

ANNUAL REPORT 2019

FROM SCIENTIFIC DISCOVERY TO PERSONALISED MEDICINE

eatris

European infrastructure
for translational medicine

EATRIS-ERIC acknowledges with gratitude the support of:

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Ministry of Education and Science



Czech Republic
Ministry of Education, Youth and Sports (MEYS)



Republic of Finland
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French Republic
Commissariat à l'Energie Atomique et aux Energies Alternatives (CEA)



Italian Republic
Istituto Superiore di Sanità (ISS)



Grand Duchy of Luxembourg
Le Gouvernement du grand-Duché de Luxembourg



Kingdom of the Netherlands
ZonMW



Kingdom of Norway
Research Council of Norway*



Republic of Portugal
INFARMED-National Authority of Medicines and Health Products



Republic of Slovenia
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Kingdom of Spain
Instituto de Salud 'Carlos III' (ISCIII)



Kingdom of Sweden
Vetenskapsrådet

Observers



Republic of Latvia
Ministry of Education and Science

* The contribution in Norway is shared between University of Oslo (UiO), University of Bergen (UiB), Norwegian University of Science and Technology (NTNU), the Arctic University of Norway (UiT) and the four Regional Health Authorities in Southeastern, Western, Central and Northern Norway

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FOREWORD



MARIANNE GRØNSLETH

Chair of the Board of Governors

EATRIS has shown a constant development during 2019, strengthening the foundations for the growth of translational medicine. EATRIS, BBMRI and ECRIN, the three Medical Research Infrastructures focusing on medical breakthroughs continued to work closely together. This is especially important with regards to the upcoming Horizon Europe framework programme and it signifies a new era in the application of biomedical research.

Furthermore, Bulgaria went from an observer to a full member, adding up to a total of twelve full members and one observer country.

All EATRIS-ERIC Members and Observers are committed to supporting EATRIS in reaching its important goal: to bridge the gap between medical research and clinical application by accelerating and optimising translational research.

Finally, the new EATRIS Scientific Advisory Board (SAB) was appointed this year. With their broad competence and extensive experience, they will help to develop EATRIS strategies and activities, and function as an external advisory body to the Board of Governors.

Sincerely,
MARIANNE GRØNSLETH



MATS LARHED

Chair of the Board of National Directors

It has been exciting to follow EATRIS' journey during my second year as chairman. Looking back, 2019 has been a successful year with a lot of new opportunities, highlights and the continuous development of the research infrastructure.

In addition, an excellent collaboration between EATRIS Coordination & Support Office (C&S) and its members led to EATRIS-Plus, one of the two flagship projects that were funded by the European Commission. It comprises a large international consortium of nineteen partners from academia, industry and patient organisations. This project will not only create new services and resources for personalised medicine research and development but also support international collaborative activities to strengthen national capacity and increase EATRIS' visibility.

The second flagship project that received funding was EU-PEARL. The goal of this project is to shape the future of clinical trials with the development of new methods, tools and frameworks and create an infrastructure that will enable the development of patient-centric platform trials. This will be possible through an integrated system where pharmaceutical companies, non-profit product developers and healthcare providers collaborate.

We have also witnessed the national coordination capacity growing and improving EATRIS' visibility locally. EATRIS is growing and for the next years to come, I am looking forward to following EATRIS' development and how this will make an impact on Europe's personalised medicine and health.

Sincerely,
MATS LARHED

**ANTON USSI**

Operations & Finance Director

**TONI ANDREU**

Scientific Director

Dear reader,

We are proud to present to you the highlights of 2019 activities for EATRIS-ERIC. As the first year of operations under the current Strategic Plan – to run until 2022 – the year can be summed up as one of new beginnings, as well as of consolidation of past achievements.

We are excited to have added several new international projects to our portfolio - in 2019 a total of seven EC-funded projects were granted, with several projects of European interest starting in the year. Of particular note is the commencement of the European Joint Programme in Rare Diseases, a €108 million initiative involving more than eighty partners in over thirty countries. EATRIS, together with our linked third parties VHIR in Barcelona, Spain and UiO in Oslo, Norway, have a leading role as co-leaders of the translational and clinical innovation pillar, and together with ISCIII in Madrid, Spain, co-lead the sustainability planning for the whole endeavour.

Alongside a strongly growing academic R&D focus, we consolidate our industry activities by continuing to serve international small-medium and large industry users. And of course, our ongoing collaboration with GSK in the unique Immune Inflammation Imaging Hub portfolio continues to expand, with several projects successfully reaching their development milestones, and novel projects added to the portfolio.

A principal component of the current Strategic Plan is to facilitate high-quality research and development for personalised medicine. To that end, EATRIS is very proud to have successfully received a positive funding review for the flagship project EATRIS-Plus in 2019, which launched in January 2020. This project will shape the EATRIS infrastructure for years to come, with a focus on facilitating high-quality multi-omic research for personalised medicine. It will also augment our multi-disciplinary approach through activities with patient communities, industry, other infrastructures, and global peers, such as those in Translation Together, which continues to thrive.

All in all, we can happily report a very exciting and successful year, in which we honed existing strategies and carefully implemented new routes to improving the process of translation. We hope you enjoy the highlights in the Annual Report 2019!

Sincerely,
ANTON USSI
TONI ANDREU

EATRIS HIGHLIGHTS

January



Medical Research Infrastructures, BBMRI – EATRIS – ECRIN, sign long-term collaboration agreement in Brussels, Belgium

February



ERIC FORUM Kick-Off meeting in Amsterdam, The Netherlands

March



Certificate of Excellence in RI Leadership received from University of Milano-Bicocca in Milan, Italy

March



2nd Conference Validation of Biomarkers, Clinimark project in Basel, Switzerland

May



Workshop on Imaging and Cell Therapies at the Advanced Therapies and Regenerative Medicine Congress in London, UK

June



BIO International Convention in Philadelphia, USA



Translation Together annual Face to Face meeting in Philadelphia, USA

July

eatris



efpia



Joint Statement from EFPIA, EATRIS, ELIXIR, BBMRI & ECRIN on the role of Research Infrastructures to boost patient-centred research and innovation in Europe

October



First visit to Bulgaria as full member by EATRIS C&S, in Sofia



First meeting of the new EATRIS SAB in Amsterdam, The Netherlands

November



PhD training course hosted in Barcelona, Spain



EATRIS co-organises session at the World Science Forum Meeting in Budapest, Hungary

December

eatris+

EATRIS-Plus Agreement Signed

2019 IN NUMBERS

100



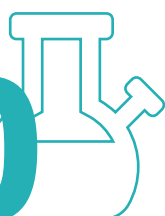
Institutions



52

University Medical Centres

800



Translational Scientists



Over

120

users of TransMed academy

Over

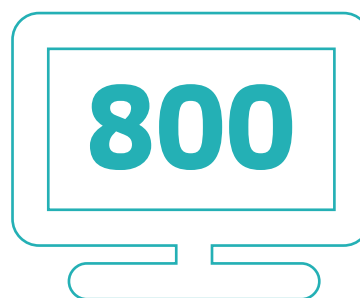
100



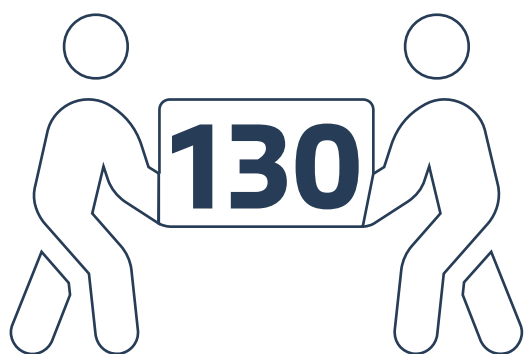
Participants to EATRIS webinars

More than

800



Views on YouTube



Partnering meetings with Industry



Research Service Requests
handled with biotech companies



Expert advices performed



Public-private partnership hub
with a Pharma company



Students at TMex
Face to Face training



Citations in scientific papers

NEW SCIENTIFIC ADVISORY BOARD

OCTOBER 24, 2019,
AMSTERDAM, THE NETHERLANDS

We are delighted to present the new Scientific Advisory Board (SAB) for EATRIS. Acting as an advisory body to the Board of Governors (BoG), the SAB provides independent feedback and advice on the scientific strategy of the organisation.

“This Board brings multi-disciplinary expertise and a broad range of professional backgrounds needed to provide guidance on the development of our strategies and activities. The new Board composition reflects the direction of EATRIS under the new Strategic Plan, whose focus on the role of translational research in personalised medicine. We are privileged to have on board a group of high-profile experts that will enrich EATRIS life, a combination of experience and expertise along the entire translational science value chain.” as stated by Toni Andreu, EATRIS Scientific Director.



Our sincerest gratitude goes out to the former members of our SAB for their invaluable contribution towards the advancement of translational research:

- José Luis Jorcano (Head of Division at Ciemat/ Professor of Bioengineering at Univ. Carlos III)
- Gerard Pasterkamp (Division Manager division Laboratories, Pharmacy and Biogenetics at UMC Utrecht)

- Leo Schalkwyk (Professor of Human Genetics at University of Essex)

Two members of the original SAB, namely Nicole Deglon and Petr Kocis, have kindly agreed to remain on the Board.



HUGO VAN HEUVERSWYN

Hugo Van Heuverswyn (Chief Executive Officer at ABC, Gent, Belgium) is one of the pioneers in turning modern biotechnology into industrial applications in Belgium. He is nowadays board member of Flanders Bio which he founded in 2003 with Rudy Dekeyser. He is also co-founder of Flanders Vaccine, a not-for-profit organisation containing a diversity of stakeholders aiming to foster national and international collaborations in the field of vaccination and immunotherapy.



PETR KOCIS

Petr Kocis (Vice President Preclinical Development at Alzheon, Boston, USA) is a drug development expert in combinatorial chemistry. He has been involved in drug discovery in cancer, immunodeficiencies, and asthma, has provided drug lead discovery leadership at various companies. Petr is on the editorial board of several journals including *Drugs of the Future*.



NICOLE DEGLON

Nicole Deglon (Professor at Lausanne University Hospital, Lausanne, Switzerland) has long-standing experience and expertise in viral gene transfer technology to deliver therapeutic candidates in the brain and modelling CNS pathologies by overexpressing disease-causing proteins. Before her position at Lausanne University Hospital, Prof. Deglon was appointed as Research Director and Deputy Director of MIRCen, a preclinical imaging platform for drug, cell and gene therapy in France.



CATHERINE LARUE

Catherine Larue Head of External Affairs at IBBL, Luxembourg). Before her CEO position at the Institute IBBL (Integrated Biobank of Luxembourg) in 2012, Dr Larue worked for Sanofi Diagnostics Pasteur at Minneapolis, USA, for three years, where she was responsible for Assay Development in the immunodiagnostic area, and several years at Bio-Rad as Director of the Business Unit. She is currently serving as an expert for the European Commission (H2020, IMI, PerMed programmes) and the Luxembourg National Cancer Plan.



ANDRES METSPALU

Andres Metspalu (Professor at the University of Tartu, Tartu, Estonia) is the former head and founder of the Molecular Diagnostic Centre of the Tartu University Hospital. He is one of the founders and directors of the P3G Consortium of Biobanks in Montreal, Canada and of BBMRI-ERIC. Prof. Metspalu is serving on several national and international committees and editorial boards and has received, among other accolades, the Order of the Estonian Red Cross 3rd Class and L'Ordre des Palmes Academiques from the Republic of France. In 2010 he was awarded Doctor Honoris Causa from Vilnius University. He is also a member of the Cancer Mission Board.



OUR INFRASTRUCTURE AND THE INSTITUTIONS IN 2019

PARTICIPATING COUNTRIES:

Bulgaria, Czech Republic,
Finland, France, Italy,
Luxembourg, The Netherlands,
Norway, Portugal, Spain,
Slovenia, Sweden, Latvia
(observer)

EATRIS INSTITUTES

100+ academic & non profit
research institutes of excellence;
more than half are university
medical centres

EATRIS

*Coordination & Support
located in Amsterdam*





OUR MEMBERS

Core activities of our Members in 2019

BULGARIA

Member representative:

Yanita Zherkova
Milena Glavcheva

National Director:

Rossitza Konakchieva
Rumen Pankov

In 2019 intensive efforts were made to introduce EATRIS-ERIC to the Bulgarian scientific community and to identify academic institutions operating with the capacities to be member institutions. Several events with the national representative audience were organised in spring and autumn 2019 with the participation of delegates from the EATRIS C&S office.

These events were followed by an intensive campaign of face-to-face meetings which generally raised great interest in collaboration with EATRIS among scientists, research officers and private stakeholders. Suitable institutions were identified and nominated to join the EATRIS Scientific Platforms. Another success of 2019 was the involvement of Bulgaria as a contributing Partner in the EATRIS-Plus project. A bilingual website dedicated to the EATRIS Bulgaria national node was built to serve as a hub of national and international communication related to EATRIS matters (<http://www.alliancecelltechnologies.eu/en/natzionalno-predstavitelstvo-eatris-balgariya>).

EATRIS Bulgaria members are now working on the establishment of a national translational biomedicine ecosystem. Key elements of this will include interaction with other European Strategy Forum on Research Infrastructures (ESFRI) Bulgaria nodes including the development of a mutual action plan in compliance with the strategic European vision, a national Research & Development (R&D) program, and events to raise the profile of the translational biomedicine community.

CZECH REPUBLIC

Member representative:

Renáta Chudáčková

National Director:

Marián Hajdúch

National Coordinator:

Miroslav Hutňan

The Czech Republic is contributing to all five technology platforms of EATRIS, with the participating institutes being: Central European Institute of Technologies (CEITEC); Charles University; Institute of Chemical Technologies Prague; Institute of Experimental Medicine ASCR; Institute of Macromolecular Chemistry Prague (IMC ASCR); Institute of Microbiology of the ASCR, v.v.i.; Institute of Organic Chemistry and Biochemistry; Czech Academy of Sciences; Masaryk University; Nuclear Physics Institute of the ASCR/UJF, v.v.i.; Palacký University Institute of Molecular and Translational Medicine (IMTM); and St. Anne's University Hospital Brno.

The Node is coordinated by the Institute of Molecular and Translational Medicine (IMTM) at the Palacký University, in Olomouc, Czech Republic.

FINLAND

Member representative:

Sirpa Nuotio
Riina Vuorento

National Director:

Seppo Ylä-Herttuala

EATRIS Finland started building collaboration with other Nordic EATRIS nodes (Sweden and Norway), with support from EATRIS C&S. Also, The Central Animal Laboratory, directed by Emrah Yatkin, at the University of Turku, joined EATRIS, as the ninth site in Finland. There were several service requests received from EATRIS C&S Office, and FIMM was selected by a company to test an extraction kit. To increase our visibility, FIMM is maintaining a LinkedIn site for EATRIS Finland.

FRANCE

Member representative:

Alix De la Coste
Eric Guittet

National Director:

Philippe Hantraye
Simone Mergui

National Coordinator:

Lauranne Duquenne

NeurATRIS, the French node of EATRIS, is a national research infrastructure dedicated to translational research in neuroscience and particularly in neurodegenerative diseases. In 2019, NeurATRIS was evaluated by the French authorities and an international scientific jury for the first time since its establishment in 2011. NeurATRIS obtained an excellent evaluation report from the jury, allowing the node to get a €3.3M funding for the next five years, thus guaranteeing its sustainability until 2025. Partnership development was a core activity for NeurATRIS in 2019, as it organised two editions of its annual event "Translational Neuroscience Day". The first was a standalone event that took place on January 25, 2019, in Paris, France. The following was a satellite event at the BioFIT 2019 partnering event, which took place on December 10, 2019, in Marseille, France. These events gather experts in neurodegenerative diseases and foster interactions between researchers, clinicians, biotech and pharmaceutical companies. NeurATRIS is also strengthening its training activities with webinars and courses dedicated to early-career scientists and translational researchers.

Number of users in 2019: about 500

ITALY

Member representative:

Maria Ferrantini
Francesca Capone

National Director:

Franca Moretti

2019 was characterised by the renewal of Governance members. President Ricciardi resigned and was replaced by President Brusaferrero; a new Executive Board was appointed in June. We decided to give priority to education and training activities with the double purpose to provide a "service" to the Italian scientific community at large and also to develop a sense of belonging and identity amongst A_IATRIS members.

In this context, a paradigmatic example is represented by the course "Biomarkers and Techniques of Diagnostics for Images in the Assessment of Inflammation in Oncology" promoted by the "Biomarkers" and "Imaging & Tracing" Platforms. The course represented a valuable opportunity for members of the two Platforms to meet and start a discussion on future activities to be developed together.

At the same time the following activities were performed:

- Facilitation of the development of common projects around priority biomedical research topics.
- Promotion of the Infrastructure, presenting activities and services offered by EATRIS and its Italian Node.
- Implementation of the activities of the Intellectual Property and Technology Transfer (IP&TT) in enhancing information and training of researchers.
- A_IATRIS scientific community maintenance and cohesion: meetings of the PP and the IP&TT group were held during the year.

LATVIA

Member representative:

Uldis Berkis

National Director:

Ilmārs Stonāns

National Coordinator:

Zaiga Nora-Krūkle

The EATRIS-Latvia National Contact Point worked on introducing the Latvian academic community to the EATRIS guidelines and the added value the organisation's activities offer. We have created an EATRIS information section on the Rīga Stradiņš University (RSU) in both Latvian and English

(www.rsu.lv/en/eatris-latvia) and identified scientific institutes that have expressed their readiness to join various EATRIS scientific platforms.

The EATRIS Directors visited Latvia in October, with the aim of introducing the Latvian scientific community to EATRIS, and to learn more about the infrastructure of scientific institutes interested in joining. Latvian EATRIS representatives participated in events throughout the year.

On November 26, the National Director gave a presentation “Rīga Stradiņš University and plans for involvement in EATRIS” at the RICH-2 (European Network of National Contact Points for Research Infrastructures) seminar, which was attended by colleagues representing BBMRI, EU-OPENSOURCE and MIRRI in Latvia. The National Coordinator attended the meeting for National Directors and Platform Chairs in Haarlem, The Netherlands in December. In 2019, a National Agreement on EATRIS Participation was prepared, with Rīga Stradiņš University, University of Latvia, Latvian Biomedical Research and Study Centre and Latvian Institute of Organic Synthesis as participating institutions.

LUXEMBOURG

Member representative:

Jean-Claude Milmeister

Lynn Wenandy

National Director:

Frank Glod

In 2019, the Institute of Health and IBBL have undergone a restructuring of the transversal translational medicine effort involving the University of Luxembourg (UL) and local hospitals. This capacity building exercise ties existing resources into an integrated operational workflow that allows the addition of new platforms and projects. One such platform is the newly created disease modeling screening platform (DMSP) with the UL.

Furthermore, the National Centre of Excellence in Research in Parkinson's Disease (NCER-PD) started its second phase and exemplifies existing research efforts spanning the entire translational pipeline. It enables a better understanding of the mechanisms of Parkinson's disease to ultimately lead to its early diagnosis and the development of highly personalised treatments for patients. NCER-PD showcases how Luxembourg translational work approach could be implemented in an European and EATRIS context. This was presented at the meeting for National Directors and Platform Chairs as part of Luxembourg translational strategy.

THE NETHERLANDS

Member representative:

Martijntje Bakker

Saco de Visser

National Director:

Gerrit Meijer

National Coordinator:

Rick van Nuland

Excellent biomedical research needs excellent research infrastructure. Health-RI (<https://health-ri.nl/>) is a joint initiative of the Dutch nodes of EATRIS, ELIXIR, BBMRI and the Dutch university medical centres, together with a broad coalition of other organisations. It is a public-private partnership to realise the infrastructure necessary to give researchers optimal access to knowledge, tools, facilities, health data and samples to enable personalised health and medicine.

The first version of Health-RI shared service centre has been implemented referencing core Health-RI related initiatives such as EATRIS, mature services such as XNAT and cBioPortal, and ongoing development projects including the Personal Health Train.

Several large national programmes have been transitioned into Health-RI to reduce fragmentation in the infrastructure landscape, in particular Translational Research IT (TraIT), Data4lifesciences, and Parelsnoer.

A professional communication programme has been implemented through the new Health-RI website, contributing to a consistent Health-RI identity with user stories, and a strategic social media presence. The national Health-RI conference provides a networking opportunity for the Dutch health data infrastructure community, with an ever-growing attendance (350 participants in 2019).

The implementation of the concepts of federated learning in the health data field were boosted with the foundation of the Personal Health Train coalition, which will work on the architecture and standards for this field.

The Dutch national node for the European Million Genome project was initiated and The Netherlands formally joined this program. The Dutch node is jointly operated by ELIXIR, BBMRI and EATRIS under the umbrella of Health-RI. The Dutch national roadmap project for integrated large-scale multi-omics infrastructure, X-Omics took off and is delivering the first infrastructure components to the Dutch community.

The Dutch University Medical Centers (UMCs) are locally establishing data centers characterised by Findability Accessibility Interoperability and Reusability (FAIR) by stewardship organisations supporting their internal scientific community in close collaboration with each other.

NORWAY

Member representative:

Marianne Grønseth

National Director:

Janna Saarela

National Coordinator:

Laetitia Abdou-Garonne

Anita Kavlie*

An important priority for EATRIS Norway during this year has been the registration of more Norwegian core facilities and expertise with the EATRIS Technology platforms. We have also organised several events as well as participated in some strategically important activities. For example, in October we hosted the first national EATRIS Norway network meeting that was attended by researchers and administrative staff from Norwegian member institutions and delegates from the Research council of Norway and South-Eastern Norway Regional Health Authority.

In June, Janna Saarela, National Director, participated at a combined science and business event in Trondheim (Health Registries, Big Data & Improving Patient Outcomes) where she took part in a panel discussion. EATRIS Norway has also been involved in scientific projects such as assessing the reproducibility of small molecules with high-throughput screening as well as whole body detection of therapeutic immune cell migration to tumours. EATRIS-Norway participates in H2020 projects such as the European Joint Programme on Rare Diseases, EATRIS-Plus and EuroNanoMed III.

* Anita Kavlie is the successor of Laetitia Abdou-Garonne

PORTUGAL

Member representative:

Rui Santos Ivo

National Director:

Cláudia Maria Coelho de Faria

National Coordinator:

Dinah Duarte

Helena Beaumont**

During 2019, EATRIS Portugal focused on building a national community through interaction with research and infrastructure partners and institutions, and coordinating activities. The National Hub was formalised in July 2019 and included fourteen specialised centres that have joined all EATRIS product platforms. The main tasks in establishing the expertise and project management structures necessary to enable efficient communication and data exchange throughout the Portuguese node were:

- Mapping the network and National network formalisation.
- Coordination and communication between the individual institutions.
- Communication with other EATRIS nodes and structures.

Within the scope of transnational research collaboration funding and in the context of the national node activities linked to EATRIS participation, Infarmed (EATRIS Portugal Coordinator) is a partner in the EATRIS-Plus project.

** Helena Baiao is the successor of Helena Beaumont

SLOVENIA

Member representative:

Albin Kralj

National Director:

Irena Mlinaric-Rascan

Žiga Jakopin

During this year, the Slovenian node made significant steps in consolidating the resources necessary for the further development of translational research. The Slovenian node joined the EATRIS Biomarkers platform. A national consortium was established between the University of Ljubljana Faculty of Pharmacy, the University of Maribor Faculty of Medicine, and the Institute of Chemistry.

In addition, the Slovenian node applied for cohesion funds from the European Regional Development Fund, for use in infrastructure development. Upgrades to research

infrastructure will improve the capacity of the national node to support research institutes. The national node provides access to resources, supports the national research community and corrects imbalances between regions, strengthening socio-economic cohesion.

EATRIS Slovenia is participating in EATRIS-Plus and Erasmus+ ADVANCE. The collaboration in both projects (funded in 2020) will support scientific quality and produce an increase in future scientific results.

Many meetings, workshops, education and training activities were organised by the node in 2019. Communications, outreach and organisation of partnering activities resulted in increased awareness of the benefits of EATRIS membership.

SPAIN

Member representative:

Gonzalo Arévalo***

Cristobal Belda

National Director:

Joan X. Comella

Fátima Núñez

National Coordinator:

Marta Marín

During 2019, the activity of the Spanish node has mainly focused on participating in European projects. In collaboration with EATRIS, the Spanish institutions have put forward eleven proposals, of which five were granted: EATRIS-Plus (VHIR, IRICYS), EU-PEARL (VHIR), EJP-RD (VHIR, IDIPAZ), EOSC-LIFE (VHIR) and RECOGNISED (VHIR). Notably, two of these projects, EATRIS-Plus and EU-PEARL, are considered EATRIS flagship projects.

In November, VHIR, together with EATRIS and “laCaixa” Foundation, organised the TMex Winter school training course in Barcelona. The five-day face-to-face workshop for PhD students and postdocs in translational medicine covered topics such as the role of clinical trials in translational medicine, innovative trial design and the engagement of patients in research.

The structure of the node has also been consolidated, with the incorporation of a National Coordinator and the identification of a contact person in each institution, to ensure an efficient communication flow. With the objective of becoming a referent for connecting translational medicine in Europe through the Spanish Health Research Institutes, EATRIS Spain is defining a new strategic plan and governance structure.

SWEDEN

Member representative:

Maria Nilsson

Håkan Billig

National Director:

Mats Larhed

National Coordinator:

Ulrika Bäckman

This year the Swedish node hosted the first national coordinator meeting. Coordinators from eight countries participated to discuss national roadmaps and EATRIS communications at the national level. Many activities focused on further building up the node with new infrastructures, outreach was also discussed. The national node participated in several conferences, including:

- The Nordic Precision Medicine Forum in Stockholm that brings together those at the very forefront of precision medicine from biologists, physicians and technology developers to data scientists, patient groups, governments and research infrastructures.
- At the Park Annual meeting with the theme of the future of health, the node had the opportunity to promote EATRIS, with one-to-one meetings and many new networking opportunities.
- For the fourth year, we participated in the Nordic Life Science Days in Malmö, Sweden, to meet with key players in the Nordic life science sector and to see and learn how the Nordic life science community is evolving.
- SwedenBio event in Stockholm, a yearly opportunity to participate in inspirational meetings, workshops and informal get-togethers.
- Invited to the Pharma development group, the node had the opportunity to present its expertise and infrastructure to several Small and Medium-sized Enterprises (SMEs) in Sweden.

The Immuno Inflammation Imaging Hub projects are ongoing, and new projects in other areas are under discussion. This hub concept creates a great opportunity for Swedish researchers with an essential role in this EATRIS flagship initiative. To further strengthen Nordic collaboration, a common application was made to NordForsk – Nordic EATRIS Hub.

*** Gonzalo Arévalo is the successor of Rafael De Andres de Medina

INSTITUTIONS OVERVIEW

- Platform participation
- Platform participation new institutions in 2019

Name	ATMP	Biomarkers	Imaging & Tracing	Small Molecules	Vaccines
CZECH REPUBLIC					
Central European Institute of Technologies (CEITEC)	●	●	●	●	●
Charles University	●	●	●	●	●
Institute of Chemical Technologies Prague	●	●	●	●	●
Institute of Experimental Medicine AS CR	●	●	●	●	●
Institute of Macromolecular Chemistry Prague (IMC ASCR)	●	●	●	●	●
Institute of microbiology of the AS CR, v.v.i	●	●	●	●	●
Institute of Organic Chemistry and Biochemistry, Czech Academy of Sciences	●	●	●	●	●
Masaryk University	●	●	●	●	●
Nuclear Physics Institute of the ASCR/UJF, v.v.i.	●	●	●	●	●
Palacký University - Institute of Molecular and Translational Medicine (IMTM)	●	●	●	●	●
St. Anne's University Hospital Brno	●	●	●	●	●
FINLAND					
Finnish Red Cross Blood Service	●	●	●	●	●
University of Eastern Finland - National Virus Vector Laboratory (NVVL)	●	●	●	●	●
University of Helsinki - Institute for Molecular Medicine Finland (FIMM)	●	●	●	●	●
University of Tampere - Regea Cell and Tissue Center	●	●	●	●	●
University of Turku and Turku University Hospital	●	●	●	●	●
VTT Technical Research Centre of Finland (VTT)	●	●	●	●	●
FRANCE					
NeurATRIS-Albert Chevalier-Henri Mondor Hospital	●	●	●	●	●
NeurATRIS-Biotherapies Institute for Rare Diseases (BIRD)	●	●	●	●	●
NeurATRIS-Brain & Spine institute IHU-A-ICM	●	●	●	●	●
NeurATRIS-French Alternative Energies and Atomic Energy Commission (CEA)	●	●	●	●	●
NeurATRIS-Neurosciences Bicêtre - Paris Sud (NBPS)	●	●	●	●	●

- Platform participation
- Platform participation new institutions in 2019

Name	ATMP	Biomarkers	Imaging & Tracing	Small Molecules	Vaccines
ITALY					
Centro di Riferimento Oncologico di Aviano (CRO Aviano)	●	●	●	●	●
Centro Medicina Rigenerativa (CMR)	●	●	●	●	●
CNCCS - IRBM Science Park	●	●	●	●	●
Fondazione IRCCS CRIBT	●	●	●	●	●
Fondazione IRCCS Fondazione Pascale	●	●	●	●	●
Fondazione IRCCS Giovanni Paolo II	●	●	●	●	●
Fondazione IRCCS Istituto Nazionale dei Tumori (INT-Milan)	●	●	●	●	●
Fondazione IRCCS Ospedale Pediatrico Bambino Gesù	●	●	●	●	●
Fondazione IRCCS SDN per la Ricerca e l'Alta Formazione in Diagnostica Nucleare	●	●	●	●	●
IDI-Fondazione IRCCS Luigi Maria Monti	●	●	●	●	●
IRCCS Istituto Ortopedico Galeazzi	●	●	●	●	●
IRCCS Foundation Santa Lucia	●	●	●	●	●
ISMETT	●	●	●	●	●
Istituti Fisioterapici Ospitalieri - Istituto Dermatologico "San Gallicano"	●	●	●	●	●
Istituti Fisioterapici Ospitalieri - Regina Elena Tumor research	●	●	●	●	●
Istituto Superiore di Sanità (ISS)	●	●	●	●	●
Mario Negri Institute for Pharmacological Research	●	●	●	●	●
National Institute for Infectious Diseases Lazzaro Spallanzani	●	●	●	●	●
Rizzoli Orthopedic Institute (IOR)	●	●	●	●	●
Scientific Institute San Raffaele (HSR)	●	●	●	●	●
LUXEMBOURG					
Integrated Biobank of Luxembourg (IBBL)	●	●	●	●	●
Luxembourg Centre for Systems Biomedicine (LCSB)	●	●	●	●	●

- Platform participation
- Platform participation new institutions in 2019

Name	ATMP	Biomarkers	Imaging & Tracing	Small Molecules	Vaccines
NETHERLANDS					
Amsterdam UMC - Academic Medical Centre (AMC)	●	●	●	●	●
Amsterdam UMC - VU Medical Center (VUmc)	●	●	●	●	●
Biomedical Primate Research Centre (BPRC)	●	●	●	●	●
Erasmus University Medical Centre	●	●	●	●	●
Intravacc	●	●	●	●	●
Leiden University Medical Centre (LUMC)	●	●	●	●	●
Maastricht University Medical Center (MUMC)	●	●	●	●	●
Netherlands Cancer Institute	●	●	●	●	●
University Medical Center St Radboud (UMCN)	●	●	●	●	●
University Medical Center Utrecht (UMCU)	●	●	●	●	●
University Medical Centre Groningen (UMCG)	●	●	●	●	●
University of Technology Eindhoven (TU/e)	●	●	●	●	●
Wageningen Bioveterinary Research	●	●	●	●	●
NORWAY					
Norwegian University of Science and Technology (NTNU)	●	●	●	●	●
University of Bergen (UiB) and Haukeland University Hospital	●	●	●	●	●
University of Oslo (UiO) and Oslo University Hospital (OUH)	●	●	●	●	●
University of Tromsø (UiT) and University Hospital North Norway	●	●	●	●	●
PORTUGAL					
3B's Research Institute, University of Minho	●	●	●	●	●
Association for Innovation and Biomedical Research on Light and Image (AIBILI)	●	●	●	●	●
Center for Neuroscience and Cell Biology; Coimbra University Hospital	●	●	●	●	●
Champalimaud Foundation	●	●	●	●	●
Coimbra Institute for Biomedical Imaging and Translational Research (CIBIT)	●	●	●	●	●
Institute for Bioengineering and Biosciences - Stem Cell Engineering Research Group (iBB - SCERG)	●	●	●	●	●
Institute of Biomedicine (IBIMED)	●	●	●	●	●
Instituto de Biologia Experimental e Tecnológica (IBET)	●	●	●	●	●
Instituto de Investigação e Inovação em Saúde (i3S)	●	●	●	●	●
Instituto de Medicina Molecular João Lobo Antunes	●	●	●	●	●
Instituto Português de Oncologia do Porto Francisco Gentil (IPO-Porto)	●	●	●	●	●
Life and Health Sciences Research Institute / Clinical Academic Centre - Braga	●	●	●	●	●
NOVA Medical School, Unicersidade NOVA de Lisboa (NMS, NOVA)	●	●	●	●	●

- Platform participation
- Platform participation new institutions in 2019

Name	ATMP	Biomarkers	Imaging & Tracing	Small Molecules	Vaccines
SLOVENIA					
University of Ljubljana	●	●	●	●	●
SPAIN					
August Pi i Sunyer Biomedical Research institute (IDIBAPS)	●	●	●	●	●
Bellvitge Biomedical Research Institute (IDIBELL)	●	●	●	●	●
BioDonostia Health Research Institute	●	●	●	●	●
FIBICO, Foundation for Biomedical Research of Cordoba (IMIBIC)	●	●	●	●	●
Fundación Jiménez Díaz Institute for Medical Research (IIS-FJD)	●	●	●	●	●
Germans Trias i Pujol Foundation (IGTP)	●	●	●	●	●
Health Research Institute of Santiago de Compostela (IDIS)	●	●	●	●	●
Hospital de la Santa Creu i Sant Pau (IR-HSCSP)	●	●	●	●	●
Hospital La Fe (IIS-La Fe)	●	●	●	●	●
Hospital La Paz Institute for Health Research (IdiPAZ)	●	●	●	●	●
INCLIVA	●	●	●	●	●
Institute of Biomedicine of Seville (IBIS)	●	●	●	●	●
Instituto Ramón y Cajal (IRYCIS)	●	●	●	●	●
Malaga Health Research Institute	●	●	●	●	●
University Hospital La Princesa (IIS-IP)	●	●	●	●	●
Val̄l d'Hebron Research Institute (VHIR)	●	●	●	●	●
SWEDEN					
Chalmers University of Technology	●	●	●	●	●
Karolinska Institute	●	●	●	●	●
KTH Royal Institute of Technology	●	●	●	●	●
Linköping University	●	●	●	●	●
Lund University	●	●	●	●	●
Stockholm University	●	●	●	●	●
Umeå University	●	●	●	●	●
University of Gothenburg	●	●	●	●	●
Uppsala University and Uppsala University Hospital	●	●	●	●	●

Publication from our nodes

MOLECULAR IMAGING TO SUPPORT THERAPEUTIC ANTIBODY DRUG DEVELOPMENT FOR THE TREATMENT OF SOLID TUMORS

IMMUNO-PET IMAGING TO ASSESS TARGET ENGAGEMENT: EXPERIENCE FROM 89ZR-ANTI-HER3 MAB (GSK2849330) IN PATIENTS WITH SOLID TUMORS

Key messages:

ImmunoPET is a sensitive, non-invasive imaging technique to measure tissue antibody-drug concentrations. In this paper, researchers from AmsterdamUMC and GSK study the biodistribution and tumor uptake of the anti-human EGFR (HER3) antibody GSK2849330. They confirm the target engagement of mAb to the HER3 receptor by showing a dose-dependent inhibition of tumor uptake by unlabeled mAb. This study further validates the use of immunoPET to directly visualise tissue drug disposition in patients with a non-invasive approach and to measure target engagement at the site of action, offering the potential for dose selection.

Synopsis:

Positron-emission tomography (PET) imaging with radiolabeled drug provides information on tumor uptake and dose-dependent target interaction to support selection of an optimal dose for future efficacy testing. In this immunoPET study of the anti-human EGFR (HER3) mAb GSK2849330, the biodistribution and tumor uptake of a 89Zr-labelled version of the mAb was investigated and target engagement was evaluated as a function of antibody mass dose.

89Zr-GSK2849330 distribution was monitored in 6 patients with HER3-positive tumors not amenable to standard treatment. Patients received two administrations of 89Zr-GSK2849330. Imaging after tracer only was performed at baseline; dose-dependent inhibition of 89Zr-GSK2849330 uptake in tumor tissues was evaluated 2 weeks later using increasing doses of unlabeled GSK2849330 in combination with the tracer. Up to 3 PET scans (2 hours post infusion [p.i.] and days 2 and 5 p.i.) were performed after tracer administration. Biodistribution and tumor targeting were assessed visually and quantitatively using standardized uptake value. The 50% and 90% inhibitory mass dose (ID50 and ID90) of target-mediated antibody uptake were calculated using a Patlak transformation.

The observations were at baseline, imaging with tracer showed good tumor uptake in all evaluable patients. Pre-dosing with unlabeled mAb reduced the tumor uptake rate in a dose-dependent manner.

Saturation of 89Zr-mAb uptake by tumors was seen at the highest dose (30 mg/kg). Despite the limited number of patients, an exploratory ID50 of 2 mg/kg and ID90 of 18 mg/kg has been determined. Target engagement is shown by dose-dependent inhibition of tumour-uptake using unlabeled antibody, illustrating a powerful technique for dose selection.

Authors:

Willemien Menke-van der Houven van Oordt, Adam McGeoch, Mats Bergstrom, Iain McSherry, Deborah Smith, Matthew Cleveland, Wasfi Al-Azzam, Liangfu Chen, Henk Verheul, Otto S Hoekstra, Danielle J Vugts, Immanuel Freedman, Marc Huisman, Chris Matheny, Guus van Dongen, Sean Zhang. *Journal of Nuclear Medicine*.

DOI: 10.2967/jnumed.118.214726

Publication from our nodes

A NOVEL BRAIN-ON-A-CHIP SCREENING SYSTEM TO SUPPORT THE SEARCH FOR PARKINSON'S DISEASE DRUGS

PROPAGATION OF ALFA-SYNUCLEIN STRAINS WITHIN HUMAN RECONSTRUCTED NEURONAL NETWORK

Key Messages:

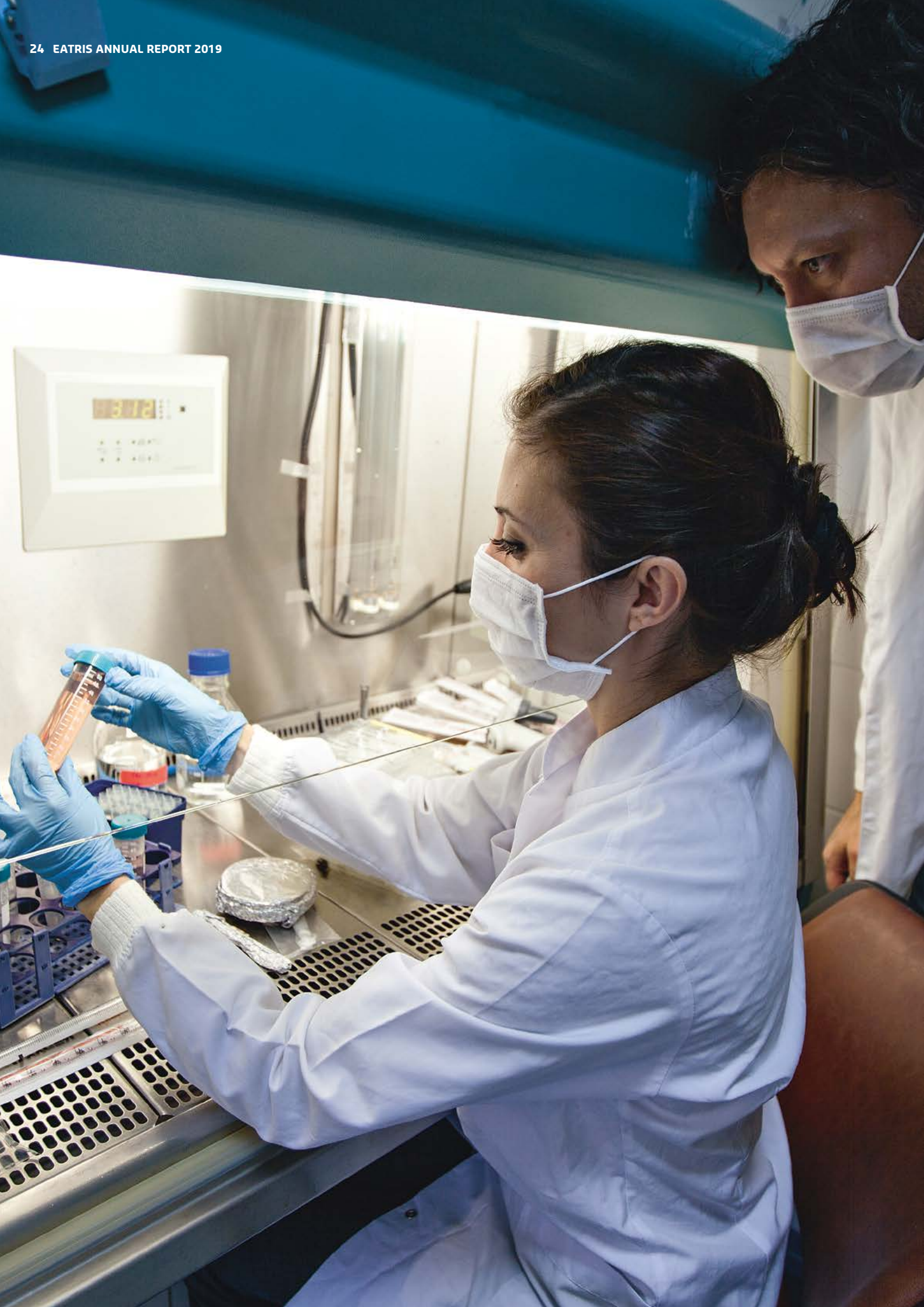
This research paper, co-authored by investigators from MirCEN (NeurATRIS), details an advanced assay that mimics the pathological hallmarks of 'prion-like' neurodegenerative diseases. They demonstrate that two different strains of alfa-Syn protein aggregates (fibrils and ribbons) are transported, move between human neurons and trigger accumulation of pathogenic proteins associated with Parkinson's disease. This platform, based on human neurons, is a promising, predictive preclinical model to screen for novel therapeutic candidates, reducing the need for animal studies.

Synopsis:

Reappraisal of neuropathological studies suggests that pathological hallmarks of Alzheimer's disease and Parkinson's disease spread progressively along predictable neuronal pathways in the human brain through unknown mechanisms. Although there is much evidence supporting the prion-like propagation and amplification of α -synuclein (α -Syn) in vitro and in rodent models, whether this scenario occurs in the human brain remains to be substantiated. Here we reconstructed in microfluidic devices corticocortical neuronal networks using human induced pluripotent stem cells derived from a healthy donor. We provide unique experimental evidence that different strains of human α -Syn disseminate in "wild-type" human neuronal networks in a prion-like manner. We show that two distinct α -Syn strains we named fibrils and ribbons are transported, traffic between neurons, and trigger to different extents, in a dose- and structure-dependent manner, the progressive accumulation of PD-like pathological hallmarks. We further demonstrate that seeded aggregation of endogenous soluble α -Syn affects synaptic integrity and mitochondria morphology.

Authors:

Simona Gribaudo, Philippe Tixador, Luc Bousset, Alexis Fenyi, Patricia Lino, Ronald Melki, Jean-Michel Peyrin and Anselme L. Perrier. Stem Cell Reports.
DOI: 10.1016/j.stemcr.2018.12.007



OUR SERVICES IN 2019

FROM SCIENTIFIC DISCOVERY TO PERSONALISED MEDICINE

2019 was the first year of implementation of the EATRIS Strategic Plan (2019 – 2022), a document that reflects EATRIS' vision for the future of the Infrastructure and defines the main pillars on which the organisation will base its progress.

The pillars that we identified are:

1. Build on our academic credentials by reinforcing EATRIS community;
2. Create an effective translational medicine ecosystem;
3. Synchronise the capacities of medical Research Infrastructures; and
4. Raise awareness of EATRIS.

This year saw the first achievements in response to the challenges addressed in our Strategic Plan, while we continued to optimise and provide access to the high-level services and expertise available in our Research Infrastructure for the advancement of translational medicine projects.

Industry research and services

In 2019, awareness among SMEs gained momentum thanks to the effort put into Business Development. Fifteen Letters of Engagement were signed with one collaboration in the making. Through the CORBEL Innovation office, we were able to offer our regulatory support service. One academic partner made use of these services, along with two European SMEs and one privately-owned biomedical research and development holding company based in the United States.

We continued to develop our technical services available at EATRIS member institutions through combining three disciplinary pillars for early decision making:

- Accessing validated analytical tools in the context of use;
- Contributing to clinical observation and understanding unmet clinical need through our clinical capacity; and
- Deep biological expertise for a mechanistic understanding.

Of note, despite delays due to uncertainty surrounding Brexit and General Data Protection Regulation (GDPR) related issues, two Data Transfer Agreements have been initiated between Queen Mary University of London, ISMETT, Italy, and St Anne's University, Czech Republic, for a project related to Complex Multimodal Biomarker Profiling in the cardiovascular field (CORBEL Open Call).

On the long-term collaboration side, one year after announcing publicly the GlaxoSmithKline (GSK) hub, a unique alliance between GSK and six EATRIS partner institutions, the project portfolio has reached €1.2M. It currently comprises three pre-clinical projects (two extended); two clinical projects to start early 2020 and five new proposals in the conceptual stage. In addition, one PhD programme was funded and ReumaNederland is exploring the opportunity to join the hub as an additional funding party.

Furthermore, we continued discussions with pharma companies on the subject of long-term collaborations along the lines of the GSK hub with the help of an industry consultant (Set-up and management of public-private innovation Hubs).

“As a charity, Prinses Beatrix Spierfonds and its fellow funders support high impact research and development to find novel treatments and to improve the quality of life of patients with muscle disorders. The translational assessment performed in 2019 by EATRIS as an independent party was very useful in making an informed decision to provide financial support to Yumen Bionics that develops an innovative bionic arm to improve the quality of life of Duchenne patients. The early Health Technology Assessment and the SWOT analysis performed by an international panel of clinical and HTA experts provided valuable insights.”

Ellen Sterrenburg, Policy and Research Manager,
Prinses Beatrix Spierfonds

“As a small company focused on rare diseases, we are relying on collaborations and innovative co-funding models. The EATRIS translational assessment provided valuable insights in the health economics aspects of our prototype product. The expert insights, collected in a systematic, independent approach were a confirmation of our endeavor to address the most pressing medical need for the patients and allowed a consideration of development bottlenecks”.

Pim Munnik, Managing Director, Yumen Bionics

In addition, we performed five translational assessments. One assessment originated from a request we received from the Princes Beatrix Spierfonds. It was regarding the evaluation of an exoskeleton for children and adults suffering Duchenne Muscular Dystrophy. The remaining assessments were all performed for ReumaNederland, the Dutch arthritis charity with which EATRIS has intensified its collaboration in the past year.

OUR SERVICES

Research Services

EATRIS C&S Office provides support to ensure that project partners reach an agreement efficiently and to facilitate partnerships while the EATRIS institutes execute the resulting study plans in direct collaboration with the users. Our catalogue comprises a wide range of high-value-added drug and diagnostic development studies. These cover most product modalities from target validation to proof of concept in humans.

Who is it for? For Industry, big pharma, biotech companies and SMEs

Consortium Building

Like Research Services, Consortium Building is a quick way to identify potential partners for funding applications. Thanks to a comprehensive database of our infrastructure's cutting-edge technologies, EATRIS helps in forming the consortium by identifying the suitable partners with specific expertise and capabilities to strengthen a project proposal.

Who is it for? Academia and SMEs

EATRIS Translational Assessment

Our Translational Assessment is a unique service in Europe. With this service, we assess the translational feasibility of projects based on various elements and criteria such as the unmet medical need, the intellectual property at play, the regulatory context, and the end-product definition. This translational assessment proactively aids in identifying potential gaps and bottlenecks which may obstruct project execution, as well as pin-pointing key enabling technologies to give confidence in the data package under generation. In addition to the translational feasibility assessment, we have developed a catalogue of centralised and decentralised services for academic users developing proposals for funding applications (see p27).

- Regulatory work package
- Translational feasibility and early Health Technology Assessment (HTA)
- Innovation & impact (feasibility and Health Technology Assessment, partnering, intellectual property)
- Training (focused on translational research)
- Hands-on development and management of flagship proposals

Who is it for? Funding agencies, Charities and Academia

Regulatory Support

Regulatory Support offers early assessment of the requirements needed for successful translational projects. It provides the necessary information to drive development plans for innovative technologies and products, which is also an essential part of the EATRIS Translational Assessment service. The regulatory experts working with EATRIS provide a range of services, including facilitating early dialogue with national competent authorities, Orphan Drug Designation applications and more.

Who is it for? Academia and SMEs

Set-up and management of public-private innovation Hubs

This service is tailored to the needs of pharma companies willing to form a long-term collaboration with multiple academic partners. It offers a novel collaboration format to enable experts in the agreement to fully focus on the scientific and technical challenges to be tackled. The Master Research Collaboration Agreement in place between the company and the institutions participating in a hub allows for fast initiation of collaborative projects. EATRIS acts as a portfolio manager, playing a key role in developing and administering the legal framework and management of the collaboration. This service originates from the success of the unique alliance put in place for GSK with six EATRIS partner institutions.

Who is it for? Pharmaceutical companies



OUR SERVICES

Academic research and services

In 2019, we saw a consolidation of our academic user group through the utilisation of our EATRIS support services for H2020 and IMI funding applications. Following the structuring in 2018 of four main levels of support, in 2019 we focused on increasing awareness of these services among the academic community. In addition, criteria for EATRIS to join a funding application as partner were made more stringent.

- **Level 1:** Consortium Building
- **Level 2:** Providing a letter of Support
- **Level 3:** Joining as Partner
- **Level 4:** Supporting EATRIS Flagship projects

As a result, our consortium building (partner finding) service was offered thirteen times and EATRIS entered as a partner in seventeen proposals (five Research Infrastructures proposals, seven Societal Challenge Health proposals and six Marie Skłodowska Curie proposals). Seven proposals received a letter of support.

The IMIBIC Fellowship Programme for Personalised and Precision Medicine, jointly developed by the University of Cordoba, the Regional Government of Andalusia (Junta de Andalucía) and the Fundación para la Investigación Biomédica de Córdoba (FIBICO) received Marie Skłodowska Curie grant funding. EATRIS is a partner in the project offering Education and Training support.

Two additional proposals were granted – RECOGNISED, a project coordinated by VHIR to develop retina biomarkers as a tool for identifying individuals with Type-2 Diabetes at a higher risk of developing cognitive decline or dementia, and PERMIT, led by ECRIN.

The objective of PERMIT is to establish thorough multi-stakeholder engagement recommendations to ensure the robustness of Personalised Medicine trials (see p61). Additional H2020 Infrastructure proposals which received funding in 2019 are ENRIITC and iNext Discovery (see p61).

Four new EU projects were initiated this year: EOSC-Life, EJP-RD, ERIC-Forum, and RI-VIS and we continued delivering on CORBEL, TRANSVAC2 and ID-EPTRI (see p62).

Three flagship initiatives granted

In 2019, EATRIS co-coordinated the preparation of the second-stage application of EU-PEARL, a €24M IMI project proposal coordinated by VHIR (EATRIS Spain) for the establishment of a platform enabling patient-centric drug development (see p32).

In addition, the two flagship projects coordinated by EATRIS, EATRIS-Plus (H2020 - INFRADEV3 proposal to support the capacity of EATRIS in Personalised Medicine) and ADVANCE (Erasmus+ funded application for the development of training in Advanced Therapy Medicinal Products (ATMPs)) were both also granted (see p30 and p72).

Summary of activity				
Core activities	2016	2017	2018	2019
Consortium Building	18	14	15	13
Matchmaking	9	14	6	10
Translational Assessment/Expert advice	3	14	2	9
Hub Partnering	1	1	1	1
Income C&S Office	2016	2017	2018	2019
Service Fees*	€ 100,150	€ 114,838	€ 32,417	€ 89,812
Grants	€ 219,035	€ 261,505	€ 309,768	€ 355,107
Income Institutions (Budget negotiated)	2016	2017	2018	2019
Industry Projects	€ 1,629,431	€ 326,571	€ 5,000	€ 818,500
EATRIS Linked Third Party grants	€ 388,859	-	€1,615,049	€ 7,713,536
Users	1,400	5,500	3,000	6,500

*non-grant/non-contribution income

INTERVIEW

EATRIS FLAGSHIP PROJECTS EATRIS-PLUS

Interview with Dr. Toni Andreu,
Scientific Director of EATRIS-ERIC

EATRIS-Plus is a H2020-funded project approved by the European Commission in September 2019. The project is one of the EATRIS flagship initiatives in Personalised Medicine and includes all 13 nodes of the infrastructure. With a budget of nearly 5 million euros, EATRIS-Plus will play a defining role in EATRIS' long-term sustainability strategy and leadership as a global research infrastructure.

What is the goal of the project?

EATRIS-Plus aims to support the long-term sustainability strategy of EATRIS as one of Europe's key European research infrastructures for Personalised Medicine. This will be achieved by consolidating EATRIS capacities in the field of Personalised Medicine, expanding our strategic partnerships with research infrastructures and other relevant stakeholders in Europe and globally, and further strengthening the long-term sustainability of EATRIS' financial model.

Why is this so important?

Significant advances have been made through the revolution of genomics. It remains important to bridge the gap between basic research findings and patient care and unleash the potential of personalised medicine for each patient. As an infrastructure with over 100 academic members across 13 countries and a track record in translational research, EATRIS can play a significant role in supporting the progress of personalised medicine.

What is the scientific focus of EATRIS-Plus?

The scientific activities of the project focus on strengthening the role of multi-omic technologies and on supporting personalised medicine. This is facilitated by offering a multi-omic toolbox to the research community, that will enable high-quality research in the context of patient stratification and accelerate the implementation of Personalised Medicine solutions. The toolbox will support cross-omics analysis and data integration in clinical samples. The omic tools will be developed and tested with a real-setting demonstrator, an already established cohort of one thousand healthy individuals in Czech Republic. Information available on this healthy individual cohort will be augmented during the project with transcriptomic, proteomic and metabolomic data.

What is the added value of the project for patients?

One of the key priorities of the project is to further drive patient empowerment in translational research, which currently remains a substantial challenge. This is why we invited the European Patients' Forum (EPF) to join the project as consortium partner. EPF will work closely with EATRIS on developing a joint advocacy programme to increase patient involvement in pre-clinical and early clinical research. Making sure patients better understand medicines development is an essential first step. Therefore, we will also develop training content, particularly e-learning materials, that help patients understand translational science and personalised medicine. Reciprocally, EPF will also provide training to our EATRIS members on patient engagement.

How will the EATRIS community be involved in this project?

All EATRIS members are represented in the consortium through the participation of all thirteen nodes of the infrastructure. Additional member institutions are also involved to carry out specific scientific activities described above. Given the decentralised nature of our infrastructure, it was a natural step to involve all our members in this flagship initiative to support our long-term sustainability. The project will also play an important role for nodes' capacity-building and sustainability planning. All EATRIS members will also benefit from the mobility grants programmes to visit fellow members or international partners, as well as from training programmes focusing on Personalised Medicine. Our yearly Summer School that will be held in Lisbon will definitely be a highlight of the project.



Dr. Toni Andreu
Scientific Director of EATRIS

INTERVIEW

EATRIS FLAGSHIP PROJECTS EU-PEARL

EU Patient-centric clinical trial platforms (EU-PEARL)

Interview with Edwin van de Ketterij,
Clinical Trial Director of EATRIS

Edwin van de Ketterij, EATRIS' C&S Clinical Project Director, leads the sustainability task through the Innovation Management Team (IMT). EATRIS is further represented on the IMT by Anton Ussi, Tamara Carapina, and Ben Lydall. Other IMT members come from other public and private partners within EU-PEARL. This task should ultimately result in the creation of the sustainable entity mentioned earlier. Edwin also holds the role of Risk Manager for the entire project and is a member of the Project Management Office (PMO).

EU-PEARL is an IMI 2 funded project, which launched in November 2019 in Barcelona, Spain. The project is one of the EATRIS flagship initiatives with an overall budget of more than 26 million euros. The project will run for 42 months, until April 2023. EU-PEARL will deliver a trusted sustainable entity ready to set up and coordinate the operation of Integrated Research Platforms (IRPs) in any disease. A Clinical Trial Platform Framework that can be used for any disease, plus four disease clinical trial platforms ready to operate at the end of the project (in Major Depressive Disorder, Tuberculosis, Non-Alcoholic Steatohepatitis (NASH), and Neurofibromatosis).

What is the goal of the project?

EU-PEARL aims to create a framework for patient-centric IRPs, through which novel techniques and treatments developed by multiple companies and organisations are tested in a platform trial. This is a more efficient, accelerated method to bring new, effective treatments to patients.

An IRP is a novel clinical development concept which centres around a master trial protocol. It can accommodate multi-sourced interventions using the existing infrastructure of hospitals and federated patient data in design, planning and execution. An optimised registration pathway for these novel treatments has been established.

EU-PEARL will deliver a trusted sustainable entity ready to set up and coordinate the operation of IRPs in any disease. A Clinical Trial Platform Framework that can be used for any disease, will include four disease clinical trial platforms ready to operate at the end of the project (Major Depressive Disorder, Tuberculosis, Non-Alcoholic Steatohepatitis (NASH), and Neurofibromatosis).

Why is this so important?

There is a clinical need to find newer treatments, faster, for a variety of diseases. In this sense, recent developments in scientific research, technological innovation and advances on big data analysis open a new world of opportunities for clinical research. Based on this new reality, EU-PEARL intends to transform the way clinical trials are conducted with the aim of improving and accelerating drug development processes.

The innovative framework of Integrated Research Platforms EU-PEARL is set to bring more efficiency to the design and implementation of clinical trial protocols, potentially improving the speed of making new drugs available to patients.

What is the added value of the project for patients?

EU-PEARL is engaging with patients from the start to co-design the platform trial framework, thus bringing on board more patient-relevant outcomes. Patients and their relatives/carers will play a central role in trial designs as their perspective on inputs and views on outcomes will be consistently incorporated. Platform trials will:

- Increase patients' prospects of receiving novel techniques and treatments during the clinical trial, rather than a placebo or standard of care; and
- Promote efficiencies in the clinical development process, potentially resulting in faster access for patients to more effective and personalised techniques and treatments.

The EU-PEARL framework will support better health and care for patients by promoting a ground-breaking collaborative paradigm.

How is EATRIS involved in this project?

EATRIS is involved in several ways. It was one of the initiators of the consortium and the development of the project proposal. EATRIS is also Co-Coordinator of EU-PEARL, with Vall d'Hebron Research Institute (VHIR). As a result, EATRIS has a seat on the project's Executive Committee.



Edwin van de Ketterij
Clinical Project Director of EATRIS

Publication from our nodes

UNRAVELLING THE MECHANISM OF ACTION OF AN ALCOHOL-ABUSE DRUG FOR REPOSITIONING IN ONCOLOGY

DISULFIRAM'S ANTI-CANCER ACTIVITY REFLECTS TARGETING NPL4, NOT INHIBITION OF ALDEHYDE DEHYDROGENASE

Key messages:

This study, from researchers at Institute of Molecular and Translational Medicine, Czech Republic, and Karolinska Institute, Sweden, provides critical insights into the mechanism of action of the existing alcohol-abuse drug disulfiram that is under investigation for oncology treatment. It is shown that the anticancer effect is not mediated through ALDH enzyme inhibition (considered a plausible target by the oncology field), but through a copper complex of a disulfiram metabolite that is rapidly formed. Using chelators in control studies it was determined that this copper complex induces aggregation of NPL4 and triggers the destruction of cancer (stem) cells. These findings corroborate further investigations of disulfiram and/or specific targeting of its metabolite as anticancer drugs.

Synopsis:

Aldehyde dehydrogenase (ALDH) is a proposed biomarker and possible target to eradicate cancer stem cells. ALDH inhibition as a treatment approach is supported by anti-cancer effects of the alcohol-abuse drug disulfiram (DSF, Antabuse). Given that metabolic products of DSF, rather than DSF itself inhibit ALDH in vivo, and that DSF's anti-cancer activity is potentiated by copper led us to investigate the relevance of ALDH as the suggested molecular cancer-relevant target of DSF. Here we show that DSF does not directly inhibit ALDH activity in diverse human cell types, while DSF's in vivo metabolite, S-methyl-N,N-diethylthiocarbamate-sulfoxide inhibits ALDH activity yet does not impair cancer cell viability. Our data indicate that the anti-cancer activity of DSF does not involve ALDH inhibition, and rather reflects the impact of DSF's copper-containing metabolite (CuET), that forms spontaneously in vivo and in cell culture media, and kills cells through aggregation of NPL4, a subunit of the p97/VCP segregase. We also show that the CuET-mediated, rather than any ALDH-inhibitory activity of DSF underlies the preferential cytotoxicity of DSF towards BRCA1- and BRCA2-deficient cells. These findings provide evidence clarifying the confusing literature about the anti-cancer mechanism of DSF, a drug currently tested in clinical trials for repositioning in oncology.

Authors:

Zdenek Skrott, Dusana Majera, Jan Gursky, Tereza Buchtova, Marian Hajduch, Martin Mistrik & Jiri Bartek. **Oncogene.** DOI: 10.1038/s41388-019-0915-2

BRCA2 MUTATIONS LINKED TO POOR TREATMENT RESPONSE, OUTCOMES IN PROSTATE CANCER

PROREPAIR-B: A PROSPECTIVE COHORT STUDY OF THE IMPACT OF GERMLINE DNA REPAIR MUTATIONS ON THE OUTCOMES OF PATIENTS WITH METASTATIC CASTRATION-RESISTANT PROSTATE CANCER

Key Messages:

PROREPAIR-B is a study coordinated by researchers at the Spanish National Cancer Research Centre (CNIO) and conducted at the EATRIS site Instituto de Investigación Biomédica de Málaga (IBIMA) in collaboration with the Instituto de Genética Médica y Molecular (INGEMM). This is the first prospective study showing that genetic aspects themselves, such as BRCA2 mutations, regardless of other factors, are responsible for poor prognosis and can have an impact on treatment responses. These mutations should be identified in patients with metastatic prostate cancer, since detecting such alterations is important for the diagnosis and management of the disease and for the patients' families, whose risk of developing breast, ovarian, or pancreatic cancer is increased.

Synopsis:

PURPOSE: Germline mutations in DNA damage repair (DDR) genes are identified in a significant proportion of patients with metastatic prostate cancer, but the clinical implications of these genes remain unclear. This prospective multicenter cohort study evaluated the prevalence and effect of germline DDR (gDDR) mutations on metastatic castration-resistance prostate cancer (mCRPC) outcomes.

PATIENTS AND METHODS: Unselected patients were enrolled at diagnosis of mCRPC and were screened for gDDR mutations in 107 genes. The primary aim was to assess the impact of ATM/BRCA1/BRCA2/PALB2 germline mutations on cause-specific survival (CSS) from diagnosis of mCRPC. Secondary aims included the association of gDDR subgroups with response outcomes for mCRPC treatments. Combined progression-free survival from the first systemic therapy (PFS) until progression on the second systemic therapy (PFS2) was also explored.

RESULTS: We identified 68 carriers (16.2%) of 419 eligible patients, including 14 with BRCA2, eight with ATM, four with BRCA1, and none with PALB2 mutations. The study did not reach its primary end point, because the difference in CSS between ATM/BRCA1/BRCA2/PALB2 carriers and noncarriers was not statistically significant (23.3 v 33.2 months; $P = .264$). CSS was halved in germline BRCA2 (g BRCA2) carriers (17.4 v 33.2 months; $P = .027$), and g BRCA2 mutations were identified as an independent prognostic factor for CCS (hazard ratio [HR], 2.11; $P = .033$). Significant interactions between g BRCA2 status and treatment type (androgen signaling inhibitor v taxane therapy) were observed (CSS adjusted $P = .014$; PFS2 adjusted $P = .005$). CSS (24.0 v 17.0 months) and PFS2 (18.9 v 8.6 months) were greater in g BRCA2 carriers treated in first line with abiraterone or enzalutamide compared with taxanes. Clinical outcomes did not differ by treatment type in noncarriers.

CONCLUSION: g BRCA2 mutations have a deleterious impact on mCRPC outcomes that may be affected by the first line of treatment used. Determination of g BRCA2 status may be of assistance for the selection of the initial treatment in mCRPC. Nonetheless, confirmatory studies are required before these results can support a change in clinical practice.

Authors:

Castro E, Romero-Laorden N, Del Pozo A, Lozano R, Medina A, Puente J, Piulats JM, Lorente D, Saez MI, Morales-Barrera R, Gonzalez-Billalabeitia E, Cendón Y, García-Carbonero I, Borrega P, Mendez Vidal MJ, Montesa A, Nombela P, Fernández-Parra E, Gonzalez Del Alba A, Villa-Guzmán JC, Ibáñez K, Rodríguez-Vida A, Magraner-Pardo L, Perez-Valderrama B, Vallespín E, Gallardo E, Vazquez S, Pritchard CC, Lapunzina P, Olmos D. *Journal of Clinical Oncology*. DOI: 10.1200/JCO.18.00358



EATRIS OUTREACH EFFORTS TOWARDS INDUSTRY IN 2019

To increase the awareness of our research services geared towards the industry, EATRIS has been present at numerous life science conferences and partnering events.

Given that the research services that can be provided via EATRIS' infrastructure ultimately start with a specific request from an industry user, a face-to-face sit-down meeting is an ideal way to discuss the current bottlenecks in R&D for a biotech SME, and whether a collaboration via EATRIS could be beneficial. In total, 118 face-to-face meetings were held at the events below, not including informal interactions during the events.

The following events were attended in 2019:

- Innovation for Health, 14 February (Rotterdam, The Netherlands)
- 14th Annual Biomarkers Conference, 21-22 February (Manchester, UK)
- Knowledge for Growth, 9 May (Ghent, Belgium)
- Advanced Therapies & Regenerative Medicine, 15-17 May (London, UK)
- BIO Convention, 3-6 June (Philadelphia, USA)
- Nordic Life Science Days, 10-12 September (Malmo, Sweden)
- Phacilitate Leaders Europe, 16-18 September (London, UK)
- Bio-Europe, 26-28 October (Hamburg, Germany)
- Dutch Life Science Conference, 28 November (Leiden, The Netherlands)
- BioFit, 10-11 December (Marseille, France)

Trends in expertise requested by industry users

Various companies have inquired whether we could provide access to specific predictive in vitro or in vivo animal models that are not easily accessible via commercial Contract Research Organisations (CROs) and available only in academia because of their novelty and innovativeness. The need for biological samples combined with well annotated clinical data, together with negotiation facilitation



is a recurring request. An additional need perceived is for early-regulatory advice. It allows companies to very quickly identify the main challenges they will face along their development programme. This is especially true for complex products in the field of ATMPs.

In addition, a number of SMEs developing novel drug delivery methods (e.g.s nano-formulation to cross the blood-brain-barrier) need to engage with disease-specific experts to ascertain unmet medical need and the benefit their technology could bring to targeted patient population. Similarly, biotech companies with an established drug development pipeline and looking for expansion in novel indications came to us for additional clinical expertise they might be lacking internally. These are prime examples of the added value of having access to a large academic infrastructure where cutting-edge disease expertise can be accessed.



PARTNERSHIPS AND LONG-TERM INITIATIVES

Engaging with key global stakeholders to collectively address the high risk of failure in medicines development is essential to EATRIS' mission. Successful translational research requires cross-sector collaboration among diverse stakeholders, namely academia, industry, funders, hospitals, regulators and patient organisations. In 2019, EATRIS took a leadership position in the Life Science Research Infrastructure community by chairing the Strategy Board and continued to build closer ties with BBMRI and ECRIN. 2019 saw the solidification of our partnership with the patient community through the European Patient Forum (EPF) which is an umbrella patient organisation that works with patients' groups in public health and health advocacy across Europe.

WORKING MORE CLOSELY WITH OTHER RESEARCH INFRASTRUCTURES

The Alliance of Medical Research Infrastructures (BBMRI, EATRIS, ECRIN) steadily growing

In 2018, all three organisations expressed joint interest in working more closely together to provide even better services to the biomedical community and to support a more cost-effective research process.

Early in 2019, the collaboration solidified through the signing of a long-term collaboration agreement that lays the groundwork for facilitating user access to pan-European medical research infrastructures and supporting the development of tools, joint services and common approaches on quality, standards and advocacy. The Alliance also continued to further build its advocacy presence by preparing joint answers to policy consultations on the future Horizon Europe programme*.

EATRIS chaired the Life Science Research Infrastructures Strategy Board

In October 2018, EATRIS succeeded EMBRC as Chair of the Life Science Research Infrastructures Strategy Board. The Board, in place since 2015, enables thirteen RIs to find alignment on strategic topics and coordinate joint advocacy actions.

Key highlights from the EATRIS mandate include:

- The official name change of the group to the Life Science RI strategy board (LS RI), whose former name (Biological and Medical Science Board) did not reflect the increasing diversity of the infrastructure cluster dedicated to the health and food domain.

- The maintaining of regular dialogue between the Board and key stakeholder groups. Anton Ussi, EATRIS Operations & Finance Director, joined a meeting of the Member States representatives composing the ESFRI Health and Food working group in London on April 30.
- The meeting was an opportunity to report back on key activities undertaken by the LS RI for international collaboration, user access and consolidation of the infrastructure landscape.
- The preparation of a joint response to the European Medicines Agency (EMA)'s public consultation on their 2025 Regulatory Strategy. This activity was an opportunity for the LS RI to increase their visibility towards the agency.
- A two-day Summer Retreat on July 10-11 2019 in Sitges, Spain to help the group brainstorm on common solutions and joint actions in the short and longer term. A summary of the discussions was shared with the Research Infrastructures Unit of the European Commission during the third annual meeting of the Board held in December 2019 in Brussels, Belgium.

In 2020, the Life Science Research Infrastructures Board will be chaired by Susan Daenke from INSTRUCT-ERIC.

* For more information, please visit:

<https://eatris.eu/insights/efpia-eatris-elixir-bbmri-ecrin-statement-role-research-infrastructures-boost-patient-centred-research-innovation-europe/>

STRENGTHENING EATRIS ROLE IN THE GLOBAL RESEARCH ENVIRONMENT

World Science Forum 2019: EATRIS joined forces with UNESCO and the International Science Council (ISC) to advocate for Open Science

EATRIS co-organised a policy session in collaboration with UNESCO and the International Science Council at the 2019 edition of the World Science Forum in Budapest, Hungary in November 2019.

The session brought together key players in the Open Science field to discuss challenges, opportunities as well as risk and benefits across the different regions of opening science to the world. The results of the discussions fed into UNESCO and ISC's programmatic, operational and normative actions on Open Science. Panel gathered diverse perspectives and geographical regions and included representatives from EATRIS, UNESCO, ISC and the European Commission, among others. The event was well-attended and helped raise further awareness about the European research infrastructures' role in fostering open science.

Shaping the future of Personalised Medicine

For the second year, Toni Andreu, EATRIS Scientific Director and member of the Personalized Medicine Coalition (PMC) Board of Directors, chaired a session at one of the key international personalised medicine conferences organised every year in November by PMC in Boston, USA. The session: "Going Global: Learning from Governmental Efforts to Advance Personalised Medicine Around the World" invited four government representatives to share their visions for the future of personalised medicine and elaborate on their efforts to accelerate progress in the field.

EATRIS Operations and Finance Director, Anton Ussi, participated as guest speaker at the Technical Workshop in Montevideo, Uruguay, in December organised by H2020-funded project EU-LAC PerMed, which aims to strengthen global efforts on Personalised Medicine and cooperation between the EU and Latin American and Caribbean (LAC) countries.

Translation Together, a global initiative to advance translational innovation

Translation Together (TT)'s mission is to conduct collaborative research projects to systematically remove barriers, catalyse translation and foster a broad understanding and appreciation for translational science among diverse stakeholders.



In 2019, the initiative formed by 6 leading translational organisations from around the world continued to meet on a regular basis and to make progress on their collaborative projects.

With the addition of Japan Agency for Medical Research and Development (AMED) in 2018, the Memorandum of Cooperation was expanded and, in 2019, each partner organisation renewed its commitment to the initiative.

The phase 1 of the High Throughput Screening (HTS) ring testing was completed, with 8 sites participating. The results obtained are under review among the centres and next steps are under development.

Among additional achievements, the fundamental characteristics of a translational scientist article was published in June 2019 in ACS Pharmacology & Translational Science.

This consensus paper identifies – and visually shows – the fundamental qualities of translational scientists.

<https://eatris.eu/insights/global-experts-define-characteristics-successful-translational-scientists/>.

The TT partners are currently working together in developing a video on the role of Translational Scientists from around the world to reflect the similarities and cultural differences and challenges impacting Translational Sciences.

With the support of the TT partners, the handbook of 100 terms used in Translational Research produced by AMED, TT partner in Japan was translated into English. A special effort was made to harmonise terminology across the TT partners. Once finalised, the document will be widely disseminated.

Translation Together's objectives are:

- To coordinate and develop programmes and resources for educating and training the next generation of translational scientists and other key stakeholders.
- To advocate for a broad understanding of and appreciation for translation and translational science among diverse stakeholders.
- To assist investigators in the conduct of translation and translational science by connecting them to resources, tools, technologies, and expertise.
- To conduct collaborative research projects to remove systemic barriers and catalyse translation.

Visit the website: <https://translationtogether.org>

FOSTERING MULTI-STAKEHOLDER ENGAGEMENT

Advocating for patient engagement in translational research

EATRIS entered a three-year collaboration agreement with the European Patients' Forum ensuring stronger patient involvement throughout the research process and demonstrating both parties' interest in advancing patient engagement in the translational research process and in implementing joint actions, particularly in the fields of advocacy and training.

To kick off this collaboration, EATRIS sponsored the EPF Congress, the first ever European Congress on patient involvement driven by leading representatives of the patient community and patient experts that took place in Brussels in November 2019. EATRIS Head of European Affairs, Anne-Charlotte Fauvel, also spoke at the Congress in the session dedicated to patient engagement in early phase of research. Additional collaboration activities are foreseen in 2020 as part of the new flagship project, EATRIS-Plus. For more information, we invite you to read our interview with Valentina Strammiello, EPF Senior Programme Manager, (see p42).

EATRIS maintains a close dialogue with regulatory authorities and extends Memorandum of Understanding with the Dutch Medicines Evaluation Board

EATRIS kept contributing to advancing regulatory science through the shaping of the EMA's 2025 Regulatory Strategy by answering to their spring public consultation on behalf of the EATRIS community.

The strategy sets out key areas where new or enhanced engagement of the European medicines regulatory network

is essential and where advances in regulatory science are necessary. Additionally, EATRIS representatives provided further feedback by participating in the multi-stakeholder workshop organised in November 2019 by the Agency in Amsterdam.

Furthermore, EATRIS continues to build trust and partnerships with national regulatory competent authorities in Europe. The Memorandum of Understanding signed with the Medicines Evaluation Board (MEB), the National Competent Authority in The Netherlands, was extended to continue supporting EATRIS users through scientific advice at early stages of drug development.

Accelerating collaboration with industry: publication of a joint statement with European Federation of Pharmaceutical Industries and Associations (EFPIA)

In July 2019, four research infrastructures including EATRIS and EFPIA published a joint statement calling on the European Institutions to provide for funding mechanisms that will strengthen public private collaboration opportunities and that will capitalise on Europe's past investments by incentivising more explicitly the use of European Research Infrastructures where appropriate in all EU-funded programmes.

The statement also acknowledges the role played by Research Infrastructures in creating, harmonising and ensuring the adoption of common standards, and in the translation of scientific knowledge into true patient benefit.

Throughout the year, EATRIS and other infrastructures regularly met with EFPIA to further explore how the role of infrastructures could be strengthened in the next European partnership for health.

INTERVIEW

PUTTING THE PATIENT AT THE CENTRE

Interview with Valentina Stramiello,
Senior Programme Manager at EPF

EPF and EATRIS hold the same vision on meaningful patient involvement and share the idea that patients should not only be involved once treatments have been made available to them. This has been the rationale behind the launch of the EPF-EATRIS collaboration, formalised with a 3-year collaboration agreement in 2019. The collaboration has already shown positive effects through the involvement of EATRIS on behalf of the of the medical Research Infrastructures, BBMRI and ECRIN, in the first EPF-led Congress on meaningful patient Involvement in November 2019 in Brussels, as well as the participation of EPF in EU-funded projects, led or co-led by EATRIS, such as EU-PEARL and EATRIS-Plus.

Could you introduce EPF to our readers in a few words?

The European Patients' Forum is the leading voice of patient organisations across Europe. It operates as an umbrella membership-based organisation that works with patients' groups in public health and health advocacy across Europe. Our seventy-four members represent specific chronic disease groups at EU level or are national coalitions of patients.

EPF is a consortium partner in the H2020-funded project, EATRIS-Plus, which focuses on personalised medicine. What will be the role of EPF in this collaboration in a nutshell?

Our role in the project is twofold: on the one hand, it relates to the involvement of patients through the moderation of a Patient Advisory Committee (PAC) that will horizontally inform EATRIS-Plus operations. We will train researchers to better engage with patients and produce a patient involvement toolkit for translational researchers. On the other hand, jointly with EATRIS, we will run advocacy work to promote early involvement of patients, and mobilise patients on topics such as data sharing and patient-driven academic research.

Patient engagement in pre-clinical and early clinical research remains an unresolved challenge. What would be your top recommendations to address this issue?

Certainly, patient engagement comes with challenges as it triggers questions around the need for resources (both human and financial) and for redesigned and adapted processes and timelines, but in the long-term it pays off simply because it shows a response to the societal and patient needs science should address and how these needs should be prioritised. As a follow-up to the above mentioned EPF Congress, we have recently released a report that summarises the key outcomes and messages from our debates (<https://www.eu-patient.eu/globalassets/events/epf-congress-report.pdf>).



Valentina Stramiello
Senior Programme Manager at EPF



EATRIS QUALITY INITIATIVE

2019 has seen some important progress in the EATRIS Quality Initiative's portfolio of projects, which is aimed at involving EATRIS member facilities in international consortia addressing data quality and reproducibility in translational medicine. EATRIS, with its 100 member-facilities, is well-suited to help tackle some of the challenges in translational medical research, e.g. by organising or participating in multi-site benchmarking studies. In order to structure our activities, the EATRIS Quality Initiative (EQI) was launched in 2015 and is an umbrella term for EATRIS activities addressing reproducibility, standards, and reference materials. Many EATRIS facilities contribute to reproducibility studies. Below we present a snapshot of ongoing studies and activities.

Development of best-practice process in somatic mutation detection by NGS

The Biomarker Platform is involved in the FDA-driven community effort SEQC2 (Sequencing Quality Control Phase II) with the aim to assess analytical issues and develop a best-practice process for the generation and bioinformatics analysis of massively parallel human sequencing data. Hundreds of scientists worldwide are contributing to the SEQC2 project to address sensitivity and quality of somatic mutation detection with NGS technologies and bioinformatics. EATRIS contributes with five sites, that provide sequencing data, and seven bioinformatics teams. Besides workshop participations and poster presentations (e.g. at the AACR 2019), the biggest achievement thus far has been the acceptance of a manuscript to Nature Biotechnology. An additional piece has been submitted and three further manuscripts are being developed. All data will be available after publication of the analyses.

Pioneering pilot studies

Under the Translation Together (TT) initiative, five institutions within the Small Molecules Platform are participating in a high-throughput screening (HTS) system ring-testing pilot study. The aim of this ring testing exercise is to identify drivers of variability in HTS, as well as to provide feedback to HTS sites on potential sources of variability in their systems. Following the completion of a pilot phase in 2018 with four sites, the study now comprises twelve research sites in total, and the data generation process is near-finalised. The results will be made available in 2020 together with guidelines and recommendations for HTS facilities (<https://www.eatris.eu/insights/insightstranslationtogether-piloting-hts-reproducibility-study>).

ctDNA as reference material

Two EATRIS sites have engaged with a private-public-consortium led by the Foundation of National Institute of Health (FNIH) with the goal to establish sensitivity thresholds and clinical applicability of ctDNA reference material. In 2019, the scope of the study was developed.

Further studies

Other activities under the EATRIS Quality Initiative umbrella include the development of a webinar series by EATRIS, which included 4 sessions on reproducibility and data quality presented by top researchers in their field. Also, EATRIS was involved in the development of an ISO guideline for quality metrics in NGS, and became an associated stakeholder in the European Quality in Preclinical Data (EQIPD) consortium funded under IMI-2 and led by Janssen Pharmaceutica and The University of Edinburgh.



Dr. Andreas Scherer
Chair of the EATRIS Quality Initiative
Co-chair Biomarker platform

Publication from our nodes

EURIPRED CONSORTIUM AIM TO OPTIMISE THE DIRECT MYCOBACTERIAL GROWTH INHIBITION ASSAY TO ASSESS REPEATABILITY AND REPRODUCIBILITY, AND HARMONISE THE ASSAY ACROSS DIFFERENT LABORATORIES

OPTIMISATION, HARMONISATION AND STANDARDISATION OF THE DIRECT MYCOBACTERIAL GROWTH INHIBITION ASSAY USING CRYOPRESERVED HUMAN PERIPHERAL BLOOD MONONUCLEAR CELLS

Key Messages:

Tuberculosis (TB) is a major global health problem, with 10 million new cases and 1.6 million deaths in 2017. BCG, the only currently available TB vaccine, has poor efficacy against adult pulmonary disease in the tropics, where TB incidence is greatest. Given the high rates of infection, insufficiency of BCG and the rising threat from drug-resistant TB, an effective vaccine is urgently required. However, vaccine development is hampered by the lack of a validated immune correlate of protection from TB. Mycobacterial growth inhibition assays (MGIsAs) represent an unbiased measure of the ability to control mycobacterial growth in vitro. Several MGIsAs have been reported in the literature but to date none has been systematically assessed for reproducibility or standardised and validated across laboratories for use in TB vaccine development. This study reported the optimisation and harmonisation efforts that resulted in demonstrable consistency in outcomes between three laboratory sites using clinically relevant samples. This represented a critical step in assay development to ensure that comparable information can be extracted from TB vaccine studies conducted across different organisations. Additional work is now required to further optimise and biologically validate the direct MGIA by demonstrating a correlation with in vivo protection from mycobacterial challenge, and to evaluate the performance of the assay in trials of novel TB vaccine candidates.

Synopsis:

A major challenge to tuberculosis (TB) vaccine development is the lack of a validated immune correlate of protection. Mycobacterial growth inhibition assays (MGIsAs) represent an unbiased measure of the ability to control mycobacterial growth in vitro. A successful MGIA could be applied to preclinical and clinical post-vaccination samples to aid in the selection of novel vaccine candidates at an early stage and provide a relevant measure of immunogenicity and protection. However, assay harmonisation is critical to ensure that comparable information can be extracted from different vaccine studies. As part of the FP7 European Research Infrastructures for Poverty Related Diseases (EURIPRED) consortium, we aimed to optimise the direct MGIA, assess repeatability and reproducibility, and harmonise the assay across different laboratories. We observed an improvement in repeatability with increased cell number and increased mycobacterial input. Furthermore, we determined that co-culturing in static 48-well plates compared with rotating 2 ml tubes resulted in a 23% increase in cell viability and a 500-fold increase in interferon-gamma (IFN- γ) production on average, as well as improved reproducibility between replicates, assay runs and sites. Applying the optimised conditions, we report repeatability to be <5% coefficient of variation (CV), intermediate precision to be <20% CV, and inter-site reproducibility to be <30% CV; levels within acceptable limits for a functional cell-based assay. Using relevant clinical samples, we demonstrated comparable results across two shared sample sets at three sites. Based on these findings, we have established a standardised operating procedure (SOP) for the use of the direct PBMC MGIA in TB vaccine development.

Authors:

Rachel Tanner, Steven G. Smith, Krista E. van Meijgaarden, Federico Giannoni, Morven Wilkie, Lucia Gabriele, Carla Palma, Hazel M. Dockrell, Tom H.M. Ottenhoff, Helen McShane
DOI: 10.1016/j.jim.2019.01.006

Publication from our nodes

MHC MATCHING ALONE IS INSUFFICIENT TO GRANT LONG-TERM SURVIVAL OF NEURONAL GRAFTS IN THE TREATMENT OF HUNTINGTON'S DISEASE

MHC MATCHING FAILS TO PREVENT LONG-TERM REJECTION OF IPSC-DERIVED NEURONS IN NON-HUMAN PRIMATES

Key Messages:

Despite the increased risk of cancer, infection and cardiovascular diseases, long-term immunosuppression is still used to protect allogeneic neural grafts from rejection. Availability of induced hPSCs (iPSCs) derived from the patient himself or from selected donors with some degree of HLA matching opens up opportunities to secure scalable sources of cell therapy products. This study from the CEA in France concluded that MHC matching alone is insufficient to grant long-term survival of neuronal grafts in an excitotoxin-lesion model of HD in Non-Human Primates (NHP). In their NHP model of Huntington's disease, in the absence of immunosuppression, haplotype-matching was insufficient to grant long-term survival of neuronal grafts and appeared to trigger a delayed/attenuated immune response in the host. In conclusion, as a result of these findings, it is clear that alternative strategies allowing cell therapies to escape altogether the host cell-mediated immune response or a combination of MHC-matching and peripheral immunosuppression should be further investigated in NHPs to allow stem cell therapy to achieve its full therapeutic potential.

Synopsis:

Cell therapy products (CTP) derived from pluripotent stem cells (iPSCs) may constitute a renewable, specifically differentiated source of cells to potentially cure patients with neurodegenerative disorders. However, the immunogenicity of CTP remains a major issue for therapeutic approaches based on transplantation of non-autologous stem cell-derived neural grafts. Despite its considerable side-effects, long-term immunosuppression, appears indispensable to mitigate neuro-inflammation and prevent rejection of allogeneic CTP. Matching iPSC donors' and patients' HLA haplotypes has been proposed as a way to access CTP with enhanced immunological compatibility, ultimately reducing the need for immunosuppression. In the present work, we challenge this paradigm by grafting autologous, MHC-matched and mis-matched neuronal grafts in a primate model of Huntington's disease. Unlike previous reports in unlesioned hosts, we show that in the absence of immunosuppression MHC matching alone is insufficient to grant long-term survival of neuronal grafts in the lesioned brain.

Authors:

Romina Aron Badin Aurore Bugi, Susannah Williams, Marta Vadori, Marie Michael, Caroline Jan, Alberto Nassi, Sophie Lecourtois, Antoine Blancher, Emanuele Cozzi, Philippe Hantraye & Anselme L. Perrier Emmet McCormack & Sonia Laín. **DOI:** 10.1038/s41467-019-12324-0

REPORT

EDUCATIONAL SESSION BIO CONVENTION USA

Novel approaches to improve reproducibility in
academia-industry research collaborations

from Florence Bietrix,
Head of Operations at EATRIS

EATRIS organised an educational session at BIO International Conference 2019 in Philadelphia, USA, bringing together outstanding scientists who play important roles in reproducibility and data quality control initiatives.

Dr. Florence Bietrix, Head of Operations at EATRIS moderated the session. She introduced the session illustrating the alarmingly high irreproducibility rate observed in biological science and the financial and societal consequences of this.

Dr. Leonard Freedman, Chief Scientific Officer at Frederick National Laboratory for Cancer Research (Frederick, USA), pointed out that the development and implementation of quality systems in biomedical research would mitigate at least some of the causes of irreproducibility. Characterisation and quality control of biological research “tools” such as cell lines and antibodies are an important aspect of standardisation and transparency across research laboratories.

Dr. Nathan Coussens previously working at the National Center for the Advancement of Translational Science (NCATS, Bethesda, USA), highlighted the fact that guidelines are essential to harmonise experiments and reporting. An example of the effort put in place at NCATS is the NCATS Assay Guidance Manual, free-of-charge, for high content screening experiments (Assay Guidance Manual, <https://ncats.nih.gov/expertise/preclinical/agm>). A second example provided by Nathan is the ring testing initiative for HTS, an initiative to understand better drivers of reproducibility in HTS through proficiency testing.

Prof. Marian Hajdúch, Director of the Institute of Molecular and Translational Medicine (IMTM) in Olomouc, Czech Republic, stressed that the authentication of cell lines in individual laboratories is crucial for the validity and transferability of research findings. Methods such as detection of protein variant using the tool CLAIRE (<https://claire.imtm.cz>), can help reveal mislabelled or contaminated cell lines.

Dr. Weida Tong from the US Food and Drug Administration (FDA), Little Rock, USA, emphasised the importance of large-scale consortia such as the FDA-driven Sequencing Quality Control consortium to assess the technical performance of genomic technologies (microarrays, GWAS and NGS) in clinic and safety evaluation. Dr. Weida concluded the session expanding on the concept of reproducibility and its relation to traceability, transferability and generalisability of research findings.



Dr. Florence Bietrix
Head of Operations at EATRIS

Publication from our nodes

A NEW EFFORT OF THE INNOVATIVE MEDICINES INITIATIVE-CANCER-ID CONSORTIUM IN THE DEVELOPMENT OF BEST PRACTICE RECOMMENDATIONS FOR LIQUID BIOPSY ASSAYS

MULTICENTER EVALUATION OF CIRCULATING CELL-FREE DNA EXTRACTION AND DOWNSTREAM ANALYSES FOR THE DEVELOPMENT OF STANDARDIZED (PRE)ANALYTICAL WORKFLOWS

Key messages:

Clinical utility of cell-free circulating tumour DNA (ccfDNA) as cancer biomarkers has attracted increasing interest to improve cancer detection, as it reflects molecular characteristics of tumour tissues and it is easy accessible. However, the integration of ccfDNA analysis into clinical practice faces a series of challenges and requires standardisation to guarantee reliable and robust results. In this study, Lampignano et al. report findings highly relevant for the development of standard operating procedures and validation of tests for the use of ccfDNA assays in clinical practice.

Synopsis:

BACKGROUND: In cancer patients, circulating cell-free DNA (ccfDNA) can contain tumor-derived DNA (ctDNA), which enables noninvasive diagnosis, real-time monitoring, and treatment susceptibility testing. However, ctDNA fractions are highly variable, which challenges downstream applications. Therefore, established preanalytical work flows in combination with cost-efficient and reproducible reference materials for ccfDNA analyses are crucial for analytical validity and subsequently for clinical decision-making.

METHODS: We describe the efforts of the Innovative Medicines Initiative consortium CANCER-ID (<http://www.cancer-id.eu>) for comparing different technologies for ccfDNA purification, quantification, and characterisation in a multicenter setting. To this end, in-house generated mononucleosomal DNA (mnDNA) from lung cancer cell lines carrying known TP53 mutations was spiked in pools of plasma from healthy donors generated from 2 different blood collection tubes (BCTs). ccfDNA extraction was performed at 15 partner sites according to their respective routine practice. Downstream analysis of ccfDNA with respect to recovery, integrity, and mutation analysis was performed centralised at 4 different sites.

RESULTS: We demonstrate suitability of mnDNA as a surrogate for ccfDNA as a process quality control from nucleic acid extraction to mutation detection. Although automated extraction protocols and quantitative PCR-based quantification methods yielded the most consistent and precise results, some kits preferentially recovered spiked mnDNA over endogenous ccfDNA. Mutated TP53 fragments derived from mnDNA were consistently detected using both next-generation sequencing-based deep sequencing and droplet digital PCR independently of BCT.

CONCLUSIONS: This comprehensive multicenter comparison of ccfDNA preanalytical and analytical work flows is an important contribution to establishing evidence-based guidelines for clinically feasible (pre)analytical work flows.

Authors:

Rita Lampignano, Martin H.D. Neumann, Sabrina Weber, Vera Kloten, Andrei Herdean, Thorsten Voss, Daniel Groelz, Anna Babayan, Marco Tibbesma, Martin Schlumpberger, Francesca Chemi, Dominic G. Rothwell, Harriet Wikman, Jean-Pierre Galizzi, Inger Riise Bergheim, Hege Russnes, Benedetta Mussolin, Serena Bonin, Christine Voigt, Hanny Musa, Pamela Pinzani, Evi Lianidou, Ged Brady, Michael R. Speicher, Klaus Pantel, Fay Betsou, Ed Schuurin, Mikael Kubista, Wim Ammerlaan, Markus Sprenger-Haussels, Thomas Schlange, and Ellen Heitzer for the Innovative Medicines Initiative CANCER-ID Consortium, Clinical Chemistry.

DOI: 10.1373/clinchem.2019.306837

Publication from our nodes

LIQUID BIOPSY FOR BREAST CANCER: A NON-INVASIVE BIOMARKER TO PREDICT THE NEOADJUVANT TREATMENT RESPONSE

PLASMA miRNA LEVELS FOR PREDICTING THERAPEUTIC RESPONSE TO NEOADJUVANT TREATMENT IN HER2-POSITIVE BREAST CANCER: RESULTS FROM THE NEOALTTO TRIAL

Key Messages:

In this study, coordinated by Istituto Nazionale dei Tumori di Milano, a test based on circulating-microRNAs has been developed as promising strategy for predicting response to single/dual HER2-targeted therapy. By profiling plasma prospectively collected from the NeoALTTO study, 4 ct-miRNA signatures associated with pathologic complete response were defined, specifically at baseline and after 2 weeks of treatment with lapatinib, and after 2 weeks of treatment with trastuzumab±lapatinib. This innovative approach is, so far, the largest retrospective study to report the predictive value of ct-miRNAs in patients with HER2 -overexpressing breast cancer treated with neoadjuvant treatment. This study is a step forward in the context of personalised medicine and opens the possibility of offering a tailored therapy to the right patient.

Synopsis:

PURPOSE: To investigate the potential of circulating-miRNAs (ct-miRNA) as non-invasive biomarkers to predict the efficacy of single/dual HER2-targeted therapy in the NeoALTTO study. **EXPERIMENTAL DESIGN:** Patients with plasma samples at baseline (T0) and/or after 2 weeks (T1) of treatment were randomised into training (n = 183) and testing (n = 246) sets. RT-PCR-based high-throughput miRNA profiling was employed in the training set. After normalization, ct-miRNAs associated with pathologic complete response (pCR) were identified by univariate analysis. Multivariate logistic regression models were implemented to generate treatment-specific signatures at T0 and T1, which were evaluated by RT-PCR in the testing set. Event-free survival (EFS) according to ct-miRNA signatures was estimated by Kaplan-Meier method and Cox regression model.

RESULTS: In the training set, starting from 51 ct-miRNAs associated with pCR, six signatures with statistically significant predictive capability in terms of area under the ROC curve (AUC) were identified. Four signatures were confirmed in the testing set: lapatinib at T0 and T1 [AUC 0.86; 95% confidence interval (CI), 0.73-0.98 and 0.71 (0.55-0.86)], respectively; trastuzumab at T1 (0.81; 0.70-0.92); lapatinib + trastuzumab at T1 (0.67; 0.51-0.83). These signatures were confirmed predictive after adjusting for known variables, including estrogen receptor status. ct-miRNA signatures failed to correlate with EFS. However, the levels of ct-miR-140-5p, included in the trastuzumab signature, were associated with EFS (HR 0.43; 95% CI, 0.22-0.84).

CONCLUSIONS: ct-miRNAs discriminate patients with and without pCR after neoadjuvant lapatinib- and/or trastuzumab-based therapy. ct-miRNAs at week two could be valuable to identify patients responsive to trastuzumab, to avoid unnecessary combination with other anti-HER2 agents, and finally to assist deescalating treatment strategies.

Authors:

Di Cosimo S, Appierto V, Pizzamiglio S, Tiberio P, Iorio MV, Hilbers F, de Azambuja E, de la Peña L, Izquierdo M, Huober J, Baselga J, Piccart M, de Braud FG, Apolone G, Verderio P, Daidone MG.,
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PRODUCT PLATFORM HIGHLIGHTS 2019

EATRIS product platforms have intensified their activities, not only due to the incorporation of new members that are reinforcing the already strong capacities of our community, but also because novel projects have emerged through cross pollinating ideas and discussions.

The wide range services of EATRIS Platforms portfolio will be further energised by new goals and perspectives. Platform chairs are actively involved in a process of analysis and dialogue that will yield in an updated platform model.

ATMP

Chairs

Maria Cristina Galli (ISS, Italy), Miguel Chillón Rodríguez (VHIR, Spain)

Platform Coordinator

David Morrow (Programme Manager EATRIS C&S)

2019 started with EATRIS presenting its capacities in cell tracking for immune cells in solid tumours at the Phacilitate conference in Miami, FL, USA. As part of the same initiative, EATRIS organised a workshop on this topic at the Advanced Therapies and Regenerative Medicines Congress in London in May which included Dr. Mangala Srinivas from Radboudumc and regulatory consulting firm Asphalion.

In addition, EATRIS held a panel discussion on the need for cell tracking in ATMP development. This panel was chaired by Dr. Seppo Ylä-Herttuala from the University of Eastern Finland and Dr. Srinivas. EATRIS was also part of the scientific Advisory Board for this conference, a role which continues into 2020. The feedback from both initiatives contributed to an EATRIS authored publication in July in Cell and Gene therapy bioinsights, titled "Broadly-applicable imaging

platforms are necessary for optimising cell therapies in solid tumours".

In 2019, EATRIS also became a supporter of the RESTORE project, presenting two posters at their November meeting in Berlin, Germany. RESTORE involves multiple EATRIS institutions and aims at a future that makes advanced therapies accessible, affordable and the standard of care for many currently incurable diseases.

In October 2019, EATRIS was invited to present at the BIOMEDICA conference in Limburg, The Netherlands to discuss our infrastructure's capacities in regenerative medicine with over 200 participants from SMEs in Europe working in this space.

In November, David Morrow attended the FEAM conference of regenerative medicine in Brussels, Belgium, where Dr. Graziella Pellegrini (Centro Medicina Rigenerativa (CMR)) presented her research on regenerative medicine. During 2019, EATRIS contributed to multiple applications in the ATMP space offering grant support through proposal review, partner finding and in several cases joining as a full partner. The Instituto de Medicina Molecular João Lobo Antunes from Portugal joined the ATMP Platform.

BIOMARKERS

Chairs Alain van Gool (Radboudumc, The Netherlands), Andreas Scherer (FIMM, Finland), Laura García Bermejo (IRYCIS, Spain)

Platform Coordinator Florence Bietrix * (Programme Manager EATRIS C&S)

In 2019, with the welcoming of the Portugal into the EATRIS Research Infrastructure, seven Portuguese institutions joined the biomarker platform, namely, the Association for Innovation and Biomedical Research on Light and Image (AIBILI), the center for Neuroscience and Cell Biology (Coimbra University)/Coimbra University Hospital, the Champalimaud Foundation, the Institute of Biomedicine (IBIMED), the Instituto de Investigacao e Inovacao em Saude (i3S), Instituto Português de Oncologia do Porto Francisco Gentil (IPO-Porto) and the Life and Health Sciences Research Institute/Clinical Academic Centre in Braga. In addition to the Portuguese institutions, additional capacities were brought to the table with the participation of the University of Bergen (UiB) and Haukeland University Hospital in Norway, the Malaga Health Research Institute (Spain) and the KTH Royal Institute of Technology and Lund University in Sweden. Sixty-two institutions are now members of the biomarker platform. The discussions initiated during the Annual Meeting 2018 in December in Ljubljana, Slovenia around “Multi-modal approaches for patient stratification” further materialised in 2019 towards the positioning of EATRIS as a Research Infrastructure enabling personalised medicine development. In this context, the concept of a multi-omic toolbox to support cross-omic analysis and data integration in clinical samples was further elaborated with the support of the biomarker chairs. Developing such a toolbox is at the heart of EATRIS-Plus. The toolbox will be developed and tested with a real-setting demonstrator, an already established cohort of 1,000 healthy individuals in Czech Republic and will contain:

- Consensus-based SOPs for omic technologies;
- Guidelines for omic analytical processes;
- Validated reference materials for analytical processes;
- Quality parameters for benchmarking quality assessment activities;
- Data analytical and FAIRification tools;
- Criteria for establishing reference values in population cohorts;
- Troubleshooting guidelines;
- Access to a repository of multi-omic reference values

A second area of focus for the biomarker platform in 2019 has been around the concept of a biomarker factory to discover and validate biomarkers dedicated to optimising paediatric patient management. This concept highlights the need for an integrated biomarker development infrastructure dedicated to this population with shared technologies, shared knowledge and shared objectives operating under good biomarker development practice to facilitate and accelerate:

1. The development of new drugs targeted at paediatric diseases;
2. The selection of appropriate dosages of already marketed drugs to prevent adverse events or secondary side effects in later stages of development;
3. Allow early diagnosis of paediatric-onset of diseases typical of adult populations.

A highlight for the Biomarker platform was the co-hosting of the 2nd conference on validation of biomarkers, on March 28, Basel, Switzerland. The event, organised in conjunction with the CliniMARK project (COST action) and Peter Groenen, Head of Translational Sciences at Idorsia, received significant attention. With keynote lecturer Joseph Menetski, Director of the Biomarkers Consortium at the Foundation for the National Institutes of Health, USA and additional speakers with various backgrounds, we examined how integrated technologies can bridge the biomarker innovation gap, with an initial focus on lung diseases.

* The biomarker platform is coordinated by Emanuela Oldoni since January 2020

EATRIS WORKSHOP AT WORLD ADVANCED THERAPIES AND REGENERATIVE MEDICINE CONGRESS 2019

In the spring of 2019 EATRIS was invited to be part of the scientific advisory board for this yearly conference in London which now boasts up to two thousand attendees and over three hundred companies.

As a member of the Advisory Board a primary goal was to contribute to the scientific scope of the meeting with must-have innovative technological approaches in addition to using the opportunity to present our contribution as an infrastructure on the advances in cell and gene therapy to the wider scientific community.

On the first day, EATRIS organised a workshop on the fundamental role of cell tracking for immune cell therapy development, in particular for the treatment of solid tumours to an audience of forty-five people.

This session was introduced by EATRIS and had keynote presentations from Dr. Mangala Srinivas, an imaging agent developer and from Dr. Christopher Mann, a regulatory expert from Asphalion. This well received educational initiative on the importance of cell tracking to assess safety and biodistribution of novel cell therapies would be the basis for a bioinsights publication developed by EATRIS titled “Broadly-applicable imaging platforms are necessary for optimizing cell therapies in solid tumours” in the months that followed.

In addition, on day two we would welcome Dr Seppo Ylä-Herttuala from the University of Eastern Finland and Dr Srinivas on to the stage for a panel discussion on the same topic, again highlighting EATRIS’s commitment to this important focus area, as the cell and gene therapy field advances into solid tumor cancers with the hope of replicating the success of cell therapies in hematological cancers.

SMALL MOLECULES

Chairs Maria Salmons (Mario Negri Institution, Italy),
Alfredo Budillon (Fondazione IRCCS, Fondazione Pascal, Italy)
Platform Coordinator Martin de Kort (Programme Manager
EATRIS C&S)

In 2019, the Small Molecules platform welcomed three new affiliate members: Instituto de Medicina Molecular João Lobo Antunes (Lisbon, Portugal), Lund University (Lund, Sweden) and the SciLifeLab Drug Development and Discovery Platform with legal representation by Uppsala University and Uppsala University Hospital (Sweden). This brings the total of advanced research facilities involved in academic drug discovery now at 32 institutions. In September, Riga Stradins University (Riga, Latvia) and the Latvian Institute of Organic Synthesis, a major drug discovery centre of the Baltic region, hosted an EATRIS delegation. It has developed eighteen original and over seventy generic medicines and offers a wide range of medicinal chemistry capabilities, including a kilo-scale facility for pilot production.

The role of ESFRI in small molecule drug research is gaining impetus by further alignment of ERICs such as EU-OPENSCREEN and INSTRUCT. With these two organisations the exploration of joint services in translational medicine was initiated. Preparation began for an Integrating Activity for Structural Biology to support the research community, the iNext-Discovery project that will launch early in 2020.

Quality and reproducibility remain key themes on the agenda of the Small Molecules Platform with five sites contributing to the second phase of the global ring test initiative (IMTM Olomouc, Czech Republic; CNCCS-IRBM Rome, Italy; FIMM Helsinki, Finland; NCMM Oslo, Norway; and IRCCS Pascale Naples, Italy), conclusion of which is anticipated in 2020. The concept of reproducibility and quality in drug development was further developed into an educational series of four webinars launched in November (see p68).

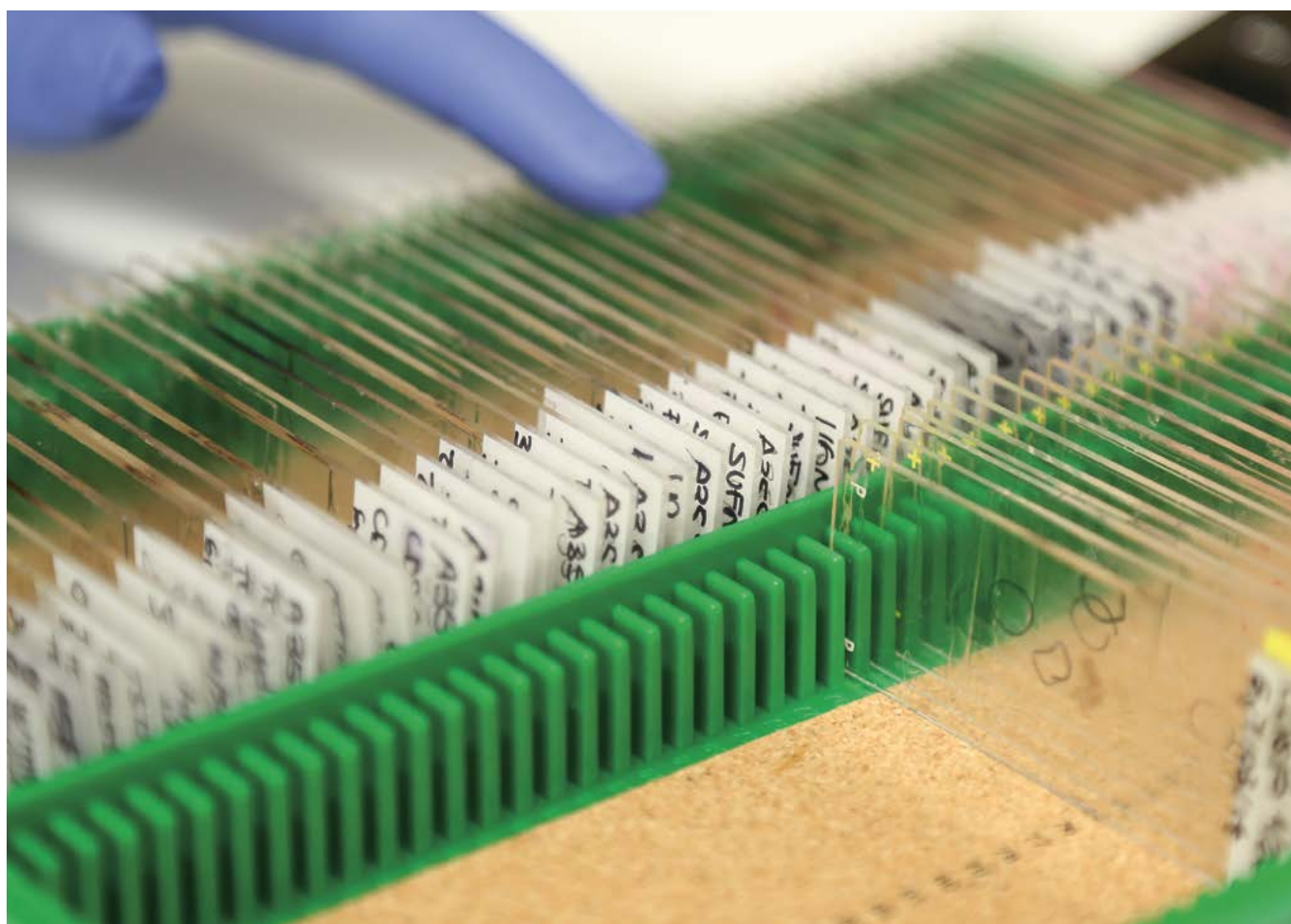
Finally, the (translational) research community was supported in their endeavours to develop international strategic initiatives, including the study of synergistic drug effects using chemoradiotherapy (led by the Mario Negri Research Institute, Milan, Italy) and innovative approaches for the sustainable exploitation of marine biologics for pharmaceutical application in collaboration with EMBRC.

IMAGING & TRACING

Chairs Cyril Poupon (CEA / NeuroSpin, France),
Albert Windhorst (VUmc, The Netherlands)
Platform Coordinator Martin de Kort (Programme Manager
EATRIS C&S)

The Imaging and Tracing Platform welcomed the first Faculty of Medicine of Charles University in Prague (Czech Republic), the University of Tromsø (UiT) and University Hospital North Norway (Norway) as new members to the Platform. In addition, 2019 marked the delivery of two major local and regional infrastructure development projects. The opening ceremonies at core facilities were attended by EATRIS. On October 15, the Comparative Medicine and Bioimage Centre of Catalonia (CMCiB), part of the Germans Trias i Pujol Research Institute (IGTP, Badalona, Spain), formally opened a unique new facility for research and training in Europe, with the most recent technology and custom-built facilities to support biomedical studies with preclinical models and new surgical techniques to the highest standards and full implementation of the principle of 3Rs research (reduction, refinement and replacement). On October 31, after a long work-intensive project, the Imaging Centre Amsterdam University Medical Centre was formally opened as Europe's largest translational imaging capacity facility in a single site. It aims to improve patient care along with diagnostics and medicines development.

In September, EATRIS gave a scientific contribution in Cambridge (UK) to the European Association of Cancer Research (EACR) community, outlining how translational molecular imaging can be used for nanomedicine development using case studies from EATRIS members, while attracting a biotech company client. In 2019, the GSK Immuno-Inflammation Imaging Hub saw the execution of its first two clinical studies and it continued to develop its project portfolio under the longstanding framework while hosting two virtual and two face to face steering committee meetings. Finally, the RECOGNISED consortium, with participation of five EATRIS institutions, prepared to kickstart its activities in 2020. This new project will broaden the expertise of the imaging platform by integrating various imaging techniques of the eye and the brain with multi-omic data to develop early diagnostic methods for cognitive decline in patients suffering from Type 2 diabetes and diabetic retinopathy.



VACCINES

Chairs Jan Langermans (BPRC, The Netherlands),
Lucia Gabriele (ISS, Italy)

Platform Coordinator David Morrow (Programme Manager
EATRIS C&S)

The Vaccine Platform's central tasks in 2019 centred around developing initiatives to benefit the vaccine researcher in the EU through the ongoing TRANSVAC project, which secured funding to continue for the year. This included finalising the regulatory database for vaccines and the development of a 2-day regulatory training course for vaccine development for up to 40 participants which was initially planned for June 2020. This course will be taught by several EATRIS experts across our network.

Progress was made on the restructuring of the vaccine platform to focus further on immunomodulation and immunomonitoring with the development of a strategy document developed by EATRIS C&S and the Chairs of the Platform. This document was shared with the Platform members for feedback with a view to moving to the next stages of development in early 2020. EATRIS C&S contributed to two submitted Horizon 2020 vaccine proposals in development by offering innovation management and regulatory support to these proposals. The end of 2019 saw the early stage of the COVID-19 pandemic develop in China. Early initiatives such as developing an inventory of COVID-19 resources began to take shape.

The EATRIS Vaccine Platform welcomed three new institutions in 2019, namely the University of Bergen (UiB) and Haukeland University Hospital from Norway and the Instituto de Medicina Molecular João Lobo Antunes from Portugal.



EC FUNDED PROJECTS: SEVEN NEW PROJECTS APPROVED

EATRIS-Plus NEW

Flagship Project In Personalised Medicine



Funding programme: H2020 (Research Infrastructures)

Total budget: € 4,900,000

Budget EATRIS: € 787,125

Coordinator: EATRIS

Website: <https://www.eatris.eu/projects/eatris-plus>

Starting - end date: January 1, 2020 – December 2023 (48 months)

EATRIS participating institutions: 13 EATRIS national nodes, 1 EATRIS institution

Project description: Our flagship project EATRIS-Plus aims to build further capabilities and deliver innovative scientific tools to support the long-term sustainability of EATRIS as one of Europe's key European research infrastructures for Personalised Medicine. The main goals of the EATRIS-Plus are: to consolidate EATRIS capacities in the field of Personalised Medicine; to drive patient empowerment; to expand strategic partnerships with research infrastructures and other relevant stakeholders; and to further strengthen the long-term sustainability of the EATRIS financial model. The project has nineteen partners (including EATRIS) from thirteen countries, and is divided into ten work packages. EATRIS is the coordinating partner and the lead for five of the work packages (Long Term Sustainability Planning, Industry Collaboration and Open Innovation Models, International Collaboration, Coordination and Management, and the Ethics Requirements).

The consortium ambition is to deliver a multi-omic toolbox to support cross-omic analysis and data integration in clinical samples.

By providing such a toolbox to the research community, EATRIS-Plus will be the engine to enable high-quality research in the context of patient stratification and to accelerate the implementation of personalised medicine solutions.

ADVANCE NEW

**Educating the Next Generation Of
ATMP Professionals**



Funding programme: Erasmus+

Total budget: € 374,927

Budget EATRIS: € 87,336

Coordinator: EATRIS

Website: <https://eatris.eu/projects/advance>

Starting - end date: November 1 2019 – April 30th 2022 (30 months)

EATRIS participating institutions: ISS (IT), University of Ljubljana (SI)

Project description: ADVANCE is a thirty-month EU training project, supported by Erasmus+ programme. Its objective is to develop a three-stage blended learning programme to support early-career biomedical scientists in developing currently missing scientific knowledge, transversal skills and competencies to meet the key challenge areas in the ATMP development cycle.

The core target group for the three-stage blended learning programme are the "next generation of ATMP developers" – i.e. early-career biomedical academics (PhDs, Postdocs), including doctors in training, clinician-scientists and SME-based professionals, who are considered to be an important component of the labour market and the critical intermediaries of the ATMP development pipeline.

The project will generate five intellectual outputs: Online Curriculum, Webinars, Workshop, Open Badges, and Sustainability plan.

The consortium consists of six partners besides EATRIS: Elevate Health (The Netherlands), Istituto Superiore di Sanita (Italy), KU Leuven (Belgium), ULB/I3Health (Belgium), University of Ljubljana (Slovenia), Takis Biotech (Italy).

EU-PEARL NEW

EU Patient-centric clinical trial Platforms



Funding programme: IMI-2

Total budget: € 26,238,048

Budget EATRIS: € 743,625

Project Leader: Janssen Pharmaceutica NV

Coordinator: VHIR (ES)

Website: <https://www.eu-pearl.eu>

Starting - end date: November 2019 – April 2023
(42 months)

Project description: The EU-PEARL project intends to develop new methods, tools and frameworks to create a novel enabling infrastructure for conducting patient-centric platform trials through an integrated system where pharmaceutical companies, non-profit product developers and healthcare providers work together.

A platform trial is a clinical trial with a single master protocol in which multiple treatments are evaluated simultaneously. Adaptive platform designs offer flexible features such as removing a treatment group for futility or adding new groups and treatments to be tested during the course of the trial. EU-PEARL intends to shape future clinical trials, making them more patient friendly by seeking patient input in trial design and therefore resulting in more patient focused outcomes. The project will develop operations ready platforms in four diseases areas: Major Depressive Disorder, Tuberculosis, Non-Alcoholic Steatohepatitis and Neurofibromatosis. In addition to these four disease areas, EU-PEARL will provide the framework for designing and executing Integrated Research Platforms (IRPs) in other disease areas as well.

The consortium consists of 36 world-leading institutions among European university hospitals, research centres, patient groups, non-profit product developers and pharmaceutical companies. The Project Leader is Janssen

Pharmaceutica NV, the Project Coordinator is Fundacio Hospital Universitari Vall D'Hebron. EATRIS is one of the initiating partners in the project, responsible for defining a future sustainability path as part of their role as Co-Coordinator for the project.

The EU-PEARL kick off meeting took place end of November 2019 in Barcelona, Spain.

INEXT-DISCOVERY NEW

Infrastructure for transnational access in structural biology and translational research



Funding programme: H2020 (Research Infrastructures)

Total budget: € 9,987,757

Budget EATRIS: € 19,375

Coordinator: Dutch Cancer Institute (NKI) – Antoni van Leeuwenhoek Hospital Amsterdam

Website: <https://www.inext-eu.org/>

Starting - end date: February 1, 2020 – January 2024
(48 months)

EATRIS role: Partner (outreach and valorisation)

Project description: iNEXt-Discovery brings together a strong network of leading structural biology facilities in partnership with regional experts and ESFRI communities in medicinal chemistry, translational medicine, biological imaging, and food research, to disseminate knowledge and services. It aims to stimulate the wider uptake of structural biology across Europe, across scientific disciplines and research sectors.

The project has 26 participants (including EATRIS) from 14 countries and is divided into 29 work packages. EATRIS will provide awareness to the structural biology community towards translational medicine and will organise together with the Coordinator NKI a workshop addressing the early development of novel therapeutics and diagnostics, with a keen focus on new drug development tools, starting SMEs, innovation management, and regulatory topics.

PERMIT NEW

Methodological Standards for Personalised Medicine



Funding programme: H2020

Total budget: € 2,000,000

Budget EATRIS: € 161,250

Coordinator: ECRIN-ERIC

Website: <https://permit-eu.org/>

Starting - end date: January 2020 – December 2021
(24 months)

EATRIS participating institutions:

University of Bergen (NO)

EATRIS role: Leader of WP5 on “Translational development of patient-stratification processes”

Project description: H2020-funded PERMIT will develop recommendations for robust and reproducible personalised medicine research. The objective of PERMIT is to establish, with all relevant stakeholders and invited experts, recommendations ensuring the robustness of personalised medicine trials, which also requires validation of the stratification methods. EATRIS-ERIC participates as leader of WP5 due to its expertise in translational research, in collaboration with the University of Bergen, a member of the EATRIS community.

ENRIITC NEW

A Pan-European Network to accelerate the translation of Open Science into Open Innovation



Funding programme: H2020 (Research Infrastructures)

Total budget: € 1,499,823.75

Budget EATRIS: € 185,312.50

Coordinator: European Spallation Source ERIC (ESS)

Website: <https://www.enriitc.eu>

Starting - end date: January 2020 – December 2022

EATRIS role: Leader of WP5 Communications

Project description: Research infrastructures (RIs) operate in complex innovation ecosystems where industry plays an increasingly important role. Pan-EU initiatives, such as the Innovation Union or the ESFRI, revolutionise the way public and private sector organisations work together, and help to create the structural frameworks which are needed to foster such collaborations. While initiatives of this type play a crucial role in enabling industry to partner with RIs (whether as a user, a supplier, or a co-creator), they do not fully utilise or engage Industrial Liaison and Contact Officers (ILOs/ICOs) which could have a central role in boosting the RI-industry partnerships. To address this gap, ENRIITC will build a permanent pan-European network of ILOs and ICOs. This will be done in a community-driven, cross-functional, cross-sectoral, multiplier-based way which will be inclusive and enable all interested parties to actively participate.

ENRIITC aims to establish a sustainable European network of ILOs and ICOs which enables mutual learning, map collaboration potential between RIs and industry, develop and refine strategies and best practices to foster these collaborations, raise awareness among industry for collaboration opportunities at research infrastructures, and demonstrate impact.

RECOGNISED NEW

Retinal and cognitive dysfunction in type 2 diabetes: unravelling the common pathways and identification of patients at risk of dementia.



Funding programme: H2020

Total budget: € 5,998,273

Budget EATRIS: € 104,000

Coordinator: VHIR (ES)

Starting - end date: January 1, 2020 – December 31, 2023 (48 months)

EATRIS role: Lead Beneficiary WP8 (Dissemination and Exploitation)

Project description: The four-year long RECOGNISED project will study the biological mechanisms that cause structural and functional alterations in the retina in people with type 2 diabetes at risk of developing cognitive impairment and dementia. Based around the concept of the eye being a “window to the brain”, RECOGNISED will determine whether evaluating the retina, easily accessible with current non-invasive technologies, could help in identifying earlier cognitive impairment in people with T2D, so that appropriate support can be given.

The project has twenty-one participants (including EATRIS) from eight countries and is divided into eight Work Packages. The role of EATRIS in the RECOGNISED project is to lead the Dissemination and Exploitation Board and develop the Innovation Management Plan to help guide the effective dissemination and exploitation of RECOGNISED project results.

EJP-RARE DISEASES UPDATE

European Joint Programme on Rare Diseases



Funding programme: H2020

Total budget: € 55,073,831

Budget EATRIS: € 376,678

Coordinator: INSERM (FR)

Website: <https://www.ejprarediseases.org/>

Starting - end date: January 2019 – December 2023 (60 months)

EATRIS role: Co-leader of Pillar IV “Accelerating Translation”; Co-leader of WP19 “Facilitate partnerships and accelerate translation” and WP3 “Sustainability”

EATRIS participating institutions: VHIR (ES), University of Oslo (NO)

Project description: The European Joint Programme on Rare Diseases (EJP RD) has two major objectives: (1) To improve the integration, the efficacy, the production and the social impact of research on Rare Diseases (RD) through the development, demonstration and promotion of European/world-wide sharing of research and clinical data, materials, processes, knowledge and know-how; (ii) To implement and further develop an efficient model of financial support for all types of research on RD (fundamental, clinical, epidemiological, social, economic, health service) coupled with accelerated exploitation of research results for the benefit of patients.

To this end the EJP RD actions are organised into four pillars assisted by the central coordination: (P1) Funding of research; (P2) Coordinated access to data and services; (P3) Capacity building; (P4) Accelerated translation of research projects and improved outcomes of clinical studies.

Within P4 EATRIS has begun developing materials for an Innovation Management Toolbox to provide resources to all RD researchers, assessing the translational potential of research projects and has established a real-time mentoring service for RD researchers. EATRIS has developed guidelines and information on sustainability and has begun assessment of sustainable elements within the project with a view to developing a sustainability roadmap.

EOSC-LIFE UPDATE

An open collaborative digital space for life science



Funding programme: H2020 (Research Infrastructures)

Total budget: € 23,745,978.25

Budget EATRIS: € 1,734,523.75

Coordinator: ELIXIR

Website: <https://www.eosc-life.eu/>

Starting - end date: March 2019 – February 2023

EATRIS participating institutions: University of Helsinki (FI), IMTM (CZ), Lygature (NL), VHIR (ES), Mario Negri Institute (IT)

EATRIS role: WP3 co-lead “Open Call on Sensitive Data”; co-lead WP8 “International Impact”, “Innovation and Sustainability”; co-lead WP9 “Training of the EOSC Life Community”, Partner WP10 “Dissemination and Outreach”

Project description: EOSC-Life is the project regrouping the 13 LS RIs in Europe into the European Open Science Cloud (EOSC) and joining forces to create an open collaborative digital space for life science.

During the past year (first year of the project), EATRIS C&S worked closely with the EATRIS data core team formed by five EATRIS linked third parties under the EOSC-life project: University of Helsinki (Finland), IMTM (Czech Republic), Lygature (The Netherlands), VHIR (Spain), and Mario Negri Institute (Italy). Initial efforts were centred around enabling the FAIRification of drug sensitivity screening through the development of MICHA (Minimal Information about Chemosensitivity Assays). A second area of effort was around the management of multi-modal sensitive data. Recommendations and guidelines are under development under WP4 (Policies, specifications and tools for the management of data for biological and medical research). The aim is to inform WP2 (Make tools and workflows interoperable and reusable) on the specific needs for data pipelines and workflows coming from the clinical and translational research community working with sensitive/ clinical data.

Further actions were undertaken by Rebecca Ludwig to better understand the education and training needs of the thirteen RIs participating in the project towards computational tools and cloud technologies. Together with Florence Bietrix and Anton Ussi, Rebecca participated in the EOSC-Life retreat organised on October 30th and 31st in Chicheley Hall, UK.

ERIC-FORUM UPDATE



Funding programme: H2020 (Research Infrastructures)

Total budget: € 1.495.281,25

Budget EATRIS: € 77.916

Coordinator: European Spallation Source ERIC (ESS)

Website: <https://www.eric-forum.eu>

Starting - end date: January 2019 – December 2022

EATRIS role: Leader of WP3 “Operations, Administration, Finance, Human Resources of ERICs”.

Project description: In January 2019, 23 ERICs from 11 countries with national nodes in all European Member States, met in Amsterdam to launch the ERIC- Forum project. For its first year of implementation, the main focus of project activities was the development of a governance model for the ERIC Forum to be effective as of 2020. EATRIS contributed to the design of the model by participating in the Governance Task Force. As leader of the work package dedicated to Operations, Administration, Finance and Human Resources, EATRIS also kicked off with the dissemination of several surveys aimed to identify remaining challenges for ERICs in those areas and help the Forum provide the right support for current and future ERICs.

RI-VIS UPDATE

Increasing the visibility of the European Research Infrastructures



Funding programme: H2020 (Research Infrastructures)

Total budget: € 1.500.000

Budget EATRIS: € 24.625

Coordinator: INSTRUCT-ERIC

Website: <https://ri-vis.eu/network/rivis/home>

Starting - end date: February 2019 – July 2022

EATRIS role: Participant in all work packages

Project description: RI-VIS aims to increase the visibility of European RIs to new communities in Europe and beyond by mapping RI services to new target communities and identifying routes to maximise the exchange of information and bases for new partnerships. During 2019 two workshops took place. The first was hosted in Faro, Portugal on June 12-13, and the second on October 1-2 in Paris, France. These workshops aimed to gather the information needed to create a database of common operating procedures and obstacles that RIs face in communicating their activities, as well as collating resources for researchers. This information provides the foundation for the development of a universal communications toolkit, an easy and useful set of tools, guidelines and resources that European research infrastructures may integrate into their communication activities. The common use of this toolkit is expected to harmonise the communication of research infrastructures in Europe, increasing visibility and stakeholder perception, and contribute to consolidating the concept of “research infrastructures”.

Project description: The ID-EPTRI project, coordinated by CVBF and funded within the H2020-INFRADEV-01-2017 programme, aims to create the framework for a new Research Infrastructure (RI) intended to enhance technology-driven paediatric research in drug discovery and early development phases to be translated into clinical research and paediatric use of medicines.

EPTRI has been envisaged to be a complementary RI in the context of the existing RIs covering the current gaps in paediatric medicines. The new RI will represent a “paediatric common service” with three already established Research Infrastructures (BBMRI, EATRIS, ECRIN) to harness efficiency and delivery of paediatric research activities and services strengthening collaboration within the scientific paediatric community.

The final result of the project is the Conceptual Design Report to realise EPTRI, the European Paediatric Translational Research Infrastructure, describing the scientific and technical requirements as well as the key components of the proposed new RI.

TRANSVAC-2 UPDATE



Funding programme: H2020 (Research Infrastructures)

Total budget: € 10,600,000

Budget EATRIS: € 211,831

Coordinator: European Vaccine Initiative (EVI)

Website: <http://www.euvaccine.eu/portfolio/project-index/transvac2>

Starting - end date: May 2017 - April 2022

EATRIS participating institutions: Masaryk University (CZ), ISS (IT)

EATRIS role: WP16 Leader – Regulatory support; WP18 – Participant – Training: responsible for the development of two regulatory workshops.

Project description: 2019 marked the third year of the TRANSVAC-2 project, where EATRIS completed three of its proposed deliverables. Firstly the regulatory database for vaccines was completed and this fully developed resource went live, initially available to all partners and to collaborators who requested access. This is now available to all EATRIS institutions.

ID-EPTRI UPDATE



Funding programme: H2020 (Research Infrastructures)

Total budget: € 3.000.000

Budget EATRIS: € 200,000

Coordinator: CBVF (IT)

Website: <https://eptri.eu/>

Starting - end date: January 2018 – April 2020

EATRIS Role: WP2 Leader “Governance and Sustainability”

Two additional resources were developed, which included a document on the regulatory challenges and bottlenecks in vaccine development and a term of reference for, and composition of consultancy expert panel designed for vaccine developers. Work began in autumn to finalise the WP18 2-day workshop on regulatory trainings to be coordinated by EATRIS and initially planned for June 2020. The TRANSVAC Annual Meeting was held in Lyon in June 2019, which was a great success. During this meeting, work also began on the development of a design study to create a Vaccine Research Infrastructure coordinated by EVI.

RITRAIN UPDATE



Funding programme: H2020 (Research Infrastructures)

Total budget: € 1.900.000

Budget EATRIS: € 35,000

Coordinator: BBMRI-ERIC

Website: <https://ritrain.eu/>

Starting - end date: September 2015- March 2020

EATRIS role: Partner WP2 "Definition of competencies" and WP5 "Continued professional development"

Project description: The Research Infrastructure Training Programme (Rltrain) aimed at improving and professionalising the training of managerial and leadership staff in RIs.

The tailored training comprises:

- 1) A series of webinars with experienced leaders in research infrastructures,
- 2) Staff Exchanges to access managerial and leadership expertise directly from leading RIs,
- 3) the Executive Master in Management of Research Infrastructures (EMMRI).

Six EATRIS C&S staff joined courses on financial management, international law, service provision, leadership, communications and received the Certificate of Excellence in Research Infrastructure Leadership. In 2019 EATRIS contributed to the organisation of the workshop "Building Leadership in European Research Infrastructures" in Brussels on November 20 & 21, 2019.

CORBEL UPDATE



Funding programme: H2020 (Research Infrastructures)

Total budget: € 14.837.800

Budget EATRIS: € 745.900

Coordinator: EMBL/ ELIXIR (UK)

Website: <https://www.corbel-project.eu/home.html>

Starting - end date: September 2015 - May 2020

EATRIS role: Leader WP8 - Accelerating Innovation

EATRIS participating institutions: Stichting Lygature (NL), Rizzoli Institute (IT), Netherlands Cancer Institute (NL)

Project description: The CORBEL programme, which integrates 13 LS RIs, was extended until May 2020 and EATRIS contributed throughout 2019 as task leader for the work package "Accelerating Innovation". Activities included scouting for industry partners for the CORBEL Open Call, provision of regulatory advice, preparing content and speakers for a repeat of the workshop on best practices in public-private research collaboration and preparation of a comprehensive guide to industry collaboration.



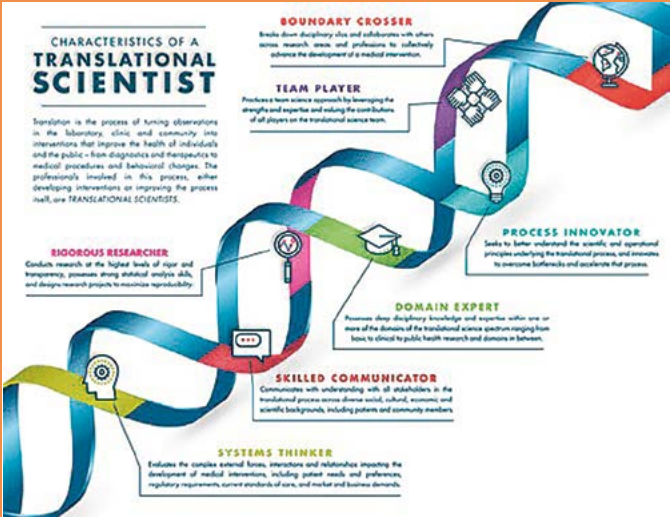
THE FUNDAMENTAL CHARACTERISTICS OF A TRANSLATIONAL SCIENTIST

Key Messages:

Translational science is focused on understanding and accelerating the process of turning health science discoveries into new medical interventions. The people working in this field are innovative and collaborative, searching for ways to break down barriers in the translation process, and ultimately to deliver more treatments to more patients more quickly. In this paper, the members of Translation Together, a global collaboration formed in 2017 (see p40) identifies seven traits of a translational scientist: boundary crosser, domain expert, team player, process innovator, skilled communicator, systems thinker and rigorous researcher.

Synopsis:

Translational science is defined as the field of investigation focused on understanding the scientific and operational principles underlying each step of the translational process. Further development of the field is advanced by describing the key desirable characteristics of individuals who seek to uncover these principles to increase the efficiency and efficacy of translation. The members of Translation Together, a newly launched international collaborative effort to advance translational innovation, present here a consensus representation of the fundamental characteristics of a translational scientist. We invite all stakeholders to contribute in the ongoing efforts to develop the field and educate the next generation of translational scientists.



Seven fundamental character traits of a translational scientist.

Authors:

C. Taylor Gilliland, Julia White, Barry Gee, Rosan Kreeftmeijer-Vegter, Florence Bietrix, Anton E. Ussi, Marian Hajduch, Petr Kocis, Nobuyoshi Chiba, Ryutaro Hirasawa, Makoto Suematsu, Justin Bryans, Stuart Newman, Matthew D. Hall, Christopher P. Austi.
DOI: 10.1021/acsptsci.9b00022

EDUCATION AND TRAINING

Education and training activities focus on providing training opportunities on the topic of translational medicine which have a high impact on researchers' daily practice and developing curricula that support the education of the next generation of translational scientists.

TRANSMED Academy - E-learning Platform powered by EATRIS

Launched in September 2019, EATRIS' very own e-learning platform was established to offer biomedical researchers a better understanding of translational research and medicines' development. TRANSMED Academy provides open access to online courses and webinars to anyone interested in learning more about hot topics in translational medicine. TRANSMED Academy is currently offering the following e-learning content:

E-LEARNING – The landscape of translational medicine

Especially for the next generation of translational scientists (PhDs, Postdocs and MDs), we have developed an online course touching upon key aspects of translational research and medicines development. Participants will learn more about target validation, predictive models, biomarkers, clinical trials, intellectual property (IP) and European regulations through a variety of learning activities including reading assignments, videos, quizzes, interactive modules and mindmaps. Learning progress of each participant is monitored and upon successful completion of all modules and the final test, a certificate can be obtained. This course requires a time investment of approximately ten hours.

'Sometimes it is difficult to find an opportunity to go deeper in fields like translational medicine. TMex helps you on that'

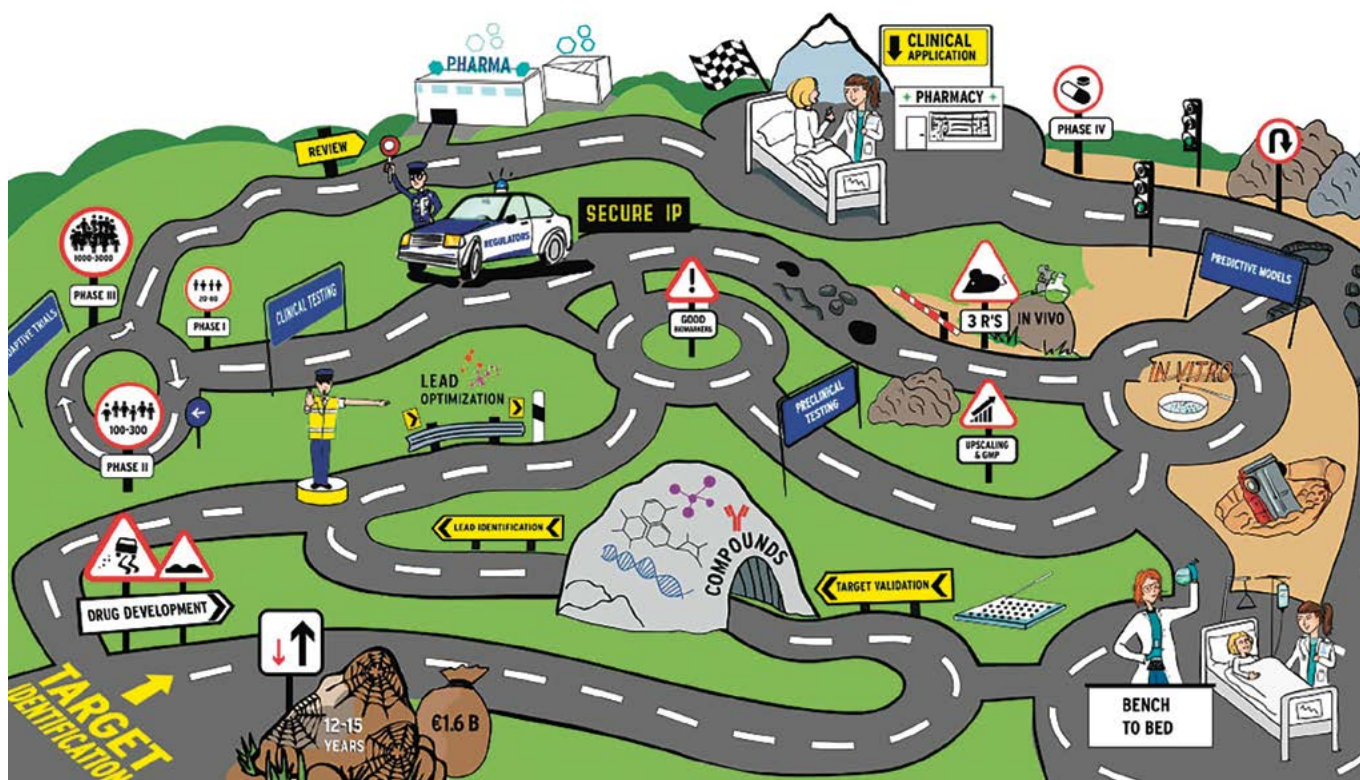
Jordi Galiano (PhD at VHIR, Spain)

EATRIS webinars

In 2019, EATRIS organised two series of webinars on translational tools and technologies. One neuroimaging series covering the usage of Ultrahigh Field MRI and other biological and technological tools to study neurodegenerative diseases was organised together with NeurATRIS. A second series was launched in the fall and looked at reproducibility issues experienced during specific phases of drug development programmes (screening, preclinical models, biomarker development & analytical platforms, clinical validation). The aim of this series was to bring best practices together and to discuss solutions designed to tackle the identified bottlenecks.

'Fantastic opportunity not only to learn about how to make research more translational to benefit patients, but also a fantastic family with people all over Europe'

Richard Crispin (Postdoc at Oslo University Hospital, Norway)



TMex Winter school on Translational Medicine

From November 11-15, 2019, twenty-seven young scientists came together at the beautiful Palau Macaya in Barcelona, Spain, for the “Translational Medicine Explained” (TMex) winter school, kindly supported by VHIR and LaCaxia Foundation. The winter school introduced the participants to the knowledge, philosophy and tools needed in translational research and medicine development, empowering them to make a difference in translational medicine. The course covered a variety of activities, including a drug discovery game, elevator pitches, students’ poster presentations, group work and lectures. Experts in the field from academia and industry addressed essential elements of the translational pipeline such as assay guidance, target validation, target product profiles, clinical trials, patient-driven research and personalised medicine.

Several innovation sessions took place, covering the business canvas model, critical success factors in the translational pathway and how to optimise the fundability of research projects. The course was held for the fourth time and had a very high recommendation rate (96%). The next edition is under preparation.

‘Thank you for the great opportunity to share my opinions with others from all over Europe and to improve my knowledge. The course itself and the evening events were so nice and everybody was so friendly. I really had a great time with you all in Barcelona.’

Natálie Kudlová (PhD at IMTM, in Olomouc, Czech Republic)

‘If you have the opportunity to take part in this course – do it. It will fundamentally change your view on how your work as a research scientist can make a difference in the real world outside your lab.’

Konstantin Kuhne (PhD at HZDR, in Dresden, Germany)

EDUCATION & TRAINING

Webinar Highlights

In vivo preclinical models for the study of neurodegenerative diseases

In this webinar Dr. Marie-Christine Birling (PHENOMIN-ICS/Celphedia) & Romina Aron Badin (MIRcen/NeurATRIS) discussed how to develop non-human primates (NHP) models for Neurodegenerative diseases and how to characterise them, using the example of the preclinical model of Tauopathy (viral overexpression) and the validation of a new gene therapy strategy for Parkinson's disease: from primate to patient (MPTP model).

Ultra high-field MR Imaging and Spectroscopy in Clinical & Translational Research

Dr. Cyril Poupon and Dr. Fawzi Boumezbeur (CEA Paris Saclay / NeuroSpin) focused on presenting the opportunities and challenges of MRI and Spectroscopy at ultra-high field and used few examples to illustrate how UHF MRI and MRS can help in better understanding the human brain in normal and pathological conditions.

The Relevance of Reproducibility for Drug Development: An Introduction

During this first webinar, Andreas Scherer (Research Coordinator/ Business development, FIMM) briefly introduced EATRIS and the EATRIS Quality Initiative, and a thorough introduction and analysis of the current reproducibility issues was given by Leonard Freedman PhD, Chief Scientific Officer at Frederick National Laboratory for Cancer Research.

Quality in Screening

This webinar focused on the need to develop standards and assays guidelines for high-throughput screening (HTS). Matthew Hall (NIH/NCATS) highlighted some initiatives such as the Assay Guidance Manual (AGM) e-book and the HTS

ring-testing project both led by NIH-NCATS to mitigate irreproducibility rates in HTS. The second part of the webinar, Dr. Wolfgang Fecke explained about EU-OPENSREEN, the infrastructure providing screening capacity in Europe and how quality is achieved across the infrastructure.

Reproducibility in preclinical and animal experimentation

Björn Gerlach (PAASP) addressed the issues of unreproducible data from *in vivo* experiments in preclinical research and pointed towards potential causes. Then the IMI project EQUIPD (European Quality in Preclinical Data) was presented as it aims to set-up a lean and fit-for-purpose quality system for preclinical research. INFRAFRONTIER, the European Research Infrastructure for the generation, phenotyping, archiving and distribution of model mammalian genomes, was represented by Michael Raess who illustrated how INFRAFRONTIER' partners across Europe work together to provide open access to a unique, standardised, high quality resource for basic and preclinical biomedical research.

Preanalytical validation and quality systems in biobanking

Monica Marchese from Integrated BioBank of Luxembourg (IBBL) addressed the importance of preanalytical quality for biomarker validation and robustness, while Andrea Wutte from BBMRI highlighted the Quality Management Service (BBMRI.QM), designed to help biobanks and researchers meet the highest quality standards for their research and the needs of their clients.

All the webinars included an audience Q&A session with the experts at the end of the session and the webinars were recorded and made available for later viewing (<https://eatris.eu/solutions/transmedacademy>).



INTERVIEW

EATRIS FLAGSHIP PROJECTS ADVANCE

Interview with Rosan Vegter and Eliis Keidong



Rosan Vegter
Education and Training manager at EATRIS*



Eliis Keidong
EU Project Manager at EATRIS

* Due to Rosan's secondment at EMA, Rosan was replaced in 2020 by Lauranne Duquenne. ADVANCE project manager is Eliis Keidong

What is/are the goals of the project?

ADVANCE is an educational project that focuses on developing new and innovative learning opportunities in the field of ATMPs. It kicked off in November 2019 and EATRIS is the coordinating partner. The project is funded by Erasmus+, lasts for thirty months and the consortium includes six partners that range from academia to a biotech and an e-learning development company.

Why is this so important?

It's important to support early career researchers in developing missing scientific knowledge, transversal skills and competencies to meet the key challenge areas existing in the ATMP development cycle.

By establishing an innovative and focused learning programme, ADVANCE aims at establishing a strategic partnership between key players from education, research and industry that contribute to innovation of ATMPs and to jointly develop curricula for early career biomedical professionals.

A blended learning programme was developed in cooperation with University of Ljubljana (Slovenia), KU Leuven (Belgium), Elevate Health (The Netherlands), Takis Biotech (Italy), Istituto Superiore di Sanita (ISS, Italy) and Université Libre De Bruxelles (Belgium).

The programme consists of three complementary elements: online learning module, webinar series, and a face-to-face workshop. The four key challenges related to ATMPs are explored: scientific, manufacturing, reimbursement/pricing, and regulatory. The online learning, as well as the webinar series are open access and free of charge for anyone to join. The face-to-face workshop is an intensive course for a select number of students (60 in 2 years) to go deeper with the topics. We hope that these students will be well positioned to carry on the important work and bring about change in their research communities in the future.

What is in it for the patients?

As with all translational research projects, the end goal should be to help patients. We strongly aim for improvements in public health by serving patients with high unmet medical needs through an appropriately educated work force who can accelerate ATMP development and therefore offer safer and more affordable treatments.

Where was the idea for the project born?

ATMPs are a class of innovative therapeutics which include gene, cells and tissue engineered products. ATMPs offer unprecedented promise for the long-term management and even cure of diseases, especially in areas of high unmet medical need, such as rare diseases, cancers and haematological, ocular, neurodegenerative and genetic diseases. However, the translation from research into patient benefit faces many challenges and requires the involvement of many stakeholders (including academic start-ups, biotech industry, regulatory agencies). For ATMPs to fulfil their potential, specific skills and knowledge in four key areas need to be available in the workforce, which are currently underdeveloped: manufacturing, clinical trials, regulatory approval and reimbursement.

How is EATRIS working towards the realisation of this?

As mentioned, EATRIS is the lead partner for the ADVANCE project. We are also responsible for developing the online learning and the digital accomplishment badges for the participants. While liaising with content experts and developing the criteria for the badges, project manager Eliis Keidong is making sure all partners are equally supported and milestones are met for each intellectual output.

How is this project going to affect operations in the field in the future?

First and foremost, we hope to enhance the quality and relevance of competencies and knowledge to the labour market in the biomedical sciences by making our materials available to a broad audience for years to come. Our aim is that early career scientists who participate in the ADVANCE Programme will improve their career opportunities and employability in the field.

A larger and further reaching goal is to foster interactions between research, education and innovation by supporting mobility between countries and between public & private sectors. Longer term benefits for Europe will include an increased number of scientific ideas turned into innovative products, bringing growth and jobs to the European economy and therefore furthering Europe's competitiveness in the field of ATMP development.

FINANCIAL SUMMARY

Development in income and expenses result:

Compared to the previous year, contributions, subsidy income as well as core projects income increased leading to a positive operating result for 2019.

In 2019 a substantial number of EU projects were acquired, most of them starting as of 1 January 2020. Because of extra subsidies anticipated from the NL government for the acquisition of these projects, extra investments were made in staff, travel and IT to prepare for the project volume growth in 2020. This extra 2019 subsidy was anticipated but for administrative reasons formally confirmed by the NL authorities in Q2 2020.

In agreement with the NL authorities, 70% of the expected subsidy amount is included as income in the 2019 audited financial report for a total of 302k. In the letter by the Netherlands Organisation for Scientific Research (NWO) of 2 June 2020, the final

2019 subsidy amount is now confirmed for a total of 431k. Otherwise, resource allocation was in line with the budget approved by the Board of Governors and in accordance with the Board's final approval of the annual accounts.

	Annual report 2019 €	Approved budget 2019 €	Annual report 2018 €
Contributions income	1,727,651	1,435,000	1,412,764
Subsidy income	557,193	320,730	309,768
Total income	2,284,844	1,755,730	1,722,532
Salaries and wages	913,304	849,639	857,037
Sub total staff	448,264	472,745	187,488
Personnel expenses	1,361,568	1,322,384	1,101,345
Depreciation	5,539	-	6,782
Other expenses	832,932	433,000	738,140
Total expenses	2,200,039	1,755,384	1,846,267
Total operating result	84,805	346	-123,735

	2019	2018	Analysis
	x € 000	x € 000	
Activa			
Tangible fixed assets	17	15	The book value of the tangible fixed assets increased as a result of investments during 2019, plus regular depreciation.
Current receivables	583	350	The increase is due to the NWO contribution recognized for 2019 to be received (302K) at year-end.
Cash at banks	1,380	394	Cash at banks increased mainly due to an increase current liabilities.
	1,980	759	

	2019	2018	Analysis
	x € 000	x € 000	
Equity & Liabilities			
Reserves	430	345	The reserve increased with a net of D85K, equal to the positive result of the financial year.
Current liabilities	1,551	414	The increase is caused by subsidy advance payments.
	1,980	759	

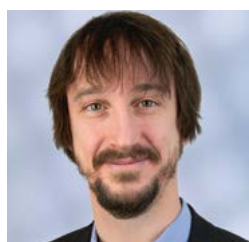
MEET THE COMMUNITY

COUNTRY	Board of Governors	Board of National Directors	National Coordinator
BULGARIA			
	Yanita Zherkova	Rossitza Konakchieva	
	Milena Glavcheva	Rumen Pankov	
CZECH REPUBLIC			
	Renáta Chudáčková	Marian Hajdúch	Miroslav Hutňan
FINLAND			
	Riina Vuorento	Seppo Ylä-Herttuala	
	Sirpa Nuotio		
FRANCE			
	Alix de la Coste	Philippe Hantraye	Lauranne Duquenne
	Eric Guittet	Simone Mergui	
ITALY			
	Maria Ferrantini	Franca Moretti	
	Francesca Capone		
LATVIA			
	Uldis Berkis	Ilmārs Stonāns	
		Zaiga Nora-Krūkle	
LUXEMBOURG			
	Lynn Wenandy	Frank Glod	
	Jean-Claude Milmeister		
THE NETHERLANDS			
	Martijntje Bakker	Rick van Nuland	
	Saco de Visser	Gerrit Meijer	
NORWAY			
	Marianne Grønseth	Janna Saarela	Anita Kavlie*
PORTUGAL			
	Rui Santos Ivo	Cláudia Maria Coelho de Faria	Dinah Duarte
			Helena Baiao
SPAIN			
	Gonzalo Arévalo Nieto**	Joan Comella	Marta Marin
	Cristóbal Belda	Fátima Núñez	
SLOVENIA			
	Albin Kralj	Irena Mlinaric-Rascan	
		Žiga Jakopin	
SWEDEN			
	Håkan Billig	Mats Larhed	Ulrika Bäckman
	Maria Nilsson		

* Anita Kavlie is the successor of Laetitia Abdou-Garonne

** Gonzalo Arévalo Nieto is the successor of Rafael De Andres de Medina

MEET THE C&S TEAM



Anton Ussi
Operations &
Finance Director



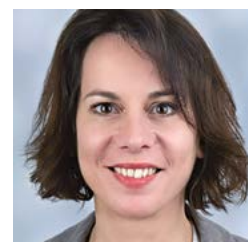
Toni Andreu
Scientific Director



Giovanni Migliaccio
Senior Advisor



Frank de Man
Governance &
Finance



Florence Bietrix
Head of Operations



Edwin van de Ketterij
Clinical Project Director



Anne-Charlotte Fauvel
Head of EU Affairs



Emanuela Oldoni
Programme Manager
Biomarker Platform



David Morrow
Senior Programme
Manager ATMP
& Vaccines platform



Martin de Kort
Senior Programme
Manager Imaging &
Tracing and Small
Molecules platform



Chris Tieken
Business Development
Manager



Rosan Vegter
Training Manager*



Lauranne Duquenne
Training Manager



Rebecca Ludwig
Training Advisor



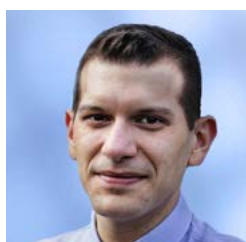
Tamara Carapina
Legal Counsel



Ben Lydall
Finance & Sustainability
Specialist



Eliis Keidong
EU Project Manager



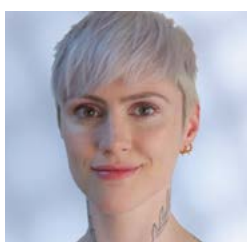
Spyros Goudelis
Communications
Manager



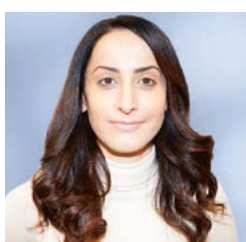
Laure Boudaud
IT & Platforms
Coordinator



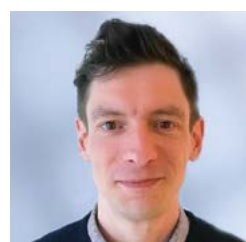
Lisa Marie Williams
Office Manager



Laura Biziou
Office Assistant



Lalageh Masihi
Financial Controller



Jean-Baptiste Trannoy
Finance Officer **



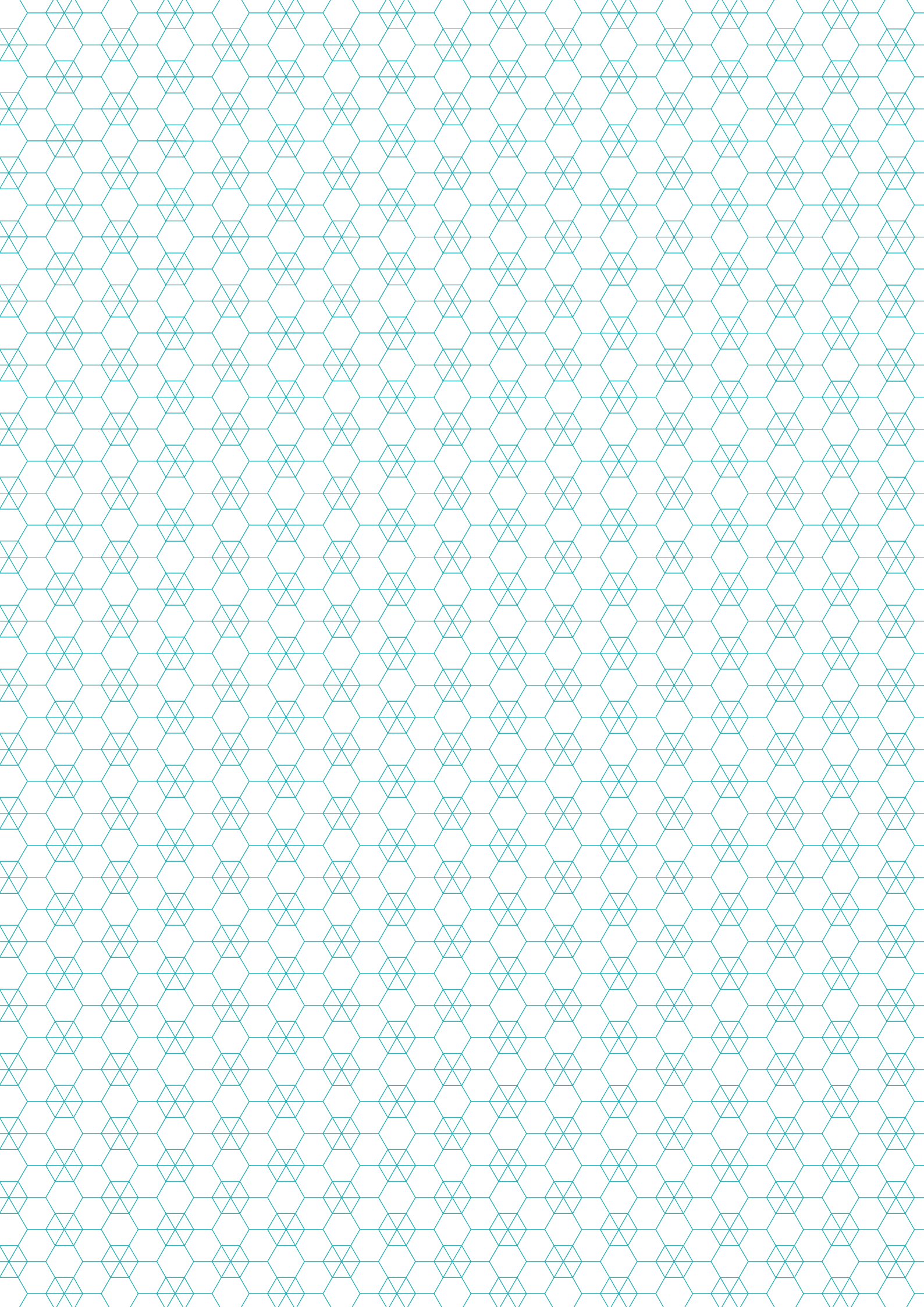
Nigel Wagstaff
Advisor Innovation
Support

*, ** Until the end of 2019

LIST OF ABBREVIATIONS

A	A_IATRIS	Italian Node of EATRIS
	ATMP	Advanced Therapy Medicinal Products
B	BBMRI-ERIC	Biobanking and BioMolecular Resources Research Infrastructure
	BMS RI	Biological and Medical Research Infrastructures
	BPRC	Biomedical Primate Research Centre
C	CAR T-Cell	Chimeric Antigen Receptor T-Cell
	C-COMEND	Competency-based course on Translational Research and Medicines Development
	CDRD	Centre for Drug Research and Development
	CEST MRI	Chemical Exchange Saturation Transfer – Magnetic Resonance Imaging
	CORBEL	Coordinated Research Infrastructures Building Enduring Life-Science Services
E	EATRIS	European Infrastructure for Translational Medicine
	EATRIS - C&S	EATRIS Coordination and Support Office
	EC	European Commission
	ECRIN	European Clinical Research Infrastructure Network
	EMA	European Medicines Agency
	EMMRI	Executive Masters in Management of Research Infrastructures
	EPF	European Patients Forum
	EPTRI	European Paediatric Translational Research Infrastructure
	EQI	EATRIS Quality Initiative
	ERIC	European Research Infrastructure Consortium
	ESFRI	The European Strategic Forum for Research Infrastructures
	ESMO	European Society for Medical Oncology
	EU	European Union
	EURIPRED	European Infrastructure for Poverty-Related Diseases
	EVI	European Vaccine Initiative
H	HESI	Health and Environment Sciences Institute
	HTA	Health Technology Assessment
	HTS	High Throughput Screening
I	IBBL	Integrated BioBank of Luxembourg
	IRP	Integrated Research Platform
	IMI	Innovative Medicines Initiative
	ISCT	International Society for Cellular Therapy
J	JTC	Joint Transnational Call

L	LAC	Latin American and Caribbean
	LoE	Letter of Engagement
	LS RI	Life Science Research
	LTP	Linked Third Party
M	MEB	Medicines Evaluation Board
	MIRCen	Molecular Imaging Research Center
	MoU	Memorandum of Understanding
	MRCA	Master Research Collaboration Agreement
N	NASH	Non-Alcoholic Steatohepatitis
	NeurATRIS	French Node of EATRIS
	NHP	Non-human primates
	NIBSC	National Institute for Biological Standards and Control
	NIH-NCATS	US National Institutes of Health – National Center for the Advancement of Translational Science
	NTNU	Norwegian University of Science and Technology
P	PAC	Patient Advisory Committee
	PI	Principal Investigator
	PMC	Personalized Medicine Coalition
R	R&D	Research and Development
	RI	Research Infrastructures
	RIS	Regulatory Information System
	RITRAIN	Research Infrastructures Training Programme
	RSU	Rīga Stradiņš University
S	SAB	Scientific Advisory Board
	SMEs	Small and medium-sized enterprises
	SOP	Standard Operating Procedure
T	TIA	Therapeutic Innovation Australia
	TraIT	Translational Research IT
	TRANSVAC2	European Network of Vaccine Research and Development
	TT	Translation Together
U	UMC	University Medical Centres
V	VHIR	Vall d’Hebron Research Institute
W	WP	Work Packages



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