FONDATION ALZHEIMER

8èmes RENCONTRES de la Fondation Alzheimer

19 & 20 novembre 2019
Cité Internationale Universitaire de Paris

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MARDI 19 NOVEMBRE 2019

Pavillon Néerlandais

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14h00 - 15h30

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- **CHECLER F.** - Understanding Aβ N-terminal truncation : a possible novel therapeutic track?
- **DHENAIN M.** - Transmission of cerebral lesions and of a neurodegenerative process by Alzheimer brains.
- **MESTRE-VOEGTLE B.** - Application of the Dynamic Combinatorial Chemistry Principle to the Amyloid-β Fibril Target

15h30 - 16h30 — Flash Posters

16h30 - 17h00 — Pause café / Posters

Pavillon Asie du Sud-Est

17h00 - 18h00 — **Conférence Pr Yaakov STERN** - Cognitive reserve: An evolving concept

18h30 — **Remise des Prix Joël Ménard**

- Prix recherche fondamentale
  remis par Marie-Claude POTIER
- Prix recherche clinique
  remis par Yaakov STERN
- Prix recherche sciences humaines et sociales
  remis par Martine BUNGENER

19h30 - 21h00 — Cocktail dînatoire

Il est souhaitable que les participants puissent **assister à l'ensemble des sessions** car, au delà des communications scientifiques, **les Rencontres de la Fondation Alzheimer sont conçues pour favoriser les discussions et les échanges informels entre participants.**

PROGRAMME

MERCREDI 20 NOVEMBRE 2019

Pavillon Néerlandais

9h30 - 10h30

2ème session : AAP and synoptic activity
Modérateurs : Raphaëlle PARDOSSI & Audrey GABELLE

- **MARIE H.** - A novel APP processing pathway and its physiological function in modulation of synaptic activity
- **MULLE C.** - Presenilin and APP in presynaptic plasticity

10h30 - 12h00

3ème session : Immunity and Inflammation in AD
Modérateurs : Marie-Claude POTIER & David WALLON

- **BONVENTO G.** - Identification of an astrocytic metabolic pathway that contributes to Alzheimer's Disease
- **DOROTHÉE G.**- Role and therapeutic potential of T cells in Tau pathology
- **NIVET E.** - Apolipoprotein E isoform-dependent human astroglial inflammation reveals an early pro-inflammatory state in APOE4 carriers underlying Alzheimer's disease

Pavillon Asie du Sud-Est

12h00 - 13h30 Déjeuner buffet

Pavillon Néerlandais

13h30 - 14h30

4ème session : New targets
Modérateurs : Nicolas SERGEANT & Olivier HANON

- **DALLEMAGNE P.** - The design of multi-target drug candidates with potential therapeutic interest against Alzheimer's disease
- **GEURS S.**- Single-nucleus Genome-plus-Transcriptome sequencing to study Somatic Genome Instability in Normal and Tauopathy Brain

14h30 - 15h00 Remise du Prix du meilleur poster

NOTES

FRÉDÉRIC **CHECLER**

IPMC, UMR7275 CNRS/UNS, Valbonne

Understanding Aβ N-terminal truncation : a possible novel therapeutic track?

N-terminal truncation of amyloid β-peptides yields toxic fragments that accumulate early in Alzheimer's-affected brains. Little is known concerning the catalytic events underlying the production of truncated fragments and their functional consequences. We have studied the involvement of two exopeptidases, namely aminopeptidase A (APA) and dipeptidyl peptidase IV (DPPIV) in the production of p3E-Aβ in vitro, in cells as well as in mice by both pharmacological and genetic approaches. We show that both APA and DPPIV contribute to N-terminal cleavages of Aβ in an additive manner. We show that pharmacological and genetic manipulation of these enzymes affect synaptic density in hippocampal organotypic slices. We also show that APA and DPPIV depletion affects learning and memory behaviors in mice. Overall, this is the first demonstration of an involvement of APA in the production of p3E-Aβ and its putative contribution in Alzheimer's pathology. Thus, the enzyme could be seen as a possible therapeutic target to prevent or slow down the progression of this neurodegenerative disease.

La coupure N-terminale du peptide amyloïde : une nouvelle cible thérapeutique ?

Le peptide amyloïde est un facteur clé dans la maladie d'Alzheimer. Il subit des coupures par des enzymes dont l'importance reste à déterminer. Notre étude se propose d'examiner l'importance de deux enzymes dans l'apparition et la progression de la maladie d'Alzheimer à l'aide de cellules et de modèles de souris.

Valverde A., Dunys J.

MARC **DHENAIN**

Laboratoire des Maladies Neurodégénératives (UMR9199),
MIINDt, MIRCen, Fontenay aux Roses

Transmission of cerebral lesions and of a neurodegenerative process by Alzheimer brains

Alzheimer's disease is characterized by cognitive alterations, cerebral atrophy and neuropathological lesions including neuronal loss, accumulation of misfolded and aggregated β-amyloid peptides (Aβ) and tau proteins. In humans and transgenic mice, administration of compounds contaminated with Aβ and Tau can induce Aβ and tau pathologies with very limited functional consequences. Unlike rodents, primates naturally express Aβ or tau under normal conditions. For the first time we demonstrate long term memory and learning impairments in a non-human primate (Microcebus murinus) following intracerebral injections with Alzheimer human brain extracts. Animals inoculated with Alzheimer brain homogenates displayed progressive cognitive impairments (clinical tests assessing cognitive and motor functions), modifications of neuronal activity (detected by electroencephalography), widespread and progressive cerebral atrophy (in vivo MRI assessing cerebral volume loss), neuronal loss in the hippocampus and entorhinal cortex (post mortem stereology). They displayed parenchymal and vascular Aβ depositions and tau lesions for some of them, in regions close to the inoculation sites. Although these lesions were sparse, they were never detected in control animals. Tau-positive animals had the lowest performances in a memory task and displayed the greatest neuronal loss.
This study show that Alzheimer brains can induce a clinically relevant encephalopathy. This raises public health issues.

Transmission de lésions cérébrales et d'une pathologie neurodégénérative par des cerveaux Alzheimer

La maladie d'Alzheimer est caractérisée par l'accumulation intracérébrale de peptides β-amyloïdes (Aβ) et de protéines Tau. Chez l'homme, l'administration de composés contaminés par Aβ et Tau peut induire des pathologies Aβ et Tau. Nous montrons chez des modèles animaux primates qu'ils peuvent aussi induire une maladie neurodégénérative.

Gary C., Lam S., Herard A.S., Koch J.E., Petit F., Gipchtein P., Sawiak S.J., Caillierez R., Eddarkaoui S., Colin M., Aujard F., Deslys J.P., French Neuropathology Network, Brouillet E., Buée L., Comoy E.E., Pifferi F., Picq J-L, Dhenain M

BÉATRICE **MESTRE-VOEGTLE**

Laboratoire de Chimie de Coordination du CNRS, Toulouse
& l'Institut des Technologies Avancées en Sciences du Vivant, Toulouse

Application of the Dynamic Combinatorial Chemistry Principle to the Amyloid-β Fibril Target

Thanks to the support of the Fondation Alzheimer in 2015, we got the opportunity to start and develop a multidisciplinary project dedicated to the application of a Dynamic Combinatorial Chemistry (DCC) approach to the fibrillar aggregated version of the Amyloid-β peptide (Aβ) implicated in the amyloid cascade associated with the Alzheimer's Disease (AD). Thus, Aβ fibrils have been chosen as the biological target of this original synthetic chemical principle to select and further identify new fluorescent probes enable to interact strongly with amyloid aggregates related to the neurotoxic process occurring in the brain of AD patient. Throughout the development of this project aiming to identify new molecular tools for the detection and the study of Aβ aggregates, we focused on the main steps of the implementation of such a DCC strategy: (i) the definition and preparation of a pool of building blocks for the generation of Dynamic Libraries (DL), (ii) the preparation of the biological target and its introduction into a model DL, (iii) the study of the best analysis conditions of a DL. The DCC principle, the main results obtained during the course of the CASPER project and the perspectives it offers will be presented.

Application du principe de Chimie Combinatoire Dynamique à la cible fibrillaire Amyloïde-β

Le projet CASPER vise à identifier par Chimie Combinatoire Dynamique de nouvelles espèces fluorescentes capables d'interagir fortement avec les agrégats d'amyloïde-β. Son principe est de proposer à la cible amyloïde-β de sélectionner dans un mélange, de nouvelles structures-outils pour la détection des agrégats amyloïdes associés à l'évolution de la maladie d'Alzheimer.

Relich I., Companys S., Gras E., Hureau C.

NOTES

MARDI 19 NOVEMBRE • 15H30

FLASH POSTERS

N°1 **Antoine P., et al.** (UMR CNRS 9193 SCALAB - Lille)
Positive Acceptance and Commitment Interventions for Caregivers

N°2 **Boucault S., et al.** (IM2A, APHP Pitié-Salpêtrière - Paris)
Randomised controlled trial pilot study of Acceptance and Commitment Therapy applied in a group setting for dementia caregivers

N°3 **Colin M., et al.** (UMRS-1172, Alzheimer&Tauopathies team - Lille)
Ectosomes, new biomakers of tau pathology

N°4 **Dahan L., et al.** (UMR 5169 CNRS, Equipe REMEMBeR - Toulouse)
Epileptiform activity during REM sleep in Alzheimer Disease

N°5 **Djelti F., et al.** (UR AFPA Laboratory - Vandoeuvre-lès-Nancy)
Glial lipoprotein receptor LSR as potential molecular link between olfactory and memory deficits and brain cholesterol homeostasis

N°6 **Gabelle A., et al.** (CMRR au CHU de Montpellier, Inserm U1061 - Montpellier)
Tau proteoforms quantification in neurodegenerative disorders

N°7 **Gerard M, et al.** (I2BC, CEA - Gif sur Yvette)
Genome-wide analysis of HDAC2-mediated epigenetic alterations of gene expression in the hippocampus of 3xTgAD mice

N°8 **Gouilly D., et al.** (Inserm UMR 1214, TONiC équipe DEVIN - Toulouse)
Immune attack : effect of Neflamapimod on neuroinflammation using DPA-714 in early Alzheimer disease.

N°9 **Helmer C., et al.** (Inserm UMR U1219, Population Health Research Center - Bordeaux)
Herpes simplex virus type 1, incidence of Alzheimer's disease and brain imaging: interaction with APOE4

N°10 **Hemonnot A.-L., et al.** (Institut de Génomique Fonctionnelle - Montpellier)
Microglial diversity in Alzheimer's Disease early stages: a key to understand the disease initiation

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MARDI 19 NOVEMBRE • 15H30

FLASH POSTERS

N°11 **Levy B., et al.** (Institut des Vaisseaux et du Sang, PARCC Inserm U970 - Paris)
Alzheimer's disease and blood vessels

N°12 **Nicolas G., et al.** (Inserm U1245 and Rouen University Hospital,Genetics and CNR-MAJ - Rouen)
Exome – Clinical Application of SequenCing in Alzheimer Disease, a multicenter French clinical utility and impact study.

N°13 **Pillet L.-E., et al.** (Alzohis - Paris)
Plasma catecholamines in Alzheimer's disease: correlations with CSF biomarkers and cognition

N°14 **Pousinha P.A., et al.** (Université Côte d'Azur, CNRS, IPMC - Valbonne)
The Amyloid Precursor Protein C-terminal domain alters CA1 neuron firing, modifying hippocampus oscillations and impairing spatial memory encoding

N°15 **Pouvreau S., et al.** (Institute for Interdisciplinary Neuroscience - Bordeaux)
Organotypic hippocampal slices as an in vitro model of AD-linked tauopathy

N°16 **Sarazin M., et al.** (Unité de Neurologie de la Mémoire et du Langage, GHU - Paris)
Therapeutic evaluation of low-dose IL-2-based immunomodulatory approach in patients with early AD

N°17 **Tautou M., et al.** (UMR-S 1172, JPArc : Neurosciences et Cancer – Lille)
New compounds targeting amyloid and Tau pathologies in Alzheimer's disease

N°18 **Vallet A., et al.** (Institut de Mécanique des Fluides de Toulouse - Toulouse)
Biomechanical response of the central nervous system is associated with frailty in patients with several neurodegenerative pathologies.

N°19 **Vigneron, P.-A., et al.** (MIRCEn, CEA-CNRS UMR 9199 - Fontenay-aux-Roses)
Chronic supplementation of L-serine, an amino-acid produced by astrocytes, improves long-term potentiation and cognitive behavior in 3xTG-AD mice, an Alzheimer's Disease mouse model

N°20 **Zimmer L., et al.** (Centre de Recherche en Neurosciences d & CERMEP, Imagerie du vivant - Lyon)
Toward PET imaging of 5-HT6 receptors during Alzheimer's disease

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MARDI 19 NOVEMBRE • 17H00

CONFÉRENCE

Pr Yaakov STERN

(Columbia University - New-York)

Cognitive reserve:
An evolving concept

NOTES

MARDI 19 NOVEMBRE • 18H30

Remise des Prix Joël Ménard 2019

2017

2018

OUVERTURE DE LA SOIRÉE

Philippe Lagayette

REMISE DES PRIX JOËL MÉNARD 2019

Lauréat·e du Prix Recherche Fondamentale
Par Marie-Claude Potier

Lauréat·e du Prix Recherche Clinique
Par Yaakov Stern

Lauréat·e du Prix Recherche Sciences Humaines et Sociales
Par Martine Bungener

CLÔTURE DE LA SOIRÉE

Professeur Joël Ménard

HÉLÈNE **MARIE**

IPMC – CNRS-UCA UMR7275,
Sophia-Antipolis - 06560 Valbonne

A novel APP processing pathway and its physiological function in modulation of synaptic activity

Deciphering the role of the different APP fragments in synaptic function is crucial to fully understand Alzheimer Disease (AD) etiology, which is believe to initiate with synapse dysfunction. In Willem et al. [(2015) Nature, 526: 443-447] we described a new APP processing pathway producing amyloid-η (Aη) peptides. We could demonstrate that the Aη-α peptide, the longest form of Aη produced by η-secretase and α-secretase cleavage, is detrimental for hippocampal function as it impairs biological mechanisms underlying memory formation. Going beyond these initial observations, we now performed an extensive analysis of its action on various parameters of plasticity at the CA3-CA1 synapse. To investigate the actions of Aη-α at the excitatory glutamatergic synapse, we performed ex-vivo field electrophysiology on hippocampal slices of adult wildtype and genetically modified mice. Electrophysiology protocols were designed to discriminate Aη-α action at the pre-, post-synapse and plasticity threshold. Our results show that both increase of Aη-α and prevention of η-dependent cleavage of APP perturb post-synaptic plasticity. In particular, it significantly modifies the induction threshold of post-synaptic long-term depression and longterm potentiation. We are currently testing how Aη-α actions at synapses translate into changes in cognition.

Un nouveau site de clivage de l'APP et la fonction physiologique des peptides associés dans la modulation de la plasticité synaptique

Nous avions découvert en 2015 un nouveau mécanisme de clivage de l'APP, protéine clé de la maladie d'Alzheimer, qui génère des morceaux d'APP et avions montré que ces fragments ont une activité biologique dans le cerveau. Nous montrons aujourd'hui qu'ils régulent la fonction des synapses nécessaires pour l'encodage de souvenirs.

Mensch M., Ma S., Dunot J., Pousinha P., Willem M., Haass C.

CHRISTOPHE **MULLE**

CNRS UMR 5297 - Interdisciplinary Institute of Neuroscience,
University of Bordeaux

Presenilin and APP in presynaptic plasticity

The loss of synapses is the best correlate to cognitive deficits in Alzheimer's disease (AD). There are also extensive experimental evidence, mainly from animal models for alterations of synaptic properties at the early stages of disease progression, before synapse loss and neuronal degeneration. A majority of studies have focused on post-synaptic elements, including impairment of long-term plasticity, spine structure, glutamate receptor-mediated transmission. Here I will present results showing that the physiopathology of neural circuits in AD includes a strong presynaptic component. I will describe studies indicating a function of major molecular players in AD, the amyloid precursor protein (APP) and the two presenilin (PS) paralogs PS1 or PS2 in presynaptic forms of synaptic plasticity. Information will also be provided about the presynaptic function of genes identified as risk factors of AD in GWAS studies, such as SV2A. I will then provide a discussion on how these physiological functions at the presynapse can explain or forecast impairment of neural circuits in the context of AD.

Rôle de la préséniline et de l'APP dans la plasticité présynaptique

Le travail présenté concerne les mécanismes par lesquels les mécanismes de libération des neurotransmetteurs au niveau des synapses, zones de contact entre les neurones, sont affectés par la perte de la préséniline et de l'APP, agents moléculaires majeurs de la maladie d'Alzheimer, ou de gènes qui lui sont liés génétiquement.

NOTES

GILLES **BONVENTO**

Laboratoire des maladies Neurodégénératives,
CNRS CEA UMR 9199, MIRCen,
18 route du Panorama, 92265 Fontenay-aux-Roses

Identification of an astrocytic metabolic pathway that contributes to Alzheimer's Disease

Recent work has shown that astrocytes, an important sub-type of glial cells, contribute to maintaining metabolic homeostasis and is involved in synaptic transmission in the mature brain. Starting from an intermediate of glycolysis (3-phosphoglycerate), astrocytes are the only cell type that can produce L-serine, a precursor of D-serine, a co-agonist of NMDA receptors essential for implementation of memory processes. We have made the hypothesis that early metabolic alterations are responsible for synaptic dysfunctions occurring in the course of Alzheimer's Disease (AD). We found that this astrocytic anabolic pathway (1) contributes to memory formation and (2) is impaired in a mouse model of AD. Supplementation with L-serine in the diet prevented both synaptic and behavioral deficits in AD mice. Our findings reveal that astrocytic glycolysis controls cognitive functions and suggest oral L-serine as a ready-to-use therapy for AD.

Identification d'une voie métabolique astrocytaire contribuant à la maladie d'Alzheimer

Notre projet montre qu'une alimentation enrichie en L-serine peut restaurer les déficits de mémoire chez des souris modèles de la maladie d'Alzheimer.

Gary C., Lam S., Herard A.S., Koch J.E., Petit F., Gipchtein P., Sawiak S.J., Caillierez R., Eddarkaoui S., Colin M., Aujard F., Deslys J.P., French Neuropathology Network, Brouillet E., Buée L., Comoy E.E., Pifferi F., Picq J-L, Dhenain M

GUILLAUME **DOROTHÉE**

Inserm, Sorbonne Université, UMRS 938 - Centre de Recherche Saint-Antoine, Team Immune System and Neuroinflammation, Hôpital Saint-Antoine, Paris, France

Role and therapeutic potential of T cells in Tauopathies

Besides innate neuroinflammation, recent data emphasize an instrumental role of T cells in the pathophysiology of Alzheimer's disease (AD). However, the impact on disease progression of T cell responses to various pathological deposits involved in AD, i.e Aβ and Tau, is still poorly defined. Whereas previous reports suggest that different anti-Aβ T cell populations could be either detrimental or beneficial, the interrelationship of T cell responses with Tau pathology remains totally unknown. Our recent studies in a mouse model strongly suggested that Tauopathy may drive the development of detrimental T cell responses that promote disease progression. However, the nature of T cell populations potentially implicated in such detrimental effects remain to be determined, as well as the impact on Tau-related pathophysiology of their modulation. Our first new data will be presented, aiming at better characterizing the role of different T cell subsets in promoting Tau-driven pathophysiology, and evaluating the therapeutic potential in Tauopathies of an optimized second-generation innovative immunomodulatory approach targeting T cell responses.

Rôle et potentialités thérapeutiques des cellules T dans les Tauopathies

Des travaux récents suggèrent que les protéines Tau impliquées dans la maladie d'Alzheimer déclencheraient une réaction de certaines cellules immunitaires, appelées lymphocytes T, qui contribueraient au processus pathologique. Nous cherchons à mieux comprendre le rôle de ces cellules, et évaluer l'impact de leur modulation sur l'évolution de la maladie.

Chou MingLi, Puchois V. , Stym-Popper G., Chaigneau T., Carvalho K., Caillierez R. , Aid S., Faivre E., Caudana P., Holzenberger M., Piaggio E., Buée L. et Blum D.

EMMANUEL **NIVET**

Institut de NeuroPhysiopathologie, UMR 7051 – CNRS ;
Aix Marseille Université - Equipes « Dégénérescence et Plasticité Neurales » et « Cellules souches, Modélisation de Maladies et Neurorégéneration »

Apolipoprotein E isoform-dependent human astroglial inflammation reveals an early pro-inflammatory state in APOE4 carriers underlying Alzheimer's disease

Glial cells – i.e. astrocytes and microglia - are increasingly seen as important in Alzheimer's disease (AD) pathology but the mechanisms by which they contribute to the disease are yet not fully understood. Astrocytes are the main source of cerebral Apolipoprotein E (APOE), a regulator of lipid homeostasis that can be expressed in three genetic isoforms in Human: APOE2, E3 and E4. The latter is the most relevant genetic risk factor for late onset sporadic AD. Leveraging on human induced pluripotent stem cell (hiPSC)-based models and CRISPR/Cas9-based genome editing strategies, we studied the impact of different APOE isoforms in human astrocytes. Our results identified that human astrocytes can autonomously contribute to a pro-amyloidogenic state that, similarly to what was found in neurons, is influenced by the APOE genotype. Moreover, we showed that the inflammatory status of human astrocytes is strongly modified in an APOE isoform-dependent manner, where APOE4 contributes to an exacerbated inflammation. Our study supports that neuroinflammatory changes driven by astrocytes, along with a pro-amyloidogenic action, are among the mechanisms underlying AD pathogenicity in APOE4 carriers.

L'Apolipoproéine E participe au contrôle de l'inflammation astrocytaire humaine et révèle un statut pro-inflammatoire précoce sous-jacent la maladie d'Alzheimer chez les porteurs d'APOE4

L'astrocyte est une cellule importante au fonctionnement cérébral. Nous avons identifié que les astrocytes humains activent un état inflammatoire exacerbé sous l'influence d'un facteur de risque génétique pour la maladie d'Alzheimer. L'inflammation astrocytaire apparait donc comme un élément de susceptibilité clé pouvant participer au déclenchement de la maladie d'Alzheimer.

Arnaud L., Greetham L., Jullien N., Garcia-Gonzalez L., Pilat D., Stephan D., Louis L., Baranger K., Rivera S.

NOTES

PATRICK **DALLEMAGNE**

Normandie Univ, UNICAEN, Centre d'Etudes et de Recherche sur le Médicament de Normandie (CERMN), Caen, France

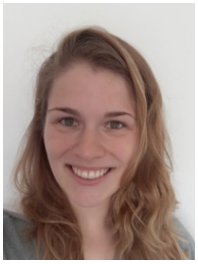
The design of multi-target drug candidates with potential therapeutic interest against Alzheimer's disease

This work describes the design, synthesis and in vitro and in vivo biological evaluation of novel Multi-Target Directed Ligands (MTDL) able to both activate 5-HT4 receptors, block 5-HT6 receptors and inhibit acetylcholinesterase activity (AChE), in order to exert a synergistic antiamnesic effect, potentially useful in Alzheimer's disease (AD). Indeed, both activation of 5-HT4 and blockage of 5-HT6 receptors led to an enhanced acetylcholine release, whose depletion would be implied in AD. The preservation of the latter through the inhibition of AChE would complete this approach and lead to an efficiently restoring of the cholinergic neurotransmission. Furthermore, 5-HT4 receptor agonists, also, appear able to promote the non-amyloidogenic cleavage of the amyloid precursor protein and to favour the production of the neurotrophic protein sAPPα. This study succeeded in yielding such pleiotropic compounds with in vivo anti-amnesic effect.

Le design de principes actifs multi-cibles d'intérêt thérapeutique potentiel dans la maladie d'Alzheimer

Le projet TRIAD vise à concevoir des principes actifs d'action plurielle, ciblant donc en même temps plusieurs protéines d'intérêt thérapeutique dans la maladie d'Alzheimer afin d'exercer par effet synergique une efficacité clinique suffisante pour ralentir l'évolution de cette maladie d'origine multifactorielle.

Rochais C., Hatat B., Yahiaoui S., Lecoutey C., Davis A., Freret T., Boulouard M., Claeysen S.



SARAH **GEURS**

KU Leuven, Department of Human Genetics, Leuven, Belgium

Single-nucleus Genome-plus-Transcriptome sequencing to study Somatic Genome Instability in Normal and Tauopathy Brain

The contribution and consequences of genome instability to the human brain remain ambiguous. Findings in Drosophila and human cell lines pointed out the possibility that Tau-mediated neurodegeneration is already determined during neurodevelopment when Tau induces mitotic problems leading to genome instability. Besides, in healthy brain, an increased genomic instability rate in the embryonic cortex compared to the adult cortex is suggested. In order to investigate acquired genome instability, we established and optimized genome-plus-transcriptome sequencing (G&T-seq) of single nuclei derived from Drosophila and frozen postmortem human brain. Single nucleus G&T-seq (snG&T-seq) enables sequencing of a cell's nuclear genome and nuclear transcriptome in parallel. The added value of this combination is the possibility to identify true copy number variation (CNV) as well as unlocking the transcriptional cell type and state, and hence, studying the functional impact of these acquired genetic variations in the same single cell. Preliminary findings from snG&T-seq on Drosophila Tauopathy model brains seem to corroborate that 4RhTau-expression during neurodevelopment induces genome instability. Furthermore, our results from snG&T-seq on five healthy human brains reveal that up to 6% of healthy neurons carry true megabase-scale copy number variants. Surprisingly, some of these CNV profiles seem to resemble chromothripsis. These findings indicate that genome instability is present and could play a major role in diseased as well as healthy human brain.

Séquençage génomique et transcriptomique de noyaux uniques pour étudier l'instabilité somatique du génome dans le cerveau normal et atteint de Tauopathie

Le cerveau humain en bonne santé présente une instabilité du génome (présence de mutations de l'ADN) qui pourrait jouer un rôle majeur dans les tauopathies. Pour étudier cela, nous caractérisons l'ADN et l'ARN de neurones individuels issus de cerveaux malades et normaux et d'un modèle de Tauopathie chez la drosophile.

Dermaut B., Rahbari R., Vanuytven S., Voet T.

NOTES

MERCREDI 20 NOVEMBRE • 14H30

CLÔTURE

Remise du
Prix du meilleur poster

FONDATION
ALZHEIMER

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@StopALZ

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