods and network analysis, we have recently developed a gene-expression based model (ATRA-21) predicting sensitivity to the anti-proliferative action of ATRA in a tumor-type independent manner (Bolis et al, Ann Oncol 2017; 28 (3): 611-621). In experimental models, ATRA-21 predictions correlate with in vitro sensitivity in a large panel of cell-lines representative of numerous tumor-types. In patients, ATRA-21 correctly identifies APL as the most sensitive acute-myelogenous-leukemia (AML) subtype. Application of the ATRA-21 model to tumor samples from the TCGA dataset indicates that uveal-melanoma and low-grade glioma are top-ranking diseases as for average predicted responsiveness to ATRA. Several other tumor types, although not predicted to be sensitive on average, include subgroups of patients with high ATRA-21 values. The predictions made with ATRA-21 in 1289 AML patients from 4 datasets suggest that the ELN-favorable-risk, CEBPA double mutant, t(8,21) and inv(16) AML subgroups are characterized by high sensitivity to ATRA. A recent clinical trial supports our predictions.
Interestingly, our model is also endowed with prognostic potential, as there is a consistent number of tumor-types for which higher ATRA-21 predictions are associated with better outcome.
In a precision medicine perspective, ATRA-21 is likely to represent a useful tool for the identification of tumor types or subtypes and the selection of single patients who may benefit from treatments based on the use of ATRA.

1) Marco Bolis, Gabriela Paroni, Adriana Zanetti, Mineko Terao, Tiziana, Enrico Garattini, Maddalena Fratelli
2) Linda Pattini
3) Castrignanò

1) IRCCS Istituto Mario Negri, Milano, Italy,
2) Politecnico di Milano, Milano, Italy,
3) CINECA-Consorzio Interuniversitario per il Calcolo Automatico, Roma, Italy

Human midbrain-specific organoids as a novel approach for in vitro disease modeling

Kathrin Hemmer

Research Associate
Luxembourg Centre for Systems Biomedicine

Kathrin Hemmer studied Biology at the Ruhr University Bochum (Germany) and specialised in advanced neuroscience. She did her PhD in the "Stem Cell Biology and Regeneration" group at the Westfälische Wilhelms-University Münster (Germany) and in the "Developmental and Cellular Biology" group headed by Prof. Schwamborn at the "Luxembourg Centre for Systems Biomedicine" (Luxembourg). During her PhD she worked on the in vivo analysis of neural stem cells for autologous cell replacement therapies. As a PostDoc in Prof. Schwamborn's group in Luxembourg she is currently working on the generation of a midbrain-specific progenitor cell line and the derivation of a midbrain-specific organoid model to study neurodegenerative processes in Parkinson's disease.

Abstract

Research on human brain development and neurological diseases is limited by the lack of advanced experimental in vitro models that truly recapitulate the complexity of the human brain. Furthermore, animal models of human neurodegenerative diseases have failed dramatically, and the success rate of clinical trials based on these models has been disappointing. Here, we describe a novel and robust human brain organoid system that is highly specific to the midbrain derived from regionally patterned neuroepithelial stem cells. These human midbrain organoids contain spatially organized groups of dopaminergic neurons, which make them an attractive model to study Parkinson's disease. Midbrain organoids are characterized in detail for neuronal, astroglial and oligodendrocyte differentiation. Furthermore, we show the presence of synaptic connections and electrophysiological activity. The complexity of this model is further highlighted by the myelination of neurites. Moreover, we show that the present midbrain organoid system can be used for advanced in vitro disease modeling and therapy development.

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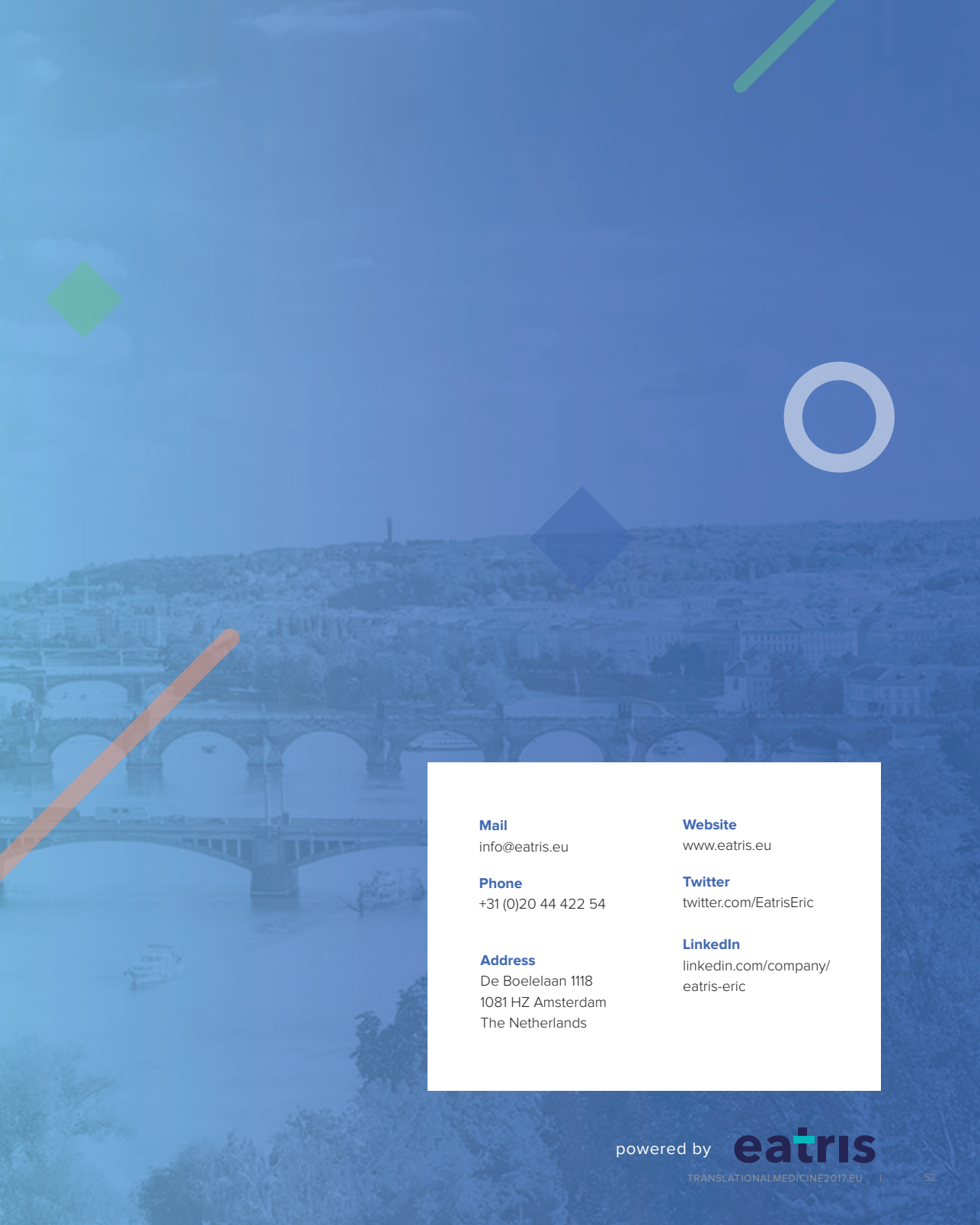
POSTERS

No.	Title	Presenter	Affiliation
1	Comparison of Ultrasound and Fluorescence techniques to monitor the progression of cancer cells in orthotopic model of pancreas	Antonio Barbieri	National Cancer Institute of Naples, Italy
2	Intraluminal Gel Ultrasound and Eco-color Doppler: New Tools for the Study of Colorectal Cancer in Mice	Antonio Barbieri	National Cancer Institute of Naples, Italy
3	Metastatic model OF Melanoma in PI3Kδ-/- mouse	Antonio Barbieri	National Cancer Institute of Naples, Italy
4	A tau peptide based in vitro assay for high-throughput screening of tau aggregation inhibitors	Narendran Annadurai	IMTM, Czech Republic
5	Transcriptional landscape of human endogenous viruses (HERVs) and other repetitive elements in psoriatic skin	Freddy Lättekivi	University of Tartu, Estonia
6	Failed Hypospadias treatment through a new advanced therapy medicinal product	Virginia Sceberras	Holostem, Italy
7	Identification of three distinct molecular subtypes in meningioma samples using microarrays for copy-number variants	Josef Srovnal	IMTM, Czech Republic
8	Preclinical evaluation of novel PET tracers for specific infection imaging	Milos Petrik	Palacky University, Czech Republic
9	The “Regina Elena” Proteomics Facility. Delving into the mechanism of action of new and old drugs for the combined treatment of glioblasto-ma multiforme patients	Marco Paggi	“Regina Elena” National Cancer Institute, Italy
10	AB61, a new potent nucleoside cytostatic: Molecular mechanisms of action and preclinical activity	Petr Džubák	IMTM, Czech Republic
11	Patient Stratification through critical molecular pathways underlying cellular plasticity and heterogeneity	Ander Matheu	Biodonostia, Spain

No.	Title	Presenter	Affiliation
12	Eight-week repeated sprint training protocol affects the circulating profile of a panel of fracture-risk associated miRNAs in young males	Giuseppe Banfi	Vita-Salute San Raffaele Unversity; IRCCS Istituto Ortopedico Galeazzi, Italy
13	DIANA assay for ultrasensitive enzyme quantification and inhibitor screening	Václav Navrátil	Institute of Organic Chemistry and Biochemistry of the Czech Academy of Sciences (CAS)
14	Cardiovascular Target Discovery: CarTarDis project	Ivana Bobeldijk-Pastorova	The Netherlands Organisation for Applied Scientific Research (TNO)
15	Microfluidic radiolabeling of peptides with PET radiometals	Daniel Seifert	Nuclear Physics Institute of the CAS
16	The nematode C. elegans as a well-established model to design and test new efficacious therapies for cardiac light chain amyloidosis	Luisa Diomede	Mario Negri Institute, Italy
17	Emergence and propagation of tau pathology in traumatic brain injury: new animal models for studying the mechanistic link between acute biomechanical injury and chronic neurodegeneration	Luisa Diomede	Mario Negri Institute, Italy
18	Radiosynthesis development and preclinical evaluation of [18F]NS12137, a novel 18F-labelled NET tracer for PET-imaging	Anna Kirjavainen	Turku PET Centre, Finland
19	Cytotoxicity profiling of new chemical compounds using high-throughput screening	Sona Gurska	IMTM, Czech Republic
20	Different treatment/culture approaches for 3-D cancer models to study novel antitumor strategies	Alfredo Budillon	National Cancer Institute of Naples, Italy
21	[18F]F-DPA for the imaging of neuroinflammation in APP/PS1-21 Mice	Tomas Keller	Turku PET Centre, Finland
22	Retro-inverso peptide inhibitors of tumor microvessel density and vascular infiltration by tumor cells	Maria Vicenza Carriero	National Cancer Institute of Naples, Italy

No.	Title	Presenter	Affiliation
23	NANBIOSIS: Integrated Infrastructure for full characterization and advisory services for Nanomedicines	Jezus Izco	CIBER-BBN, Spain
24	The marmoset as a preclinical model for neurological disorders	Ingrid Philippens	BPRC, Netherlands
25	Preclinical study of pharmacokinetics parameters of a novel potent pair of prodrug-drug of triterpenoids	Barbora Lišková	IMTM, Czech Republic
26	GMP production of [18F]FMPEP-d2 at Turku PET Centre	Salla Lahdenpohja	University of Turku, Finland
27	CORBEL: Harmonisation of access to Europe's biomedical research infrastructures	Nigel Wagstaff	EATRIS
28	Novel translational approaches for preclinical research in the area of non-alcoholic fatty liver disease	Lars Verschuren	The Netherlands Organisation for Applied Scientific Research (TNO)
29	C-COMEND: an Erasmus+ funded project to train the next generation of translational scientists	Rosan Vegter	EATRIS
30	EATRIS Quality Initiative	Andreas Scherer	EATRIS Finland, Institute for Molecular Medicine (FIMM)
31	EATRIS inside: Translational feasibility assessment to optimise project design	Florence Bietrix	EATRIS



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