BEYOND INNOVATION, SOCIAL AND ETHICAL PERSPECTIVES ON BIO-DERIVED AND NIO-DIGITAL TECHNOLOGIES : PROMISE AND RISKS

SUMMER SCHOOL 2026 EDITION
GRADUATE PROGRAMME «PRECISION HEALTH»

DATES
6th to 8th of July

LOCATION
Hub Eurasanté & ESJ Lille

CONTACT
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Between technical feats and scientific hubris, technoscience is making its way into healthcare practices, ranging from the repair of the human body to its enhancement. Is this, then, a promise or madness? A myth or reality? A miracle or mirage? Through lectures by renowned speakers, roundtable discussions, and the presentations of our students' scientific work, this summer school will offer an opportunity to reflect on the consequences of dominant technoscientific paradigms for humanity - both in terms of progress for our societies and as a threat to the future - drawing in particular on example such as brain-machine interfaces, digital twins, and mirror bacteria.

PROGRAMME

July 6, 2026 – Hub Eurasanté

13h30	**Accueil**
	Session 1 Modération : Sophie LESTAVEL & Margaux LEDUC
14h-15h	**Raphaël BENTEGEAC** MD-PhD, santé publique et médecine sociale, CHU LILLE, INSERM u1167, RIDAGE, Institut Pasteur de Lille **"Intérêt et danger de l'utilisation de l'IA pour l'analyse des données de santé "**
15h-16h	**Blaise YVERT** DR Inserm, responsable équipe neurotechnologies et dynamiques des réseaux, Institut des neurosciences, Grenoble **"Interfaces cerveau machine et neuroprothèses : fonctionnement, perspectives et questions éthiques associées"**
16h-16h20	**Flash-talks par les étudiants PhD** • Alessio BURIN (LilNCog) • Léna CHESNAIS (LilNCog) • Marine GAUTIER-Martins (LilNCog) • Narod TASHJIAN (RID-AGE)
16h20-18h30	**Session posters** Présentation orale par les PhD devant un jury, discussions interactives
18h30	**Dégustation "Saveurs et savoirs"**

July 7, 2026 – Ecole Supérieure de Journalisme de Lille (ESJ)

9h30	**Accueil café**
	Session 2 Modération : Benoit POURCET & Julian LALOYAUX
10h-11h	**Hervé CHNEIWEISS** PH Neuro-oncologie Salpêtrière, Directeur du Comité d'éthique de l'Inserm, Paris **"Au-delà de l'innovation : pour une éthique des systèmes bio-numériques en santé de précision -** Jumeaux numériques, bactéries miroirs et interfaces cerveau-machine entre promesses biomédicales, incertitudes épistémiques et responsabilité collective"
11h-12h	**Ariel LINDNER** DR Inserm, Sorbonne Université, cofondateur du Learning Planet Institute, Paris Titre à confirmer **"Défis sociaux et éthiques de la biologie d'ingénierie contemporaine"**
12h-12h20	**Flash-talks par les étudiants PhD** • Salomé FARGE (U1011) • Zeineb RAMNAL (U8199) • Arman SHAHRISA (U1190) • Elise WREVEN (U1190)
12h20-14h	**Cocktail déjeunatoire**
	Session 3 Modération : Julien CHAPUIS & Ibtiha HEIZILI
14h-15h	**Claire CHERY** Responsable documentaire INA Hauts-de-France & Normandie "**Science et médias : la représentation des innovations scientifiques à la télévision française**"
15h-15h20	**Flash-talks par les étudiants PhD** • Charlotte BOCQUET (U1011) • Tiffany GENCARELLI (U1190) • Adel GUIOT (PRISM) • Hugo SEGURA (UGSF)
15h20-15h45	**Pause café**
16h - 17h30	**Table ronde** réflexion sur les enjeux sociétaux et éthiques des innovations scientifiques • **Claire CHERY** Responsable documentaire INA HdF & Normandie • **Hervé CHNEIWEISS** Neurologue, Directeur du Comité d'éthique de l'Inserm, Paris • **Ariel LINDNER** DR Inserm, Sorbonne Université • **Stéphane ZYGART** PhD, Professeur de Philosophie, Université de Lille
18h	**Fin de la journée – possibilité de prolonger les discussions au café "L'écart"**

July 8, 2026 - Ecole Supérieure de Journalisme de Lille (ESJ)

9h	**Accueil** **Session 4 "CDP MOSAIC"** Modération : Alexandre GRASSART & Arij HAMOUD
9h-9h40	**Corentin SCHOLAERT** IR, IEMN (Institut d'Electronique, de Microélectronique et de Nanotechnologie), Univ Lille **"Organic Bioelectronics: Bridging Electronics and Living Systems"**
9h40-10h20	**Samy GOBAA** Chercheur, Institut Pasteur Paris **"Modelling viral and bacterial infections in human advanced *in vitro* models"**
10h20-10h35	**Flash-talks par les étudiants PhD** • Lucie LIEFOOGHE (U1167) • Thibault NICOD (U1172) • Quentin VANPEENE (CIIL-IEMN)
10h35 - 11h	**Pause café**
11h - 11h40	**Fabien MILANOVIC** Sociologue, enseignant chercheur Sup'Biotech Département des sciences humaines, économiques et sociales, Univ Paris Descartes **"Au-delà de la biologie, les organoïdes en société. Une approche en sciences sociales"**
11h40 - 12h20	**Samuel ARRABAL** Agence de Biomédecine. **"Enjeux éthiques et réglementaires sur les organoïdes, cérébroïdes, embryoïdes"**
12h20-12h30	**Discussion Générale**
12h30	**Prix poster et prix flash-talk**
12h35	**Déjeuner de cloture – Fin de l'évènement**

SPEAKER BIOPIC

RAPHAËL BENTEGEAC
MD, MPH, Chef de Clinique-Assistant (CCA) at Lille University Hospital and Lille University

INTÉRÊT ET DANGER DE L'UTILISATION DE L'IA POUR L'ANALYSE DES DONNÉES DE SANTÉ

He is a Public Health Specialist and is currently pursuing his PhD under the co-direction of Dr. Aghiles Hamroun within Team 1 of the Inserm UMR 1167 RID-AGE research unit at the Pasteur Institute of Lille. His doctoral research is deeply anchored at the intersection of epidemiology, clinical reasoning, and computer science, focusing on the methodological evaluation, reliability, and safety of large language models (LLMs) in medicine, with a particular application to nephrology. As a researcher and software engineer, Raphaël explores how generative AI can be rigorously integrated into medical workflows and real-world data reuse without compromising clinical safety. He is the sole creator and lead developer of ECOSBot, an innovative generative AI-based tool for clinical simulation and objective structured clinical examination (OSCE/ECOS) training. He also serves as a key methodological and technical investigator in major AI-driven clinical trials and projects, including the international REFINe trial on AI-assisted clinical reasoning and the French ministerial DAtAE CEPHALAG.IA project.

SPEAKER BIOPIC

BLAISE YVERT
PhD in Biomedical Engineering
Researcher leading the team Neurotechnology and Network Dynamics at the Grenoble Institute of Neuroscience

INTERFACES CERVEAU MACHINE ET NEUROPROTHÈSES : FONCTIONNEMENT, PERSPECTIVES ET QUESTIONS ÉTHIQUES ASSOCIÉES

He received his Engineering degree from Ecole Centrale de Lyon and Cornell University in 1993, his PhD in Biomedical Engineering from Insa Lyon in 1996, and his habilitation (HDR) in 2008. In his early carrier, by started to work on human brain imaging of auditory areas using EEG, MEG and intracranial EEG (SEEG). From 2003, he then developed neurotechnologies to better interface the central nervous system using electrophysiological devices and improve neural stimulation for rehabilitation systems. In 2012- 2013 he became appointed Fulbright Visiting Scholar at the Brown Institute for Brain Sciences (directed by John P. Donoghue) in the field of human brain-computer interfaces (BCIs). Since 2013, his research interests focus on the development of new cortical interfaces and BCI systems to restore speech by decoding brain signals. He coordinates several collaborative projects and networks in the field of neurotechnologies, including the annual international Neurotech School, as well as the Grenoble Initiative in Medical Devices (GIMeD) Labex aiming at promoting early research for health technologies.

SPEAKER BIOPIC

HERVÉ CHNEIWEISS

Neurologist and Neuroscientist, Emeritus Research Director (CNRS) at the Centre for Neuroscience Sorbonne University (NeuroSU, and its former head 2014-2024) and neuro-oncologist at hospital La Salpétrière (AP-HP)

AU-DELÀ DE L'INNOVATION : POUR UNE ÉTHIQUE DES SYSTÈMES BIO-NUMÉRIQUES EN SANTÉ DE PRÉCISION

Trained as a neurologist (movement disorders, neurogenetics and then brain tumors), his scientific work was dedicated to the molecular biology (stathmin, PEA15) and plasticity of astrocytes and for the last 20-y their roles in brain tumor origin (identifying stem-like cancer cells), progression and treatment resistance, identifying new metabolic drivers and therapeutic avenues. He has authored more than 200 academic papers.

He is also involved in bioethics, presently chair Inserm Ethics Committee, EMBL Ethics Board, EBRAINS Science and Society and ARRIGE, member and past-chair of UNESCO International Bioethics Committee (2014-2021), former member French National Ethics Committee (CCNE, 2013-2017), WHO advisory committee on developing global standards for governance and oversight of human genome editing (2019-2021), expert for OECD for neurotechnology (2015-present). He was also co-chair of the AHEG UNESCO to draft the recommendation on ethics of neurotechnology (2024) and chair of the intergovernmental committee leading to their final adoption (General conference Samarkand nov. 2025). Member of several scientific councils such as Fondation Brocher (Switzerland, since 2018) or Fondation pour la recherche médicale (FRM, France, chair 2020-2026). He wrote several books or chapters on bioethics of human embryos, stem cells, genetics and neuroscience.

SPEAKER BIOPIC

ARIEL LINDNER
Research director at the French National Institute of Health and Medical Research (INSERM) and Sorbonne University
CSO of the Paris Biofoundry
Co-founder of the Learning Planet Institute

DÉFIS SOCIAUX ET ÉTHIQUES DE LA BIOLOGIE D'INGÉNIERIE CONTEMPORAINE

Member of the iGEM Foundation and member of the International Bioethics Committee (UNESCO), he is graduated from the 'Amirim' interdisciplinary program with a major in Chemistry (Hebrew University, Jerusalem) and received his M.Sc. and Ph.D. from the Weizmann Institute of Science for work on enzyme models, antibody conformational changes and directed evolution. After a research period on protein structures at the Scripps Institute (California, USA), and postdoctoral work in Paris on bacterial genetics, he tenured at INSERM and now direct the U1284 SEED (Systems Engineering and Evolution Dynamics) Unit. His research interests revolve around applying Physical, Chemical and Systems/Synthetic Biological approaches to study variability between clonal individuals on one hand and engineer bacteria on the other. Major contributions in past 5 years include publications in PLoS, eLife, Nature, Science, Cell and PNAS journals . He coordinated the Citizen CyberLab European project (citizencyberlab.eu), he took part in the Axa foundation Chair on Longevity. He co-created the CRI Masters and PhD programs, based on novel adaptive learning using ICT and organized numerous interdisciplinary research/education workshops around the world.
More on his lab's work here: https://elis-labs.org
In addition, he is involved in research at the interface between art & science.
See his latest project at http://www.ramedhanlevi.com/measure-for-measure-the-project/

SPEAKER BIOPIC

CLAIRE CHERY
Head of Documentation at the INA Nord regional office

SCIENCE ET MÉDIAS : LA REPRÉSENTATION DES INNOVATIONS SCIENTIFIQUES À LA TÉLÉVISION FRANÇAISE

She helps carry out the missions of the National Audiovisual Institute (INA) and represents the institute in the Hauts-de-France and Normandy regions. Her work primarily involves collecting, preserving, and promoting the audiovisual heritage among the general public, as well as educational and academic communities and professionals.

SPEAKER BIOPIC

STÉPHANE ZYGART
PhD in philosophy
Teach at the University of Lille and Sciences Po Lille

RÉFLEXION SUR LES ENJEUX SOCIÉTAUX ET ÉTHIQUES DES INNOVATIONS SCIENTIFIQUES

Member of the Hauts-de-France Regional Ethics Think Tank and the Ethics and Scientific Committee of the Lille University Hospital Health Data Repository. His work focuses on the epistemology of medicine and psychiatry, medical ethics, and health policy.

His most recent book is « Life, Activity, Disability: Rehabilitation and Medical-Social Standards » (Éditions de la Sorbonne, 2023).

Other texts and works are available on the website: https://transfinis.eu

SPEAKER BIOPIC

CORENTIN SCHOLAERT
Research Engineer at the Institute of Electronics, Microelectronics and Nanotechnology (CNRS)

ORGANIC BIOELECTRONICS: BRIDGING ELECTRONICS AND LIVING SYSTEMS

He develops devices for interfacing with living systems. He earned his PhD through research on the growth and properties of conducting polymer fibers for applications in unconventional computing and electrophysiology. His current work focuses on the fabrication of transparent microelectrode arrays based on organic electronics. Leveraging conventional microfabrication processes derived from the semiconductor industry, he develops innovative bioelectronic interfaces. In his presentation, he will discuss recent advances in organic bioelectronics and highlight the key technological challenges facing the field.

SPEAKER BIOPIC

SAMY GOBAA
Engineer, Head of the Organ-on-Chip Center& Head of the Biomaterials and Microfluidics core facility at the Institut Pasteur of Paris

MODELLING VIRAL AND BACTERIAL INFECTIONS IN HUMAN ADVANCED IN VITRO MODELS

My work touched on developing various approaches to better understand tissue complexity and homeostasis. On the engineering side I designed multiple tools/devices tailored for investigating the cell-microenvironment multifactorial interactions in high throughput. I also contributed to the design and implementation of microfluidic assays capable of recapitulating tissue level organization on chip. On the biological side, I tried to address cell- and tissue-level questions including the impact of the biophysical and biochemical cues on stem cell differentiation. In 2015 I joined Institut Pasteur with the objective of implementing bioengineering tools development as core facility services. Today the facility is proposing multiple solutions for the development and use of advanced in vitro culture systems based on organ on chip and organoid technologies.

SPEAKER BIOPIC

FABIEN MILANOVIC
Sociologist
Faculty member at SupBiotech

AU-DELÀ DE LA BIOLOGIE, LES ORGANOÏDES EN SOCIÉTÉ. UNE APPROCHE EN SCIENCES SOCIALES

He heads the Department of Humanities, Economics, and Social Sciences, as well as the SupBiotech school's social sciences research laboratory, PBS.
Specializing in Science & Technology Studies, he has spent the past twenty years studying living organisms (humans, animals, and plants), particularly the activities involved in their banking and the uses to which they are put.
He is currently working on two research areas: one on biomedicine (with an ANR grant he coordinates on organoids, https://organact.fr), and the other on the environment (through an interdisciplinary research project funded by FranceAgrimer on innovations related to biocontrol in agriculture, utilizing viruses and bacteriophages).
Finally, he will defend his HDR thesis next fall at EHESS, focusing on living organisms and biotechnologies.

SPEAKER BIOPIC

SAMUEL ARRABAL

Ph.D. in science and serves as head of the Research, Europe, International Affairs, and Monitoring Division at the French Biomedicine Agency

ASPECTS ÉTHIQUES ET RÉGLEMENTAIRES DE LA RECHERCHE SUR LES ORGANOÏDES, CÉRÉBROÏDES ET EMBRYOÏDES

He is particularly interested in issues of governance and regulation in biomedical research and has been working for more than fifteen years on issues related to research on human embryos, stem cells, and new life sciences technologies. He also contributes to national and European discussions on the regulatory framework for this research.

FLASHTALK: POSTER 1

ALESSIO BURIN
LilNCog

LET'S STICK TOGETHER: MOLECULAR GLUES AS A NOVEL TOOL TO BLOCK LRRK2 KINASE ACTIVATION

Authors:
Alessio Burin[1], Margaux Morez[1,] Beatrice Masotti[3], Antonio Jesús Lara Ordóñez[1], Chloé Annicotte[1], Arjan Kortholt[4], Maarten Altelaar[2], Elisa Greggio[3], Christian Ottmann[2,5], Jean-Marc Taymans[1]

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2Ambagon Therapeutics, Eindhoven, The Netherlands
3University of Padova, Department of Biology, Padova, Italy
4Department of Cell Biochemistry, University of Groningen, Groningen, The Netherlands
5Laboratory of Chemical Biology, Department of Biomedical Engineering and Institute for Complex Molecular Systems, Eindhoven University of Technology, Eindhoven, The Netherlands

Scientific context:
A fundamental principle of therapeutic targeting of LRRK2 is to attenuate its kinase activity, that is hyperactivated in Parkinson's disease (PD).
Objectives:
In this study, we evaluated an alternative approach to target LRRK2 kinase activation, LRRK2:14-3-3 complex stabilization with molecular glues.
Materials and methods:
In this work we use 2 LRRK2:14-3-3 tool compounds previously developed in our consortium and explore the effects of LRRK2:14-3-3 stabilization on LRRK2 activity in activation conditions.
Results and discussion:
Our results confirm that chloroquine treatment causes significant LRRK2 activation, as measured by the phosphorylation of the LRRK2 substrate Rab10, and we show that pre-treatment with 1 μM of molecular glues blocks chloroquine induced activation in LRRK2 expressing SH-SY5Y cells. Conversely, LRRK2:14-3-3 complex disruption by difopein can increase Rab10 phosphorylation, and combining chloroquine treatment with difopein expression enhances this effect.
Conclusions:
Our work demonstrates the effectiveness of stabilizing the LRRK2:14-3-3 complex to block LRRK2 activation, establishing molecular glues as a promising LRRK2 targeting approach for PD therapy.

FLASHTALK: POSTER 2

LÉNA CHESNAIS
LilNCog

ROLE OF TAUOPATHY AND ASSOCIATED ASTROCYTIC A2A ADENOSINE RECEPTORS DYSREGULATION IN DEPRESSIVE SYMPTOMS ASSOCIATED WITH ALZHEIMER'S DISEASE.

Authors:
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Abstract :

Alzheimer's disease (AD) is characterized by an hippocampal tauopathy that contributes to cognitive decline. Beyond memory impairment, depression is a common and burdensome symptom, although its mechanisms and links to tauopathy remain poorly understood. Enhanced activity of glutamatergic projections from the ventral hippocampus (vHPC-CA1) -an early site of tauopathy development in AD- to the nucleus accumbens (NAc) promotes susceptibility to anhedonia and social withdrawal. Interestingly, in the AD brain, development of tauopathy and memory deficits are associated to the upregulation of astrocytic adenosine A2A receptors (A2AR), one target of caffeine. Our team has recently shown that such A2AR upregulation reduces astrocytic GLT-1 expression, contributing to impaired glutamate uptake and hippocampal neuronal hyperexcitability. Together, these observations suggest that hippocampal tauopathy may disrupt the vHPC–NAc circuit, increasing vulnerability to depression-like behaviors through astrocytic A2AR dysregulation in vHPC.
The present project aims at investigating (1) the impact of neuronal tauopathy to the vHPC on vHPC–NAc circuit excitability, astrocytic responses (GFAP, GLT-1), and depressive-like behaviors; (2) the effects of astrocytic A2AR upregulation towards these processes; and (3) the therapeutic potential of the FDA-approved selective A2AR antagonist Istradefylline (KW6002).
To achieve this, we will combine (1) viral-vector approaches in mice (males and females), to selectively induce neuronal tauopathy or astrocytic A2AR overexpression in vHPC ; (2) behavioral assays, (3) retrograde tracing coupled to ΔFosB imaging to monitor neuronal excitability and (4) vHPC patch-clamp recordings.
Our preliminary data indicate that astrocytic A2AR upregulation in the vHPC induces social withdrawal and behavioral despair in males. These results indicate that astrocytic A2AR upregulation, promoted by tauopathy in AD, is sufficient to favor depression-like phenotypes.

FLASHTALK: POSTER 3

MARINE GAUTIER-MARTINS
LilNCog

INTER-BRAIN SYNCHRONY AS A DIAGNOSTIC AND PROGNOSTIC MARKER OF SOCIAL COGNITION IN NEURODEVELOPMENTAL CONTEXTS

Marine Gautier–Martins[1], C.Cornillot[1], S. Leclercq[1] , S. Szaffarczyk[1], R. Ramadour[2], C-A. Seux[1], K. Chachlaki[1], V. Prévot[1], G. Dumas[2] & R. Jardri[1]

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[2] Univ. Montréal, CHU Ste-Justine, Montreal, QC, H3T 1C5, Canada

Interpersonal synchrony operates across behavioural, physiological, and neural levels and varies depending on interaction context and dyad type. This project aims to identify diagnostic and prognostic biomarkers of social cognition impairments using multimodal interpersonal synchrony. Specifically, it investigates behavioural, physiological, and neural markers across two neurodevelopmental windows: infancy and adolescence. The goal is to characterise how these markers relate to social cognition impairments and therapeutic outcomes.

Two parallel studies were conducted using a shared multimodal high-density electroencephalography hyperscanning framework in naturalistic, free-interaction paradigms, including electrocardiography and video recordings. For the infancy period, mother–infant dyads were recruited across three groups: term-born, preterm without nitric oxide treatment, and preterm treated with nitric oxide. For adolescents, dyads consisted of therapists and patients, divided into psychotherapy and control groups, with pre/post assessments. A dedicated pipeline was developed with EEG preprocessing, an automated mutual gaze detection system, cardiac synchrony and semantic alignment analyses.

Preliminary analyses reveal observable patterns of neural coupling. In infancy, early observations suggest potential differences in synchrony patterns between preterm and term dyads, supporting the hypothesis that prematurity affects social cognition mechanisms. In adolescence, pilot data indicate possible restructuring of neural and physiological synchrony following psychotherapy, aligning with models of therapeutic alliance and interbrain plasticity.

This work proposes a unified, multimodal framework to assess social cognition through interpersonal synchrony across development. By integrating neural, physiological, and behavioural measures in naturalistic interactions, this approach offers a promising avenue for identifying biomarkers of social cognition impairments.

FLASHTALK: POSTER 4

NAROD TASHJIAN
RID-AGE

ESCAPE OF FRMPD4 FROM X-CHROMOSOME INACTIVATION IN ALZHEIMER'S DISEASE

Julie Le Borgne, Raphael Margueron[2], Michel Wassef[2], Jean-Charles Lambert [1], Julien Chapuis [1].

1 : Université de Lille, Inserm, CHU Lille, Institut Pasteur de Lille, U-1167 - RID-AGE – Facteurs de risques et déterminants moléculaires des maladies liées au vieillissement, Lille 59000 France. Région Haut de France, Université de Lille
2 : Génétique et Biologie du Développement
Institut Curie [Paris], Institut National de la Santé et de la Recherche Médicale, Sorbonne Université, Centre National de la Recherche Scientifique

Background: Women are disproportionately affected by Alzheimer's disease (AD), although the mechanisms underlying this sex difference remain unclear. Recently, X-chromosome-wide association studies (XWAS) have identified FRMPD4 (FERM and PDZ domain-containing 4) as an AD-associated locus on the X chromosome. Interestingly, Interestingly, downregulation of FRMPD4 (also known as PSD-95-interacting regulator of spine morphogenesis or Preso1) has been shown to protect neurons from glutamate-induced excitotoxicity. Moreover, FRMPD4 has also been reported among genes that escape X-chromosome inactivation (XCI), a process that mediates dosage compensation in females. Since age-associated destabilization of XCI has been linked to amyloid pathology and cognitive decline, we hypothesize that incomplete inactivation of FRMPD4 may lead to deleterious overexpression in females.
Methods: To investigate the impact of X-chromosome genetic variants on AD risk, we conducted an in-depth XWAS including 115,841 AD cases or proxy cases and 613,671 controls. Escape from XCI was induced using a CRISPRi system to silence XIST expression. XCI maintenance was assessed by immunofluorescent detection of Barr body-associated markers and ChIP-seq analysis of H3K27me3 marks. FRMPD4 expression was examined by immunofluorescence and Western blotting in human neurons derived from induced pluripotent stem cells (iPSCs).
Results: XWAS analyses identified FRMPD4 as an AD-associated locus on the X chromosome. Synaptic expression of FRMPD4 was confirmed in human neurons. Reduced enrichment of repressive chromatin marks at the FRMPD4 locus following XCI escape was consistent with increased expression after X-chromosome reactivation.
Conclusion: All together our results suggested that escape from XCI could induce through sex-specific genetic risk factors an increase in synaptic vulnerability.

FLASHTALK: POSTER 5

SALOMÉ FARGE
U1011

THE NUCLEAR RECEPTOR REV-ERB-α CONTROLS ATHEROSCLEROTIC PLAQUE NEOVASCULARIZATION

Farge S[1], Bellengier C[1], Ferri L[1], Duhem C[1], Diedisheim M[2], Kara Ali G[1], Delhaye S[1], Ory K[1], Bongiovanni A[3], Hebras A[1], Leduc M[1], Bicharel M[1], Sebti Y[1], Venteclef N[2], Staels B[1], Haas J[1], Tardivel M[3], Gauthier JF[2], Duez H[1] & Pourcet B[1]

1 Université de Lille, INSERM, Institut Pasteur de Lille, EGID-U1011
2 Université Paris Cité, Institut Necker Enfants Malades, INSERM-U1151
3 Université de Lille, BiCel-US41

Plaque instability is the most deleterious atherogenic event leading to its rupture. Among destabilizing processes, intraplaque neovascularization accelerates progression, promotes rupture and limits statin benefits. Yet, its mechanisms remain unclear.
Using a combinatorial approach on human endarterectomies and diabetic patients at different cardiovascular risks, we identified Rev-erb-a as a key regulator of plaque complexity and neovascularization. While previously linked to lipid metabolism and inflammation, we further investigated its role in neovascularization. Bulk RNAseq analysis showed upregulation of pro-angiogenic pathways in 18-month-old Rev-erbα+/+LDLr-/- and Rev-erbα-/-LDLr-/- mice. Accordingly, scRNAseq revealed an enrichment of dysfunctional luminal endothelial cells when Rev-erbα is deleted.
We confirmed the presence of intraplaque neovessels in brachiocephalic arteries from 18-month-old LDLr-/- mice using whole organ imaging. Strikingly, Rev-erbα deficiency was associated with a denser and immature vascular network. Unexpectedly, neovessels also emerged from the lumen and from isolated endothelial cells, suggesting both angiogenic and vasculogenic processes. In vitro, we confirmed that Rev-erb-α modulates the pro-angiogenic program regulating tip-stalk cell shuffling and endothelial progenitor cell recruitment.

In conclusion, Rev-erb-α inhibits intraplaque neovascularization and may be a therapeutic target for plaque stabilization in very high cardiovascular risk patients.

FLASHTALK: POSTER 6

ZEINEB RAMMAL
U8199

EPIGENETIC SIGNATURES OF AGING AND INSULIN SENSITIVITY IN HUMAN SKELETAL MUSCLE

Zeinab Rammal[1,2], Lucas Maurin[1,2], Marie Fourcot[1,2], Bénédicte Toussaint[1,2], Souhila Amanzougarene[1,2], Mehdi Derhourhi[1,2], Violeta Raverdy[2,3], François Pattou[2,3], Amélie Bonnefond[1,2], Philippe Froguel[1,2,4], Amna Khamis[1,2,4]

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2Univ. Lille, Inserm, CHU Lille, Institut Pasteur de Lille, EGID, F-59000 Lille, France.
3Inserm, Translational Research in Diabetes (U1190), Lille, France.
4Department of Metabolism, Digestion and Reproduction, Imperial College London, London, United Kingdom.

Introduction: Skeletal muscle is the primary site of insulin-stimulated glucose uptake and a major determinant of insulin resistance in type 2 diabetes (T2D). Aging is a strong risk factor for T2D, yet the epigenetic mechanisms linking skeletal muscle aging to impaired insulin signaling remain poorly understood.
Methods: Skeletal muscle biopsies were obtained from 84 individuals (27–45 years). DNA methylation was profiled using Illumina MethylationEPIC (850K) arrays, and age-associated epigenome-wide association studies (EWAS) were performed. RNA sequencing and genome-wide genotyping (Omni2.5M array) were integrated to identify cis-regulatory targets, with causality assessed by Mendelian randomization (MR).
Results: Age exhibited the strongest epigenetic signal, identifying 307 DNA methylation changes, including established age-associated loci (ELOVL2 and FHL2). Integrative analyses identified 124 target genes (±1Mb), with CpGs enriched in promoter and enhancer regions overlapping key transcription factor binding sites (i.e., CTCF). MR supported causal effects of methylation on gene expression. Notably, methylation negatively regulated the insulin receptor (INSR), directly implicating epigenetic modulation of insulin signaling. Additional causal targets included mitochondrial (COQ9, UQCR11), oxidative stress (NQO1), and structural muscle genes (MYOM2), implicating age-related pathways that converge on insulin resistance. Direct associations between methylation and glycemic traits (HOMA2-IR, HbA1c, fasting glucose etc.) were limited, indicating that muscle epigenetic changes are primarily age-dependent and likely act upstream of metabolic dysfunction.
Interpretation: Our comprehensive, multi-omic work indicates that skeletal muscle epigenetic aging drives transcriptional remodeling of insulin signaling and metabolic pathways, positioning age-related DNA methylation as an upstream regulatory layer of metabolic dysfunction.

FLASHTALK: POSTER 7

ARMAN SHAHRISA
U1190

BASELINE LIVER TRANSCRIPTOMIC SIGNATURE OF FIBROSIS NON-RESPONSE 5 YEARS AFTER BARIATRIC SURGERY

Arman shahrisa[1], Guillaume Lassailly[2], Violeta Raverdy[1,3], and Stefano Romeo[4,5,6,7,8] and François Pattou[1,3*]
1. Translational Research for Diabetes UMR 1190, University of Lille, Inserm, Institut Pasteur Lille, CHU Lille, Lille, France2. Inserm, U1190, F-59000 Lille, France
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Background
Bariatric surgery dramatically improves metabolic parameters, yet liver fibrosis persists in a subset of patients. Distinguishing the unique baseline molecular vulnerabilities of these «non-responders» from general fibrosis markers is essential for predicting patient trajectories and optimizing long-term monitoring.
Objectives
To uncouple general fibrosis pathways from the specific baseline transcriptomic signature unique to patients who exhibit persistent liver fibrosis 5 years post-bariatric surgery.
Methods
We employed a dual-stratification strategy on a French bariatric cohort, analyzing baseline liver microarray transcriptomics. Patients were first stratified by their baseline fibrosis severity to identify common disease pathways, and then independently stratified by their 60-month outcomes (responders with regression vs. persistent non-responders). Partial Least Squares Regression (PLS-R) and False Discovery Rate (FDR)-adjusted Spearman correlations were used across both models. Comparing the two approaches allowed us to filter out common fibrotic traits and isolate the transcriptomic features uniquely driving non-response.
Results
Cross-referencing stratification models successfully isolated the pre-operative non-responder phenotype from generic fibrosis. Feature selection (VIP > 1) and FDR analysis revealed a distinct baseline signature strictly unique to future non-responders: significant downregulation of MT1B and MT1JP, alongside elevated ZMAT3. Mechanistically, the loss of MT1B relieves AKT/PI3K inhibition to promote scar tissue formation, while decreased MT1JP impairs p53 translation, suppressing apoptosis. Conversely, elevated ZMAT3 drives P21 degradation and CDK2/4 activation, forcing cellular proliferation. Ultimately, non-responders possess an exclusive pre-existing hepatic environment—characterized by unchecked fibrogenesis, blocked apoptosis, and dysregulated cell cycling—that general fibrosis patients do not share.
Conclusion
By comparing baseline and 5-year outcome stratifications, we successfully isolated the specific transcriptomic vulnerabilities of non-responders from common fibrosis markers. The unique baseline signature of high ZMAT3 coupled with low MT1B and MT1JP identifies patients inherently resistant to fibrosis regression, providing precise prognostic biomarkers for post-operative care.

FLASHTALK: POSTER 8

ELISE WREVEN
U1190

MONLUNABANT : A BETTER STRATEGY TO TACKLE TYPE 1 DIABETES ?

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Introduction : Cannabinoid type 1 receptor (CB1R) blockade in islets prevents immune cell infiltration (insulitis) in type 1 diabetes (T1D), an autoimmune disease characterized by beta (β)-cell loss leading to insulinodeficiency and hyperglycemia. Mechanistically, CB1R blockade prevents islet nitric oxide (NO) production and lowers chemokine expression/sécrétion. While it improve β-cell function, it also drives glucose-stimulated insulin secretion (GSIS) beyond normal levels, possibly due to excessive Gαi–adenylal cyclase–cAMP signaling, which could be detrimental over time. We hypothesize that the β-arrestin–biased CB1R-inverse agonist monlunabant may prevent insulitis without causing insulin oversecretion.

Methods : Human islets ± same organs donor's immune cells (ex vivo model of insulitis), were treated with 1-100nM monlunabant (S-MRI-1891) or vehicle in the presence of proinflammatory cytokines (IL1β, TNFα, and IFNγ). β-cell function and insultis were assessed by GSIS, Seahorse Analyzer, continuous cell imaging, qPCR, and ELISA.

Results-Discussion : Monlunabant at 1 and 10nM preserved human β-cell function in proinflammatory conditions, without enhancing GSIS beyond control levels. Monlunabant protected mitochondrial function, preserving ATP production and further enhancing it 2-fold over control conditions. Monlunabant (10nM) also ameliorated insulitis : 1) prevented cytokine-induced NO production, 2) reduced 50±4% IL1B and CXCL10 expression/secretion, and 3) prevented immune cell infiltration into islets. These findings demonstrate that β-arrestin–CB1R signaling modulates islets inflammation, mitochondrial metabolism and GSIS. Its blockade succesfully preserves functional β-cell responses without leading to insulin oversecretion and potential β-cell exhaustion.

Conclusion : Monlunabant therefore represents a promising therapeutic candidate to preserve functional β-cell mass longterm in T1D.

FLASHTALK: POSTER 9

CHARLOTTE BOCQUET
U1011

CHARACTERIZATION AND FIBRINOLYTIC SUSCEPTIBILITY OF RIVAROXABAN-ASSOCIATED INTRACEREBRAL HEMATOMAS USING A CLINICAL-SCALE EX VIVO MODEL MIMICKING THE MINIMALLY INVASIVE SURGERY WITH THROMBOLYSIS FOR INTRACEREBRAL HEMORRHAGE EVACUATION (MISTIE) PROCEDURE

Charlotte Bocquet[1], Mickael Rosa[1], Mélanie Daniel[1], Delphine Corseaux[1], Timothée Bigot[1], Alexandre Ung[1], Antoine Rauch[1], Grégory Kuchcinski[2], Audrey M. Thiebaut[3], Laurent Puy[2], Charlotte Cordonnier[2], Jérôme Parcq[3], Sophie Susen[1], Annabelle Dupont[1]

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Scientific context
Intracerebral hemorrhage (ICH) is the most severe form of stroke (10–15% of cases), with high mortality, disability, and healthcare costs. The Minimally Invasive Surgery with Thrombolysis for ICH Evacuation (MISTIE) procedure is a promising treatment strategy; however, patients at high bleeding risk, particularly those treated with direct oral anticoagulants (DOAC), were excluded from clinical trials due to lack of preclinical data.

Objectives
Assess how rivaroxaban (largely prescribed DOAC) affects hematoma structure and fibrinolytic response in a model mimicking the MISTIE procedure.

Materials and methods
We developed a human ex vivo intracerebral hematoma model reproducing the MISTIE procedure (haematoma size, catheter placement, fibrinolytic delivery, drainage and treatment times). Hematomas were generated from 15 ml whole blood of healthy volunteers with or without rivaroxaban (400 ng/mL). Structure and composition were analyzed by immunofluorescence staining, scanning electron microscopy, and dynamic gadolinium-enhanced MRI. Fibrinolytic efficacy of alteplase and tenecteplase was evaluated by hematoma weight loss.

Results and discussion
Rivaroxaban significantly altered hematoma architecture, with a looser and less dense fibrin network, thicker and longer fibers, and larger pores. These changes were associated with increased hematoma permeability, with faster gadolinium diffusion on MRI. Moreover, rivaroxaban-associated hematomas had lower baseline weight, consistent with an increase of permeability due to altered fibrin organization. Fibrinolytic efficacy of alteplase and tenecteplase was not significantly different between control and rivaroxaban, though interindividual variability was notable.

Conclusion
Rivaroxaban alters hematoma structure and permeability without impairing fibrinolytic efficacy in a ex vivo MISTIE model. These findings support consideration of DOAC-treated patients in future ICH evacuation strategies using the MISTIE procedure.

FLASHTALK: POSTER 10

TIFANNI GENCARELLI
U1190

DEVELOPMENT OF CELL THERAPY FOR PARATHYROID AUTO-, ALLO- AND XENOGRAFTS FOR THE TREATMENT OF HYPOPARATHYROIDISM

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Hypoparathyroidism is a rare yet debilitating endocrine disorder caused by insufficient parathyroid hormone (PTH) secretion, resulting in chronic hypocalcemia and a range of neuromuscular and renal complications. When conventional treatments, including calcium and vitamin D supplementation, recombinant PTH, or autotransplantation, fail, new therapeutic strategies are required.
This PhD project aims to develop and standardize parathyroid transplantation using minced or enzymatically digested human hyperplastic tissue from living donors. The digested approach, based on a collagenase protocol inspired by pancreatic islet transplantation, offers advantages such as injectability and standardization but remains underexplored.
In vitro, digested cells were characterized by flow cytometry, RT-qPCR, and static incubation assays to assess cellular phenotype, viability, parathyroid marker expression, and calcium-dependent PTH secretion. In vivo, immunodeficient mice received renal subcapsular or intramuscular grafts using minced or enzymatically digested tissue. Human PTH secretion was monitored over time, and histology at day 30 assessed endocrine volume, vascularization, fibrosis, and proliferation.
Enzymatic digestion produced highly viable cells with minimal necrosis and preserved expression profiles, although temporal downregulation was expected and observed. Renal subcapsular grafts sustained PTH secretion and showed comparable integration, with reduced fibrosis in digested tissue. In contrast, intramuscular transplantation showed limited efficacy, likely due to the intrinsically pro-fibrotic nature of skeletal muscle, a less favorable environment for endocrine graft survival.
Overall, these findings confirm the feasibility of enzymatically digested grafts and highlight the potential of digested tissue for minimally invasive, injectable transplantation. Future work focuses on intramuscular transplantation in a minipig model to enable clinical translation.

FLASHTALK: POSTER 11

ADEL GUIOT
PRISM

HARDWARE AND SOFTWARE-BASED DEVELOPMENTS TOWARDS IN-VIVO MASS SPECTROMETRY IMAGING

GUIOT Adel[1], CHAILLOU Paul[2], CHERVILLE Barnabé[1], ZIREM Yanis[1], LEDOUX Léa[1], PICCINALI Thibaud[2], HAMHOUM Oumaima[1], FOURNIER Isabelle[1]

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Keywords : Mass Spectrometry Imaging, Open-Source, Modularity, Software, Python, MatLab, SOFA, Soft-Robotics

Cancer surgeries are very time-sensitive operations during which surgeons need as much information on the tumour as they can get. Mass Spectrometry (MS) has proven capable of providing extensive and highly accurate tissular information in real time, but MS Imaging (MSI) has seldom been used in this context. We have previously developed an ambient ionization technique, that could be used for intraoperative MSI and are currently working on using a deformable robot to allow for the use of this technique in minimally invasive surgeries, such as laparoscopies. Those hardware developments have led us to create our own software that could enable MSI acquisitions using a variety of hardware components, novel imaging modalities (i.e., Continuous imaging, 3D-MSI…) better suited to intraoperative constraints and that could provide a variety of tools for data processing.
The software's capabilities were tested on our MSI system by imaging (or profiling) fresh frozen rat brain and beef liver samples in positive and negative mode with no prior sample preparation. 3D-MSI was performed by adding a depth sensor to our classical imaging pipeline on mice breast tumours, as well as on several other samples such as thick beef liver sections and carved apple slices. 2D MSI data was exported to our own visualizer or Bruker's SCiLS for validation. Experiments regarding augmented reality were also carried out for 3D samples. Proof of concepts for soft robotics were obtained by bringing the robot to several points of interest on a carved apple with a custom controller in Python and assessing the difference in observed molecular profiles.
Through this work, we have been able to overcome three main limitations of in-man MSI: the topographical features of Regions Of Interest (ROI) on patients were tackled with triangulation sensors, imaging time was reduced by 21x by implementing continuous imaging down to a few minutes per cm2, and we have proven that a soft robot could be used to retrieve MS data through trocars.

FLASHTALK: POSTER 12

HUGO SEGURA
UGSF

A NOVEL REGULATORY PATHWAY FOR AMYLOPECTIN DEPOSITION IN TOXOPLASMA GONDII REVEALED THROUGH INACTIVATION OF TREHALOSE-6-PHOSPHATE SYNTHASE/PHOSPHATASE (TPSP).

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2 Univ. Lille, CNRS, Inserm, CHU Lille, Institut Pasteur de Lille, U1019-UMR 9017-CIIL-Center for Infection and Immunity of Lille, F-59000 Lille, France.

Current treatments for toxoplasmosis target only the tachyzoite stage, the actively replicating form of Toxoplasma gondii. However, the parasite can differentiate into bradyzoites, a dormant and highly resilient stage responsible for chronic infection. Reactivation of bradyzoites may lead to severe forms of toxoplasmosis, particularly in immunocompromised individuals. Previous studies on phosphatase TgPP1 showed that alterations in the phosphorylation status of trehalose-6-phosphate synthase/phosphatase (TPSP) lead to unexpected deposition of amylopectin in tachyzoites, suggesting a regulatory link between trehalose metabolism and carbohydrate storage.
This project aims to characterize the enzymatic properties of TPSP and its individual catalytic domains and to determine their role in amylopectin accumulation. Kinetic parameters of the recombinant enzymes will be established, while quantification of amylopectin, trehalose, and trehalose-6-phosphate (T6P) levels will be quantified in T. gondii mutant strains. The overall objective is to elucidate the molecular pathway connecting trehalose metabolism to amylopectin storage in the parasite.
To achieve these goals, expression vectors encoding the full-length TPSP and its catalytic domains were constructed. Recombinant protein production and purification strategies are currently being optimized. Enzymatic activities will be assessed using specific biochemical assays, whereas amylopectin content will be quantified by an enzymatic assay and trehalose and T6P levels by GC-FID.
To date, all expression constructs have been successfully generated. Initial expression trials revealed limited solubility of the recombinant proteins and optimization of production is ongoing.

FLASHTALK: POSTER 13

LUCIE LIEFOOGHE
U1167

4R ISOFORMS OF HUMAN TAU PROTEIN ALTER SYNAPTIC TRANSMISSION IN DROSOPHILA

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Tau neurofibrillary tangles, a hallmark of Alzheimer's disease (AD), spread trans-synaptically, progressively affecting connected neurons. This propagation correlates with the early synaptic loss and cognitive decline observed in AD. This work aimed to characterize the neurotoxic effects of human Tau on neuronal activity and synaptic transmission using Drosophila retina as a model system. In this system, electroretinogram (ERG) allows assessment of both photoreceptor neuron activity and synaptic transmission, through the measurement of retina depolarization and transient currents upon light stimulation.
We set up ERG recordings by standardizing light distance, intensity, and Drosophila eye color. We validated synaptic transmission readouts by showing an abolition of the transient currents upon tetanus toxin expression. The 6 human cerebral Tau isoforms, and some phospho-deficient/mimetic and R406W mutated variants were expressed in photoreceptor neurons and confirmed by western blot. Tau toxicity correlated with the number of microtubule-binding regions: 2N4R induced the strongest reduction in photoreceptor response amplitude, followed by 1N4R and 0N4R, while the 3R isoforms did not show any toxicity. Interestingly, 2N4R and 1N4R displayed synaptic toxicity prior to neuronal toxicity, suggesting a sequence of events in which synaptic dysfunction precedes neurodegeneration. The 2N4R-induced neurodegeneration was light-dependent. The phosphodeficient form of 0N4R was less toxic than the wild-type isoform, while R406W mutation exacerbated the toxicity of the 0N4R isoform, consistent with Tau phosphorylation and mutation being pathogenic.
These findings highlight the toxicity of 4R Tau isoforms especially at the synaptic level.

FLASHTALK: POSTER 14

THIBAULT NICOD
U1172

STUDY OF NEURON–ASTROCYTE INTERACTIONS IN THE CONTEXT OF ALZHEIMER'S DISEASE: MODELING USING MICROFLUIDIC SYSTEMS AND/OR MICROELECTRODE ARRAYS (MEA)

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LilNCog, Lille Neurodegeneration, Inserm UMR 1172

Alzheimer's disease (AD) is characterized by the accumulation in the brain of two pathological protein aggregates: amyloid-β peptides and abnormally phosphorylated tau. The progressive cognitive decline observed strongly correlates with the synaptic loss. An overexpression of the A_2A receptor, an adenosine receptor, has also been observed. In astrocytes, this overexpression is believed to contribute to excitotoxicity and to an imbalance between excitation and inhibition by impairing neurotransmitter transporter function in the tripartite synapse. These alterations contribute also in the progression of the hallmark pathological features of AD. This project objective is to study the relationship between tau pathology and the overexpression of the A_2AR by astrocytes, as well as their effects on synaptic function and neuronal circuit activity.
To analyze cellular interactions at the synaptic level, a microfluidic system reconstructs a neural circuit with three separated chambers linked by microchannels. Presynaptic neurons are on one side and postsynaptic neurons on the other, which form synaptic connections with the middle chamber in which astrocytes are integrated. Coupled with a MEA, this system allows the recording of neuronal activity in both chambers, thereby enabling the calculation of a connectivity between pre and post synaptic compartments and the functional evolution of synapses throughout the culture period.
With the overexpression of A2AR induced by an AAV, a significant increase of the activity has been shown in the postsynaptic chambers. However, the connectivity intra and inter chamber does not change. A2AR overexpression induces cascades that modify astrocytic calcium, promote the release of gliotransmitters and decrease the efficiency of glutamate reuptake by astrocytic transporters that lead to a stronger and longer activation of postsynaptic receptors. Tau recombinant protein will be added in this culture to modelise tau pathology and a glutamate assay in the synaptic cleft will allow the quantification of extracellular glutamate levels and their correlation with functional connectivity between the chambers.

FLASHTALK: POSTER 15

QUENTIN VANPEENE
CIIL-IEMN

DEVELOPMENT OF A HUMAN GUT-ON-A-CHIP INTEGRATING A MICROELECTRODE ARRAY TO INVESTIGATE SHIGELLA INFECTION DYNAMICS

Quentin Vanpeene[1,2], Corentin Scholaert[2], Anne-Sophie Vaillard[2], Sandra Weller[1], Yannick Coffinier[2] & Alexandre Grassart[1,3]

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Shigella is a major human-restricted enteric pathogen that invades the intestinal epithelium and spreads from cell to cell, yet its relationship with epithelial barrier integrity remains poorly understood. We aim to develop a human gut-on-a-chip model enabling real-time study of Shigella infection together with dynamic barrier monitoring. Our approach combines an in-house microfluidic chip, a transparent PEDOT:PSS-based microelectrode array for impedance-based TEER-like measurements, and hiPSC-derived intestinal organoids as a human relevant epithelial source. Preliminary results support the feasibility of the platform: we fabricated a biocompatible MEA device, obtained first impedance measurements, and generated hiPSC-derived intestinal organoids that were seeded into a microfluidic chip, where organoid-derived cells reached about 80% surface coverage after 7 days under static conditions. Flow will next be introduced to improve tissue coverage and differentiation. This platform will provide a relevant framework to study host-pathogen interactions in human intestinal models.
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POSTER 16

ADEL GUIOT

HARDWARE AND SOFTWARE-BASED DEVELOPMENTS TOWARDS IN-VIVO MASS SPECTROMETRY IMAGING

GUIOT Adel[1], CHAILLOU Paul[2], CHERVILLE Barnabé[1], ZIREM Yanis[1], LEDOUX Léa[1], PICCINALI Thibaud[2], HAMHOUM Oumaima[1], FOURNIER Isabelle[1]

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POSTER 17

JÉROMINE CARRET

INTEGRATED STRUCTURAL AND POPULA ON ANALYSIS OF PATHOGENIC MISSENSE VARIANTS IN THE MEDIATOR COMPLEX

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Scientific context
The Mediator complex is a central regulator of RNA polymerase II-dependent transcrip on. Pathogenic variants in several Mediator subunits have been associated with a growing group of neurodevelopmental disorders collec vely referred to as MEDopathies. Although numerous pathogenic missense variants have been reported, their molecular interpreta on remains challenging owing to the structural complexity of the Mediator complex.
Objectives
This study aimed to establish a systema c structural framework for the interpreta on of pathogenic missense variants across Mediator subunits. Specifically, we sought to iden fy recurrent structural signatures, and inves gate the dis nct molecular contexts underlying MED13 and MED13L pathogenic variants.
Materials & methods
A total of 134 pathogenic missense variants curated from HGMD (2024) and distributed across eleven disease-associated Mediator subunits were analyzed. In silico mutagenesis was performed on AlphaFold2 models using ChimeraX (v1.10), and five physicochemical descriptors were extracted. Unsupervised analyses, including Principal Component Analysis (PCA), were applied to iden fy pa erns of structural perturba on.
Results & discussion
Unsupervised analyses iden fied four structural impact classes among the 134 Mediator missense variants. C1 (n=4) corresponds to a MED13L-specific hydrophobic cluster; C2 (n=29) groups bulky subs tu ons in folded regions; C3 (n=23) captures variants in intrinsically disordered regions ; and C4 (n=78) represents func onal hotspot variants. MED13L variants in C1 are concentrated in a C-terminal region proximal to the ubiqui na on site, while MED13 variants in C3 converge on a phosphodegron hotspot, sugges ng convergent but mechanis cally dis nct perturba on of protein turnover between the two paralogs.
Conclusion & perspectives
Our results support MEDopathies as a coherent family of structural disorders affec ng modules of the Mediator complex. Structural descriptors derived provide informa on complementary to sequence-based pathogenicity predictors, and reveal dis nct molecular signatures for MED13 and MED13L variants. Extending this approach to addi onal Mediator subunits will further delineate the structural landscape of MEDopathies