INTERNATIONAL SYMPOSIUM
P2M
PATHWAYS PRECISION MEDICINE

THE THIRD P2M ROUEN INTERNATIONAL SYMPOSIUM

ROUEN SCHOOL OF HEALTH SCIENCES
UFR SANTÉ ROUEN

APRIL 3RD | 4TH 2025

ROUEN NORMANDIE FRANCE

Pathways *to* PRECISION MEDICINE

FROM RARE TO COMMON DISEASES

Prof. Soumeya BEKRI (President)
Prof. Abdellah TEBANI (Chair)

PROGRAM

DEAN'S WELCOME MESSAGE

Dear all,

In this era of rapid biomedical and technological transformation, Precision Medicine stands at the forefront of a healthcare revolution. It aims to collect, link, and leverage large-scale scientific knowledge about health, from the molecular basis of disease to clinical, environmental, psychosocial and lifestyle data. This allows to decipher why individuals respond differently to health care management and treatment, and to help guide more precise, predictive and equitable medicine.

The symposium boldly advocates for the universal potential impact of Precision Medicine. From the rare to the most complex and chronic diseases, we are witnessing an unprecedented, yet promising, convergence of science, technology, and patient-centered care. However, alongside these breakthroughs come critical ethical, societal, and workforce challenges that require interdisciplinary collaboration.

Over these two enriching days, I invite you to engage in insightful discussions led by distinguished international experts from across the healthcare ecosystem.

Welcome to this immersive event is not only an opportunity to learn and exchange ideas but also a platform to forge collaborations that will shape the future of healthcare. Let us seize this moment to challenge conventional thinking, push the boundaries of science, and drive actionable change that empowers patients and advances human health worldwide

We look forward to hosting you all in Rouen for an inspiring and engaging event!

Prof. Benoit VEBER
Dean
UFR Santé Rouen (Rouen School of Health Sciences)
Rouen Normandie University

WELCOME MESSAGE

We are pleased to welcome you to **the third edition of the International Pathways to Precision Medicine Symposium (P2M Symposium)** organized by Soumeya BEKRI and Abdellah TEBANI (Metabolic Biochemistry Department – Rouen Normandie University) which takes place at the Rouen Health Campus (UFR Santé – Bâtiment Stewart) on 3rd and 4th, April 2025.

Precision Medicine opens a new medical era and reimagines medicine to focus on the prediction, prevention and treatment of diseases with high technological precision and clinical accuracy. In a game-changing move, healthcare providers leverage patient-specific data to understand disease susceptibility and tailor intervention. This approach is set to revolutionize how we diagnose and treat diseases, paving the way for more personalized, effective healthcare solutions and accountable data-driven medicine.

This symposium brings together international leaders in the different fields of Precision Medicine. Academic, industrial, and healthcare stakeholders will meet for two days to foster collaboration, address challenges, and define actions for large-scale leverage of an integrated data healthcare ecosystem for a single purpose: to improve human health. Get ready for the future of healthcare!

This edition will cover a wide range of topics, from the ever-changing role of AI in medicine to the ethical considerations guiding precision medicine practices. The foundational principles to develop accountable and effective data-driven medicine will be discussed. We will also explore innovative approaches to treating rare diseases and reimagining therapies. Parsing disease complexities through phenotype investigative lenses will be presented.

We will dive into cutting-edge medical imaging advancements and data-driven disease management strategies. Along these conversations, we will ponder the transformative potential of generative AI in reshaping medicine. As we navigate social determinants of health disparities, we will advocate for inclusivity and patient empowerment in the precision medicine era. Additionally, we will discuss healthcare readiness, and workforce empowerment, highlighting the importance of nurturing the next generation of healthcare professionals to improve patient outcomes and streamline operational efficiency.

Discover drug repositioning, gene therapy, diagnostics, biomarkers, omics-based molecular profiling, medical imaging, large-scale screening, critical care, rare diseases, cancer, and more. We will also demystify, electronic health records, federated learning, blockchain, artificial intelligence, large language models, generative AI, digital health, and empowered clinical trials. But the journey doesn't stop there – we'll also challenge the implementation, ethical, and societal issues raised by precision medicine.

Embracing precision medicine is a bold yet essential move towards a technically efficient, clinically relevant, and ethically accountable healthcare system.

Join us for an exciting journey into the world of Precision Medicine and be the change you want to see in healthcare!

Prof. Soumeya BEKRI
Symposium President
(Co-Founder)
Head of the Department
of Metabolic Biochemistry
AIMS - Systems Medicine Lab
Rouen University Hospital
Rouen Medical School
Rouen – France

Prof. Abdellah TEBANI
Symposium Chair
(Co-Founder)
Department of Metabolic
Biochemistry
AIMS - Systems Medicine Lab
Rouen University Hospital
Rouen Medical School
Rouen - France

SUMMARY | **PROGRAM**

SUMMARY | **ABSTRACT**

SPEAKERS

—
Hatim ABDULHUSSEIN
Health Innovation Kent Surrey Sussex, Keele, UK

—
Shadi ALBARQOUNI
University of Bonn
Bonn, GERMANY

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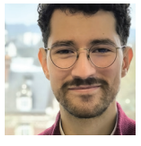
Soumeya BEKRI
Rouen University Hospital
AIMS - Systems Medicine Lab
Rouen, FRANCE



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Nassim BOUTOUCHENT
Rouen University Hospital
Rouen, FRANCE

—
Guillaume CANAUD
Necker Enfants Malades - Assistance Publique-Hôpitaux de Paris
Paris, FRANCE

—
Fouad CHEBIB
Mayo Clinic Florida
Florida, USA

—
Pierre-Alexis DA COSTA
Sorbonne University
Paris, FRANCE

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Mie Seest DAM
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Copenhagen, DENMARK

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Franklin DUCATEZ
Boston Children's Hospital
Boston, USA

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Ellen GRANT
Harvard Medical School
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Boston, USA

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Ursula HEINS-MARROQUIN
Luxembourg Center for Systems Biomedicine,
Esch-sur-Alzette, LUXEMBOURG

—
Simon JONES
Manchester Center for Genomic Medicine
Manchester, UK

—
Didier LACOMBE
Bordeaux University Hospital, Bordeaux, FRANCE

—
Peter LAUSSEN
Harvard Medical School
Boston Children's Hospital
Boston, USA

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Zacharia MESBAH
Henri Becquerel Cancer Center, Rouen, FRANCE

—
Joseph NADEAU
Maine Medical Center Research Institute,
Maine, USA

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Mette Nordahl SVENDSEN
University of Copenhagen
Copenhagen, DENMARK

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Mark RUBIN
University of Bern
Bern, SWITZERLAND

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Manuel SCHIFF
Necker Enfants Malades - Assistance Publique Hôpitaux de Paris
Paris, FRANCE

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Abdellah TEBANI
Rouen University Hospital
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—
Yannick THIRIET
Thermo Fisher Scientific
FRANCE

—
Sarah WAMALA ANDERSSON
Mälardalen University
Västerås, SWEDEN

—
Eva WINKLER
Heidelberg University Hospital
Heidelberg, GERMANY

DAY 1 THURSDAY APRIL 3RD, 2025

8 AM > 8:55 AM REGISTRATION

9 AM > 9:55 AM
OPENING CEREMONY / WELCOME ADDRESS
Chairs: Soumeya BEKRI & Abdellah TEBANI, Rouen University Hospital, Rouen, FRANCE

10 AM > 10:55 AM
SESSION 1 - OPENING KEYNOTE - THE HUMAN TOUCH
Chair: Abdellah TEBANI, Rouen University Hospital, Rouen, FRANCE

The Human Factor in AI-Driven Medicine.
Peter LAUSSEN, Harvard Medical School, Boston Children's Hospital, Boston, USA

11 AM > 11:25 AM COFFEE BREAK

11:30 AM > 1 PM
SESSION 2 - BEYOND PROMISES
Chair: Carole LINSTER, Luxembourg University, Esch-sur-Alzette, LUXEMBOURG

The Ethical Landscape in Precision Medicine.
Eva WINKLER, Heidelberg University Hospital, Heidelberg, GERMANY
Newborn Screening of Spinal Muscular Atrophy: A Pilote Program in France.
Didier LACOMBE, Bordeaux University Hospital, Bordeaux, FRANCE
Newborn Screening for Lysosomal Diseases: Insights from the LysoNeo Study.
Abdellah TEBANI & Soumeya BEKRI, Rouen University Hospital, Rouen, FRANCE

1:05 PM > 1:55 PM LUNCH BREAK

2 PM > 2:30 PM
SESSION 3 - PRECISE CARE FOR RARE
Chair: Olivier LIDOVE, La Croix Saint Simon Hospital, Paris, FRANCE

Mechanism-Driven Therapies in Rare Diseases.
Manuel SCHIFF, Necker Enfants Malades - Assistance Publique, Hôpitaux de Paris, Paris, FRANCE

2:35 PM > 3 PM
POSTER FLASH TALKS

Searching for small molecule-based therapies for ATP13A2 deficiencies.
Ursula HEINS-MARROQUIN, Luxembourg Centre for Systems Biomedicine, Esch-sur-Alzette , LUXEMBOURG
Deciphering cellular and molecular mechanisms of immune infiltration and Tertiary Lymphoid Structure organization in Non-Small Cell Lung Cancer.
Pierre-Alexis DA COSTA, Sorbonne University, Paris, FRANCE
Antibiotic resistance genes diversity and antimicrobial effects in the vaginal microbiome during pregnancy.
Nassim BOUTOUCHENT, Rouen University Hospital, Rouen, FRANCE
Predicting NSCLC patient response to radio-chemotherapy.
Zacharia MESBAH, Henri Becquerel Cancer Center, Rouen, FRANCE
Use of Fourier transformation of monitoring waveforms movement detection in sedated patients.
Franklin DUCATEZ, Boston Children's Hospital, Boston, USA

3:05 PM > 4:05 PM
SATELLITE EVENT - ORCHARD Orchard therapeutics

Autologous Ex Vivo Gene Therapies Development in Rare Diseases: in the Perspective of the Global Gene Therapy Landscape.
Simon JONES, Manchester Center for Genomic Medicine, Manchester, UK

4:10 PM > 4:25 PM COFFEE BREAK

4:30 PM > 5:30 PM
SESSION 4 - PLENARY KEYNOTE - HIDDEN PATTERNS
Chair: Soumeya BEKRI, Rouen University Hospital, Rouen, FRANCE

Parsing Disease Complexity: A Phenotype-guided Perspective.
Joseph NADEAU, Maine Medical Center Research Institute, Main, USA

DAY 2 FRIDAY APRIL 4TH, 2025

8 AM > 8:40 AM REGISTRATION

8:45 AM > 10:25 AM
SESSION 5 - TOWARDS EMPOWERMENT
Chairs: Pierre VERA, Henri Becquerel Cancer Center, Rouen, FRANCE
& Stefan DARMONI, Rouen University Hospital, Rouen, FRANCE

Digital Transformation and Social Determinants of Health: Beyond Disparities.
Sarah WAMALA ANDERSSON, Mälardalen University, Västerås, SWEDEN
Enabling Next-Gen Healthcare Workforce: From Vision to Reality.
Hatim ABDULHUSSEIN, Health Innovation Kent Surrey Sussex, Keele, UK
Empowering the Patient in the Precision Medicine Era.
Mette Nordahl SVENDSEN and Mie Seest DAM, University of Copenhagen, Copenhagen, DENMARK

10:30 AM > 10:55 AM COFFEE BREAK

11 AM > 11:30 AM
SESSION 6 - BEYOND THE LABEL
Chair: Frédéric BARBEY, Lausanne University Hospital, Lausanne, SWITZERLAND

Drug repositioning in CLOVES Syndrom.
Guillaume CANAUD, Necker Enfants Malades - Assistance Publique, Hôpitaux de Paris, Paris, FRANCE

11:35 AM > 12:05 PM
WORKSHOP - THERMOFISHER SCIENTIFIC

Expanding Capabilities Towards Omics-Based Workflows In Precision Medicine
Technology innovations to LC-MS platforms that increase the speed of biomarker verification and validation through expanded experimental capacity.
Yannick THIRIET, Thermo Fisher Scientific

12:10 PM > 1:20 PM LUNCH BREAK

1:25 PM > 3:05 PM
SESSION 7 - FILLING THE GAPS
Chairs: Ivana DABAJ, Rouen University Hospital, Rouen, FRANCE
& Pierre DECAZES, Henri Becquerel Cancer Center, Rouen, FRANCE

Next-Generation Imaging in Fetal and Newborn Medicine.
Ellen GRANT, Harvard Medical School, Boston Children's Hospital, Boston, USA
Data-Empowered Strategies in Polykystic Kidney Disease.
Fouad CHEBIB. Mayo Clinic, Florida, USA
Leveraging Collective Intelligence for inclusive Global Healthcare.
Shadi ALBARQOUNI, University of Bonn, Bonn, GERMANY

3:10 PM > 3:55 PM
SESSION 8 - CLOSING KEYNOTE - A LEARNING JOURNEY
Chair: Nathalie BEDNAREK, Reims University Hospital, Reims, FRANCE

Precision Medicine: Lessons From the Fields.
Mark RUBIN, University of Bern, Bern, SWITZERLAND

4 PM > 4:15 PM
POSTER PRIZES - CLOSING REMARKS
Chairs: Soumeya BEKRI & Abdellah TEBANI, Rouen University Hospital, Rouen, FRANCE

DAY 1 THURSDAY APRIL 3RD, 2025

SESSION 1 I **THE HUMAN TOUCH**

The Human Factor in AI-Driven Medicine.

Peter LAUSSEN

The human factor in AI-driven medicine is an essential aspect for integrating artificial intelligence (AI) into healthcare. AI in medicine is intended to augment human capabilities, and in some cases automate them, but not replace them.

There are several key elements to the human factor within AI development and utilization. AI creation requires humans to understand the problem(s) to be solved. Upstream, humans are needed to harness and harden data through its generation, collection, access and linkages. This requires a structure, a governance or stewardship, that humans create related to policies around sharing, unlocking data, analysis and deployment.

AI tools are powerful at analyzing vast amounts of data, but currently do not have the nuanced understanding of individual patient contexts and biologic variability. AI may suggest possible diagnoses or treatment options, but humans are needed to make the final decision; this is true in almost all high-risk industries outside of healthcare where there is complexity or ambiguity. AI does not replace the human connection and holistic care between a healthcare provider and a patient and family.

The application and adoption of AI as a translational or decision support tool requires an understanding of the macro- and micro-systems into which the AI is being deployed. This is particularly important for leaders in healthcare systems as they manage the ever-increasing costs. To be successfully deployed and adopted, humans need to have trust in the AI output, that there are no biases or hallucinations in the data or analyses, and that the output is believable, explainable and actionable.

Healthcare providers must be trained to work with AI technologies, ensuring they understand how to interpret AI outputs and when to challenge or override recommendations. Legal and ethical considerations are still evolving, including determining accountability in cases of potential AI failure.

AI will transform healthcare and sits at the interface between humans, data and technology. Aligning people with the intelligence generated from data aggregated through episodes of care is fundamental for deriving wisdom and eventually changing our behaviors and care delivery.

SESSION 2 I **BEYOND PROMISES**

The Ethical Landscape in Precision Medicine

Eva WINKLER

Precision medicine promises to revolutionize healthcare by tailoring treatments to individual patients based on genetic, environmental, and lifestyle factors. However, this shift raises critical ethical questions:

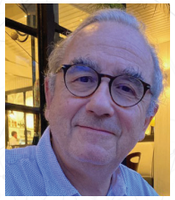
How can we ensure equity in access to precision treatments?

What safeguards are needed to balance data-driven insights with patient autonomy and privacy?

What oversight is needed for genomic data sharing, and how should we handle incidental findings or the reinterpretation of sequencing results over time?

And how do we navigate the role of AI in clinical decision-making while maintaining accountability?

This talk will explore the ethical principles that must guide precision medicine, addressing issues of fairness, transparency, and trust in an era of rapidly evolving medical technology.



SESSION 2 | **BEYOND PROMISES**

Newborn Screening of Spinal Muscular Atrophy: A Pilote Program in France.

Didier LACOMBE

Spinal muscular atrophy (SMA) is a neuromuscular genetic disorder characterized by loss of motor neurons from the anterior horn of the spinal cord. Inheritance is autosomal recessive. SMN1 gene is implicated in the survival of the motor neurons. In 95% of cases of the disease, there is a biallelic deletion of exon 7 of SMN1. An homologous gene to SMN1, SMN2, is not functional, because of splicing of exon 7 of SMN2, but the severity of the disease is linked to the number of SMN2 copies. There are four types of SMA and 60% of SMA type 1 die at age 18 months. Recently, three drugs have been evaluated in SMA and have the authorization in France for presymptomatic use up to three copies of SMN2. Nusinersen is an antisense oligonucleotide known to functionalize SMN2 gene. Administration is by regular intrathecal injections. A gene therapy (Onasemnogene abeparvovec, Zolgensma®) is an unique injection. Benefit is better with an early administration of the product, and for this reason, newborn screening has been promoted. A third drug (Risdiplam) is an oral treatment. SMA fullfill the Wilson criteria for newborn screening. Newborn screening for SMA is available in many countries, as Belgium, Germany, Taiwan, USA, Japan, Australia... In France, a pilot project is in process in two areas (Nouvelle Aquitaine and Grand Est). We will test 2 x 55 000 babies/year, whether 32 children expected to be affected in two years. Newborn screening is effective by molecularly testing SMN1 gene biallelic deletion. Biological confirmation will include the analysis of the copy number of SMN2. When the diagnosis is confirmed, the patient will be included in a French « RCP » meeting to discuss the treatment modality.

This communication will present the current results of this pilot program.

SESSION 2 | **BEYOND PROMISES**

Newborn Screening for Lysosomal Diseases: Insights from the LysoNeo Study

Soumeya BEKRI & Abdellah TEBANI

Spinal muscular atrophy (SMA) is a neuromuscular genetic disorder characterized by loss of motor neurons from the anterior horn of the spinal cord. Inheritance is autosomal recessive. SMN1 gene is implicated in the survival of the motor neurons. In 95% of cases of the disease, there is a biallelic deletion of exon 7 of SMN1. An homologous gene to SMN1, SMN2, is not functional, because of splicing of exon 7 of SMN2, but the severity of the disease is linked to the number of SMN2 copies. There are four types of SMA and 60% of SMA type 1 die at age 18 months. Recently, three drugs have been evaluated in SMA and have the authorization in France for presymptomatic use up to three copies of SMN2. Nusinersen is an antisense oligonucleotide known to functionalize SMN2 gene. Administration is by regular intrathecal injections. A gene therapy (Onasemnogene abeparvovec, Zolgensma®) is an unique injection. Benefit is better with an early administration of the product, and for this reason, newborn screening has been promoted. A third drug (Risdiplam) is an oral treatment. SMA fullfill the Wilson criteria for newborn screening. Newborn screening for SMA is available in many countries, as Belgium, Germany, Taiwan, USA, Japan, Australia... In France, a pilot project is in process in two areas (Nouvelle Aquitaine and Grand Est). We will test 2 x 55 000 babies/year, whether 32 children expected to be affected in two years. Newborn screening is effective by molecularly testing SMN1 gene biallelic deletion. Biological confirmation will include the analysis of the copy number of SMN2. When the diagnosis is confirmed, the patient will be included in a French « RCP » meeting to discuss the treatment modality. This communication will present the current results of this pilot program.

SESSION 3 | **PRECISE CARE FOR RARE**

Mechanism-Driven Therapies in Rare Diseases: Innovative therapies for inborn errors of metabolism: the example of MSUD

Manuel SCHIFF

Monogenic inborn errors of metabolism (IEMs) are relevant targets for genetic therapies as they are autosomal recessive conditions with well-characterized pathophysiology and highly informative biochemical readouts; yet their therapeutic management remains complex and often cumbersome with numerous unmet therapeutic needs. Among these, maple syrup urine disease (MSUD) is a rare recessive IEM caused by the dysfunction of the branched-chain keto acid dehydrogenase (BCKD) enzyme which leads to accumulation of branched-chain amino- and keto- acids causing neonatal death if untreated. MSUD represents an unmet need as its current management is based on a life-long low-protein diet, which does not prevent the risk of acute decompensations and long-term neuropsychiatric defects. The curative effect of liver transplant in MSUD patients was an incentive for testing liver-directed innovative therapies in MSUD mice.

In the talk, we will introduce innovative therapies (mainly mRNA and gene therapies) for IEMs. Then, we will present experimental data in mice showing successful rescue of severe neonatal phenotypes in 2 mouse models of MSUD on the one hand with AAV8 gene therapy and on the other hand liver-directed mRNA therapy.

The demonstration of efficacy of these innovative therapies for MSUD demonstrate their potential for clinical translation.

POSTER FLASH TALKS

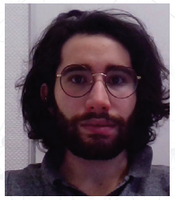
Searching for small molecule-based therapies for ATP13A2 deficiencies

Ursula HEINS-MARROQUIN

Mutations in ATP13A2 cause the Kufor-Rakeb Syndrome, a rare early-onset form of Parkinsonism with dementia. Interestingly, other mutations in the same gene lead to neuronal ceroid lipofuscinosis or Spastic Paraplegia-78. The most commonly reported phenotypes in ATP13A2-deficient models include mitochondrial and lysosomal dysfunction, alpha-synuclein aggregation, and decreased heavy metals resistance. Recently, functional studies identified ATP13A2 as a conserved lysosomal polyamine exporter.

Despite these advances, the connection between the function of ATP13A2 and related disease phenotypes remains elusive and no efficient treatments exist for ATP13A2 deficiencies. We generated yeast and zebrafish models of ATP13A2 deficiency to screen for compounds with therapeutic potential. A drug repurposing screen was performed in the yeast model using a phenotypic assay based on decreased heavy metal resistance. Hit compound validations were performed in the zebrafish model, ATP13A2-deficient SH-SY5Y cells, and midbrain neurons obtained by differentiation of patient-derived induced pluripotent stem cells. Promising therapeutic compound candidates, including N-acetylcysteine and furaltadone, from our yeast-based repurposing screen could be validated in the zebrafish model. Deep phenotyping of ATP13A2-deficient SH-SY5Y cells and the patient-derived midbrain neurons allowed to identify robust readouts that are currently being used to test our lead compounds in these disease-relevant cell models and to further decipher cellular pathways leading to neuronal death. Perturbations of lipidic profiles are among the most striking changes that we could identify in our ATP13A2-deficient models. Although the molecular function of ATP13A2 is known, its role in neurodegenerative disease is still a mystery. The combination of a phenotypic rescue screen in a simple model followed by validation in patient-derived models might accelerate the identification of small compound drugs that can be repurposed for the treatment of disorders caused by ATP13A2 deficiency.

Finally, our findings position ATP13A2 as an important player in lipid homeostasis, suggesting new therapeutic leads.



POSTER FLASH TALKS
Deciphering cellular and molecular mechanisms of immune infiltration and Tertiary Lymphoid Structure organization in Non-Small Cell Lung Cancer

Pierre-Alexis DA COSTA

Background: The Tumor MicroEnvironment (TME) of Non-Small-Cell Lung Cancer (NSCLC) is highly complex, comprising tumor cells, immune cells, cancer-associated fibroblasts (CAFs), and endothelial cells. Immune cells, especially B and T lymphocytes, can organize in Tertiary Lymphoid Structures (TLS), which are linked to better prognosis and immunotherapy response. Conversely, low adaptive immune infiltration or absence of TLS correlates with poor clinical outcomes. The mechanisms driving immune infiltration and TLS formation in the TME remain poorly understood. We hypothesize that immune infiltration and TLS organization depend on tumor cell phenotype, blood and lymphatic vessel activation and patterning, CAF subsets, and extracellular matrix composition and structure. The study aims to identify a TME signature associated with immune infiltration and TLS organization in NSCLC.

Material and methods: We are analyzing a retrospective cohort of 211 patients who underwent surgery in 2018 at Cochin Hospital, with available clinical data. Immune infiltrate in the TME was characterized using multiplex immunofluorescence. We quantified B and T cell densities, TLS presence/maturation, high endothelial venules, cell proliferation, and tumor cell density. In parallel, we have started quantifying stromal components like CAF subsets and blood/lymphatic vessels. These features were quantified using HALO AI software, followed by bioinformatics analyses to classify the cohort based on immune cell density and TLS presence and maturity.

Results: Preliminary results show that 204 out of 211 patients have at least one mature TLS. High secondary follicle-like TLS density (above median) correlates with better overall survival. Based on this classification, we have selected two patient groups: 9 with low TLS density and 9 with high TLS density. These patients will be analyzed using bulk and spatial transcriptomics (Visium HD, 10X Genomics).

Conclusion: This study will provide insights into the relationship between various TME components particularly CAFs and blood/lymphatic vessels, and immune infiltration, along with transcriptomic profiles of distinct TME subtypes.

POSTER FLASH TALKS
Antibiotic resistance genes diversity and antimicrobial effects in the vaginal microbiome during pregnancy

Nassim BOUTOUCHENT

Background: Materno-fetal infections are a leading cause of morbidity and mortality, often requiring complex antibiotic treatments due to increasing antibiotic resistance. However, the determinants and dynamics of resistance in vaginal microbial communities are poorly understood. Methods In this prospective observational study, we performed whole genome shotgun metagenomic analysis of vaginal samples collected from pregnant women in their third trimester. Microbial taxonomic assignment was performed using a dedicated in-house vaginal microbiota Kraken2 database, with species-level abundance adjusted using Bracken. Clinically relevant antibiotic resistance genes (ARGs) in vaginal resistome were identified using the ResFinder database. Normalized read count tables were analyzed to characterize the vaginal resistome and evaluate shifts associated with antibiotic exposure during pregnancy. ARGs diversity was assessed through and -diversity metrics. In addition, ARGs phenotype predictions similarities were used to construct a phenotypic resistance tree, facilitating the development of a novel diversity index specific to clinically relevant ARGs.

Results We analyzed 1,938 samples from 1,543 pregnant women, including 395 with two samples taken at different timepoints. The vaginal resistome revealed 547 distinct ARGs, 60% (328/547) conferring resistance to beta-lactams. The average ARG richness was 6.8 (SD ± 8). Most abundant ARGs conferred resistance to macrolides (47.4%), tetracyclines (30.7%), and beta-lactams (7.1%). lsa(C) and tet(M) were the most frequent and abundant ARGs. These genes were predominantly harbored by species from the Lactobacillales order, whereas species from the Enterobacterales order harbored a broader diversity of ARGs across different antibiotic classes, including beta-lactams, aminoglycosides, and sulfonamides. Comparative analysis based on antibiotic use during pregnancy (wATB vs. woATB) showed a twofold increase in beta-lactam resistance ARGs relative abundance in the wATB group at delivery ($p = 0.007$). The Shannon diversity index revealed a significant difference in ARGs intra-sample diversity between the wATB and woATB groups during pregnancy ($p = 0.02$), but not at delivery. The novel phenotypic resistance diversity index (PRDI) captured significant differences at both timepoint ($p = 0.003$ and 0.02 respectively), indicating that while no differences in richness and evenness were observed at delivery, the predictive ARGs resistance phenotypes differed, with a broader spectrum of resistant phenotypes in the vaginal ecosystem at delivery for women who received antibiotic therapy during pregnancy.

Conclusion Clinically relevant ARGs in the vaginal resistome predominantly confer resistance to macrolides and tetracyclines and are partly harbored by the core communities of the vaginal microbiota. A functionally aware analysis, using PRDI, provides a novel approach to assess ARGs diversity, beyond traditional metrics. By considering the individual variability of the microbiome and resistome, this approach could deepen our understanding of resistome dynamics across different ecosystems and lead to more targeted strategies for improving maternal and child health. Conflict of interest None to declare.

POSTER FLASH TALKS
Predicting NSCLC patient response to radio-chemotherapy

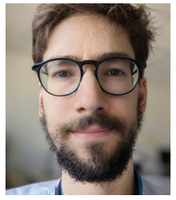
Zacharia MESBAH

Background: The RTEP7 study is a phase II-III study originally designed to prove the safety of dose escalation up to 74 Gy (boost) of the radiotherapy (RT) treatment, based on 18F-FDG-PET/CT imaging after 42 Gy of treatment (PET/CT 2).

This study focuses on patients with stage III inoperable non small cell lung cancer (NSCLC) Patients were split in two treatment arms :
• an experimental arm (arm A) in which patients with residual malignant uptake on PET/CT 2 received a RT boost (dose escalation to 74 Gy), while the patients with no uptake received the classic dose (66 Gy)
• a control arm (arm B) in which all patients receive the standard RT dose We are looking to:
- detect patients which could benefit from a boost, since the initial exam (PET/CT 1)
- estimate the risk of death or progression for a patient using the pre-radiotherapy and per-radiotherapy scans

Material and Methods: In total, 138 patients were included in our analysis, 67 in the experimental arm, which benefited from adaptative treatment and 71 in the control arm. The lesions (Tumor + Lymph nodes) were manually delineated by a physician. We then extracted 204 radiomics features (107 on the CT, 107 on the PET). Clinical data (Age, sex, cancer histology and stage) are added to the pool of features. For the frst task, we keep the features most correlated to the target value, using Spearman correlation. For survival prediction we used an univariate Cox Proportional Hazards (CoxPH) analysis instead. We use a Bagged SVM as classifier for classification, and a CoxNet and fast Survival SVM (FS-SVM) are compared for survival estimation. Models were evaluated using corrected accuracy, specificity and sensitivity for the classification task ; and using the Concordance Index (C-Index) for survival estimation. All reslts were obtained by averaging over 10 runs a 6 folds, cross-validation.

Results: Patients classification using PET/CT 1 : accuracy is 51.98 %, sensitivity is 53.21 % and specificity is 50.74 % Survival estimation using both PET/CT exams: (FS-SVM) gave the best results with C-Index of .649 for overall survival (OS) and .663 for Progression Free Survival (PFS) on arm A and .566 for OS and .529 for PFS for all patients.



POSTER FLASH TALKS
Use of Fourier transformation of monitoring waveforms movement detection in sedated patients

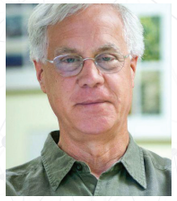
Franklin DUCATEZ

Background: Sedation and analgesia are essential to the care of critically ill infants and children. However, sedative agents also carry significant risks, and thus best practices focus on titrating sedation to the minimum dose required to maintain comfort. The quantification of sedation level remains a critical task in sedation provision. Current practice is for bedside staff to perform intermittent, active assessments of sedation level according to standardized scales. However, these methods are time-intensive, intermittent, and subjective. Establishing a continuously measured, objective metric of sedation level may improve the rigor of sedation assessments, and advance the science of sedation practices in infants and children. The purpose of this work was to quantify patient movement using artifact in photoplethysmograph (PPG) readings in sedated patients.

Methods: 844 hours of continuous PPG waveform were recovered from 39 patients. Waveforms were divided into 10 second increments on which discrete Fourier transformation (FT) was performed. The resulting frequency matrix was then filtered and normalized. For each 10 second increment, the maximum amplitude of the FT-data was identified and used to normalize the entire FT signature. Thereafter, we computed the sum of all FT-amplitudes across the filtered spectrum from 0 to 10 Hz. This resulted in the computation of a single number between 0 and 25 that represented the degree of motion artifact within a 10 second sample, with 0 being perfectly still (i.e. no artifact present) and 25 being nearly all artifact motion artifact.

Results: Raw waveforms (Figure 1A, top) underwent Fourier transformation (Figure 1A, middle), then summarized as a single numerical value assigned to the 10-second sample (Figure 1A, bottom). Analysis and visualization of all 10-second epochs together allowed for a potential visualization of patient movement over time (Figure 1B).

Conclusions: FT of raw waveforms may be useful to quantify patient movement. Validation of these methods against human interpretations of waveform artifact, then of patient motion, are critical next steps.



SESSION 3 | **HIDDEN PATTERNS**

Parsing Disease Complexity: A Phenotype-guided Perspective

Joseph NADEAU

What if our ideas about phenotypic variation and disease risk overlook a primary determinant? Fisher's century-old model, phenotypic variance VP = genetics VG + environment VE + error Ve, continues to guide many areas of biomedical research. But substantial variation is not included in this model. On average, 50% of variability has neither genetic nor environmental origins. We propose that considerable non-genetic and non-environmental variation emerges during development, arising from stochastic noise that triggers probabilistic epigenetic changes, and that once established are deterministically propagated throughout life. These epigenetic changes lead to wide variation in phenotypic outcomes across many traits, in many species, and in health and disease. Clearly, managing disease, even with Precision Medicine approaches, will remain challenging if 50% of risk remains outside the scope of current research. Our ongoing work in humans and model organisms addresses many of the conceptual, study design, technical and analytical challenges. In particular, a focus on variability itself reveals common, clinically relevant cancer and metabolic subtypes that elude discovery with conventional approaches. Together these observations support a phenotype-guided virtuous cycle of human-model organism studies with discovery and experimentation in model organisms integrated with validation and refinement in humans.

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SESSION 5 | **TOWARDS EMPOWERMENT**

Digital Transformation and Social Determinants of Health: Beyond Disparities

Sarah WAMALA ANDERSSON

As global life expectancy continues to rise, maintaining good health has become an increasingly sought-after goal for many, with technological advancements offering promising solutions. Digital Health Technologies (DHTs) have the potential to revolutionize healthcare by enabling virtual care, remote monitoring, improved disease management, and more personalized treatment options (1).

DHTs encompass telemedicine, mobile applications, wearable devices, electronic health records, and artificial intelligence (AI). These technologies facilitate real-time data collection on patients' vital signs, lifestyles, and medical histories, supporting more effective care pathways, personalized treatments, and predictive healthcare. Moreover, DHTs and AI have the potential to reduce healthcare costs while simultaneously improving the quality of care.

However, one significant barrier to fully leveraging the potential of DHTs is digital health literacy. Without sufficient understanding of how to use these technologies, their value in transforming healthcare cannot be fully realized, hindering efforts toward achieving digital health equity. Additional challenges include insufficient research-based evaluations, skepticism, resistance to change, and limited access to digital tools (2). Digital health literacy is a multifaceted concept, requiring a comprehensive approach to ensure better outcomes.

Policymakers, healthcare professionals, and technology developers are increasingly recognizing that the successful adoption of technology and innovation in healthcare demands more than just financial investment. It also requires a focus on usability and accessibility.

The future of healthcare delivery is expected to shift towards empowering patients to take control of their health management through the use of DHTs, facilitating better communication with healthcare providers and professionals. The World Health Organization (WHO) has underscored the importance of developing and implementing digital health technologies in ways that promote equity, affordability, and accessibility. In its Regional Digital Health Action Plan 2023-2030, the WHO highlights Digital Health Literacy (dHL) as a critical factor in achieving universal health coverage and ensuring that all populations benefit from digital health solutions.

The WHO defines dHL as the ability to seek, find, understand, and appraise health information from electronic sources, and to apply that knowledge to solve health-related problems (2). Achieving dHL is therefore essential for both patients and healthcare professionals, enabling them to effectively access, evaluate, and apply health information from digital platforms. This requires not only technical skills for operating digital tools but also cognitive skills for interpreting and communicating health data. Consequently, digital health literacy should be incorporated into lifelong learning initiatives.

This talk aims to underscore the significance of dHL, identify existing research gaps, share lessons from the IDEAHL EU project, and explore strategies for accelerating digital transformation in healthcare.

SESSION 5 | **TOWARDS EMPOWERMENT**

Enabling Next-Gen Healthcare Workforce

Hatim ABDULHUSSEIN

In this talk, we will explore the transformative vision set forth by the Topol Review, which aims to prepare the healthcare workforce to deliver the digital future. We will delve into how the NHS is adapting to and preparing for new technologies, with a particular focus on the impact of artificial intelligence (AI) on the workforce. Drawing from our extensive work within the NHS, we will highlight key insights and lessons learned in understanding the workforce implications of AI. Additionally, we will discuss the proactive measures being taken at Health Innovation KSS to equip the future healthcare workforce with the necessary skills and knowledge to thrive in an increasingly digital and data-driven environment. Join us as we navigate the journey from vision to reality, ensuring that our healthcare professionals are well-prepared to embrace the innovations of tomorrow.

SESSION 5 | **TOWARDS EMPOWERMENT**

Empowering the Patient in the Precision Medicine Era

Mette Nordahl SVENDSEN & Mie Seest DAM

In this talk we explore selection practices in precision medicine. Precision medicine holds the great hope of selecting genetically fit medicine for the patient. However, in on-the-ground clinical practices, precision medicine is oriented towards selecting clinically and genetically fit patients for available therapies. Based on ethnographic research in oncology clinics and experimental labs, we show that matching patients with treatment is inseparable from dealing organizationally and morally with the large group of patients identified as unlikely to benefit from personalized cancer therapies. On one hand, precision medicine empowers patients who fit therapies or experimental trials. On the other hand, patients who have contributed their tissue and time to precision medicine, but do not match available therapies feel disempowered. They show us the huge challenges of turning the absence of personalized treatment options into care for patients.

SESSION 6 | **BEYOND THE LABEL**

Drug repositioning in CLOVES Syndrom

Guillaume CANAUD

CLOVES syndrome (congenital lipomatous overgrowth, vascular malformations, epidermal naevi, scoliosis/skeletal and spinal syndrome) is a genetic disorder that results from somatic, mosaic gain-of-function mutations of the PIK3CA gene, and belongs to the spectrum of PIK3CA-related overgrowth syndromes (PROS). This rare condition has no specific treatment and a poor survival rate. Here, we describe a postnatal mouse model of PROS/CLOVES that partially recapitulates the human disease, and demonstrate the efficacy of BYL719, an inhibitor of PIK3CA, in preventing and improving organ dysfunction. On the basis of these results, we used BYL719 to treat nineteen patients with PROS. The drug improved the disease symptoms in all patients. Previously intractable vascular tumours became smaller, congestive heart failure was improved, hemihypertrophy was reduced, and scoliosis was attenuated. The treatment was not associated with any substantial side effects. In conclusion, this study provides the first direct evidence supporting PIK3CA inhibition as a promising therapeutic strategy in patients with PROS.

SESSION 7 | **FILLING THE GAPS**

Next-Generation Imaging in Fetal and Newborn Medicine

Ellen GRANT

This session will describe novel strategies for image acquisition and analysis aimed at enhancing the clinical management of fetuses and infants. Discussions will delve into the interplay between placental function and fetal brain development, alongside the repercussions of hypoxic stress. Moreover, the session will highlight the burgeoning role of artificial intelligence (AI) in fetal deep phenotyping and in neonatal outcome prediction for hypoxic ischemic encephalopathy (HIE). The potential for vital monitor waveform data combined with novel frequency domain near infrared spectroscopy / diffuse correlation spectroscopy to improve clinical management in the neonatal intensive care unit and provide more nuanced outcome prediction will also be discussed.

SESSION 7 | **FILLING THE GAPS**

Data-Empowered Strategies in Polykystic Kidney Disease

Fouad CHEBIB

Precision Imaging in ADPKD: AI-Driven Radiogenomics for Diagnosis and Predicting Disease Progression

In the evolving landscape of precision medicine, artificial intelligence (AI) is transforming the diagnosis and prognostication of complex genetic disorders, particularly Autosomal Dominant Polycystic Kidney Disease (ADPKD). Our research employs advanced AI methodologies, including machine learning and neural networks, to perform high-resolution quantitative analyses of radiological data, uncovering distinct radiomic signatures associated with ADPKD. By systematically assessing key imaging biomarkers—such as total cyst number, volume and cyst parenchymal surface area—we are constructing a comprehensive digital phenotype that enhances the precision of ADPKD characterization.

This digital phenotype facilitates the stratification of ADPKD subtypes, including ADPKD-PKD1, ADPKD-PKD2, ADPKD-GANAB, ADPKD-IFT140, and ADPKD-DNAJB11, each exhibiting distinct radiological profiles reflective of their genetic underpinnings. By integrating AI-driven radiomic profiling with quantitative radiogenomics, we aim to refine diagnostic accuracy and develop predictive models for individualized disease progression. A key focus is forecasting the onset of kidney failure (KF), which in ADPKD patients demonstrates striking heterogeneity, occurring as early as the third decade of life or as late as the eighth.

In this lecture, I will illustrate how AI and radiomic innovations are driving paradigm shifts in ADPKD diagnosis, risk stratification, and prognosis. We will explore how AI-powered imaging biomarkers can inform individualized treatment strategies and optimize clinical decision-making, marking a critical step toward precision nephrology. By leveraging AI in radiogenomics, we move closer to a future where early intervention and tailored therapeutic approaches mitigate disease burden and improve patient outcomes.

SESSION 7 | **FILLING THE GAPS**

Leveraging Collective Intelligence for inclusive Global Healthcare

Shadi ALBARQOUNI

Deep Learning (DL) stands at the forefront of artificial intelligence, revolutionizing computer science with its prowess in various tasks, especially in computer vision and medical applications. Yet, its success hinges on vast data resources, a challenge exacerbated in healthcare by privacy concerns. Enter Federated Learning, a groundbreaking technology poised to transform how DL models are trained without compromising data security. By allowing local hospitals to share only trained parameters with a centralized DL model, Federated Learning fosters collaboration while preserving privacy. However, hurdles persist, including heterogeneity, domain shift, data scarcity, and multi-modal complexities inherent in medical imaging. In this illuminating talk, we delve into the clinical workflow and confront the common challenges facing AI in Medicine. Our focus then shifts to Federated Learning, exploring its promise, pitfalls, and potential solutions. Drawing from recent breakthroughs, including a compelling MR Brain imaging case study published in Nature Machine Intelligence, we navigate the landscape of secure and efficient AI adoption in healthcare.

SESSION 8 | **CLOSING KEYNOTE**
A LEARNING JOURNEY
Precision Medicine: Lessons from the Fields
Mark RUBIN

Precision medicine strives to identify the right treatment at the right time for the right patient. Over the past decade, there have been several success stories in precision medicine. What is often less appreciated are the challenges faced by the broad biomedical community and healthcare systems in implementing precision medicine into our daily practice. In the lecture, I hope to provide background on the elements needed to create a learning system that will allow precision medicine to improve our care of patients. I will give specific examples of precision medicine successes and pathways for making precision medicine success a more common event.

SATELLITE EVENT - ORCHARD
Autologous Ex Vivo Gene Therapies Development in Rare Diseases: in the Perspective of the Global Gene Therapy Landscape.
Simon JONES

WORKSHOP - THERMOFISHER SCIENTIFIC
Expanding Capabilities Towards Omics-Based Workflows In Precision Medicine.
Yannick THIRIET

Translational research and precision medicine require workflows that can support the expanded scale needed to identify and transfer promising biomarker candidates to verification and validation phases. Translational research of biomarkers is pivotal in bridging the gap between laboratory discoveries and clinical practice, underpinning personalized medicine by enabling tailored treatment plans based on individual molecular profiles. With best-in-class components covering everything from targeted sample preparation, maximum separation performance, orthogonal selectivity, to sensitive data acquisition and downstream data processing, we will discuss innovations to our LC-MS portfolios designed to increase the speed of biomarker verification and validation through enhanced laboratory productivity and expanded experimental capacity.

Orchard therapeutics

ThermoFisher SCIENTIFIC

revvity

Takeda

Amicus Therapeutics

Olink

Fondation Daniel Hunt Normandie

Chiesi Global Rare Diseases

LUPIN NEUROSCIENCES

BIOMARIN

sanofi

ALEXION AstraZeneca Rare Disease

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