

Background

Université de Montréal



PhD Neurobiology
Neuronal plasticity



Unil

UNIL | Université de Lausanne

Postdoctoral fellowship:
Neuron-astrocyte communication



Centre de recherche en neurosciences
Centre for Research in Neuroscience

Centre universitaire de santé McGill McGill University Health Centre

Douglas
INSTITUT MENTAL HEALTH
UNIVERSITAIRE EN UNIVERSITÄT
SANTÉ MENTALE INSTITUTE



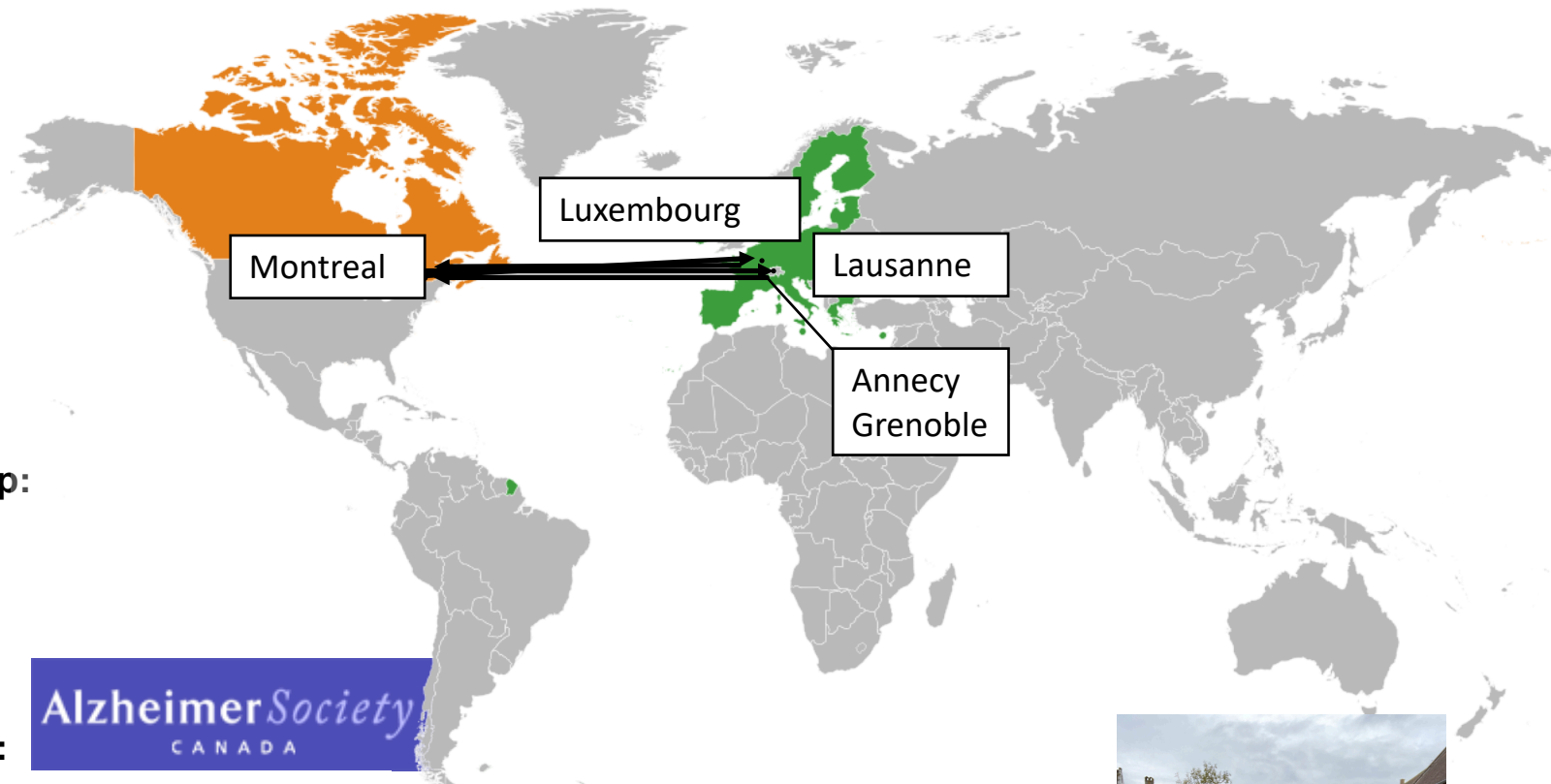
Luxembourg Centre
for Systems Biomedicine



Fonds de recherche Santé
Québec



Prof. Michel Mittelbronn
Luxembourg Centre of Neuropathology (LCNP) Team



Awards, donations

- Fondation Gustave et Simone Prévot 2016 Award
- Fondation Gustave et Simone Prévot 2017 Award
- 1st Prize Rotary Espoir en tête 2017
- Donations Rotary Bassin Esch Minier 2018_Conservatoire
- Diverse Donations from private 2018
- Donation Agaajani Family 2019
- 1st Prize Rotary Espoir en tête 2019
- FRN AFR for Félicia Jeannelle (PhD grant)
- Prix Fondation pour la recherche sur Alzheimer (France) 2021
- 1st Prize Rotary Espoir en tête 2021



Espoir en tête
Les Rotariens aident la recherche sur le cerveau



Dons famille
Agaajani
(en mémoire de
Rahim)



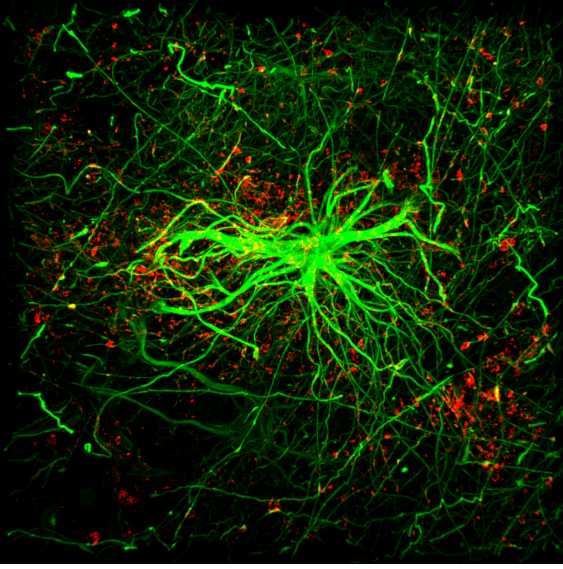
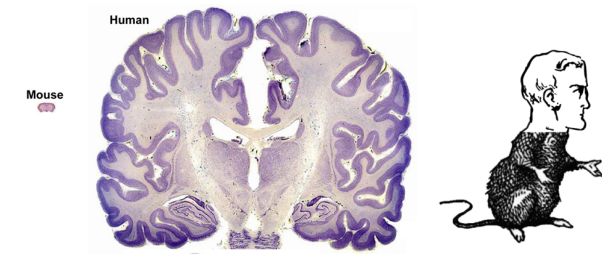
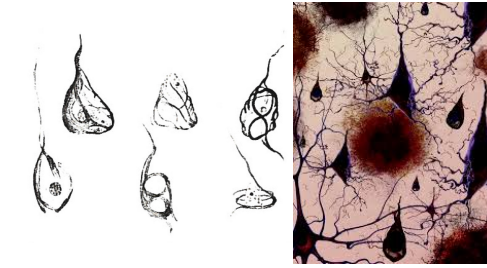
David Bouvier_ AD_LCSB



Alzheimer's Disease

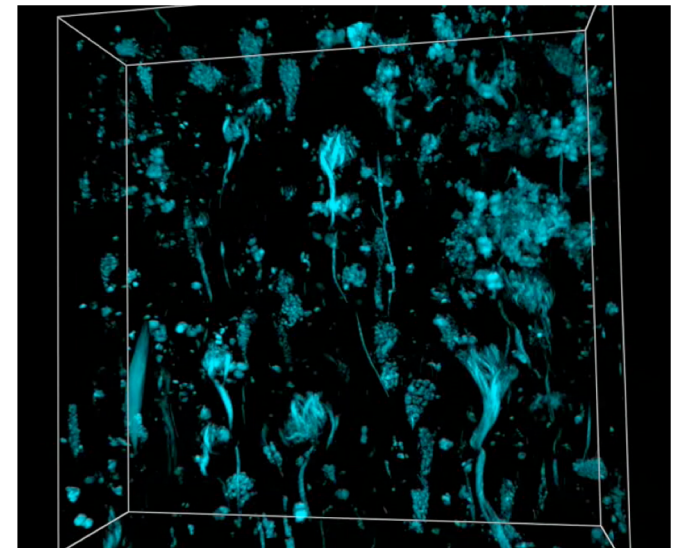
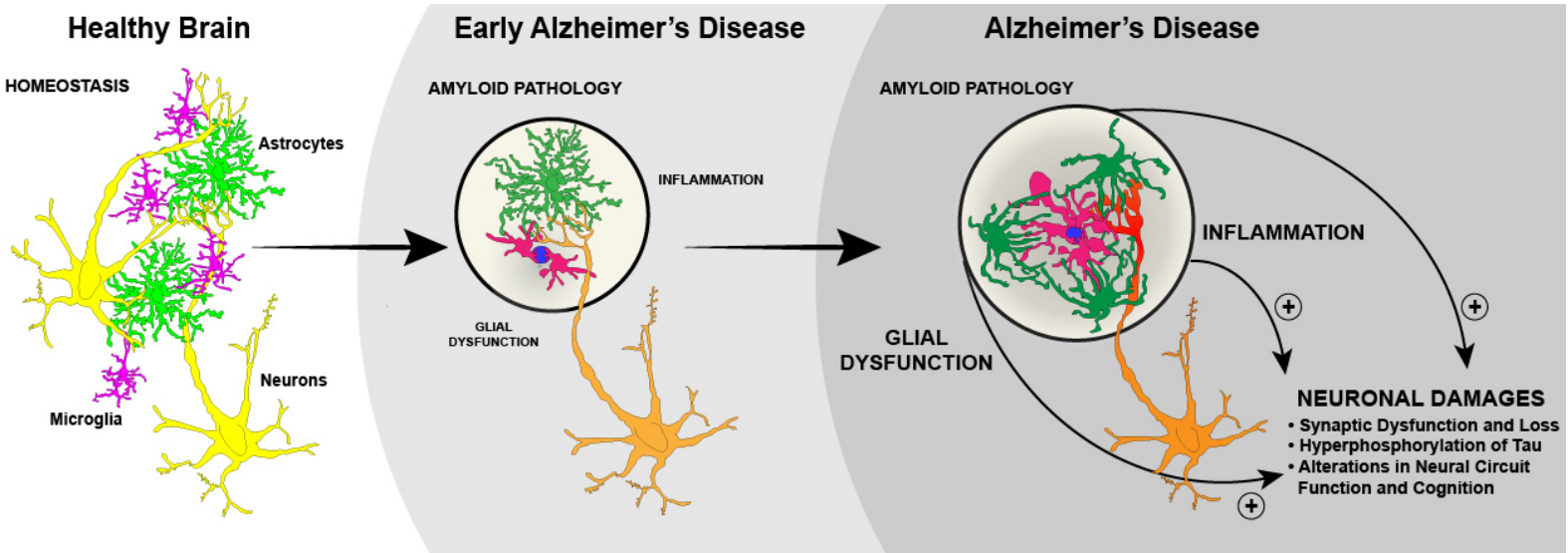
Neurodegeneration *Cell Death*
Inflammation *Human samples*
Cellular heterogeneity *Memory*
Microglia *Single-Cell RNAseq* *Astrocytes*
Toxic cells signatures *STED* *Epigenome*
 High-content Microscopy

Dementia with
 Lewy Bodies

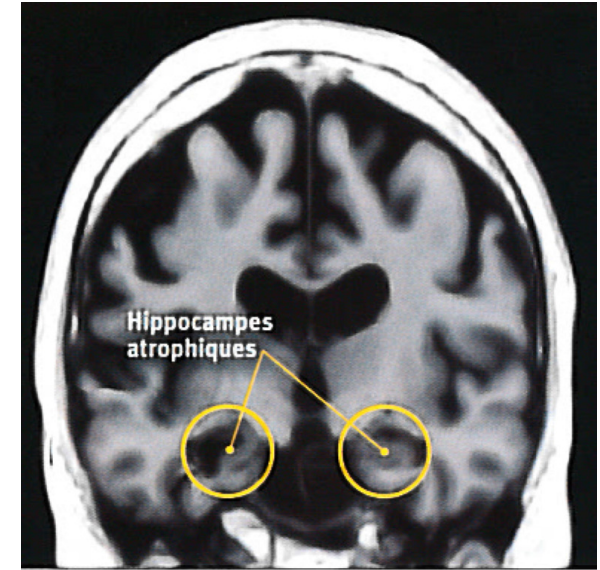
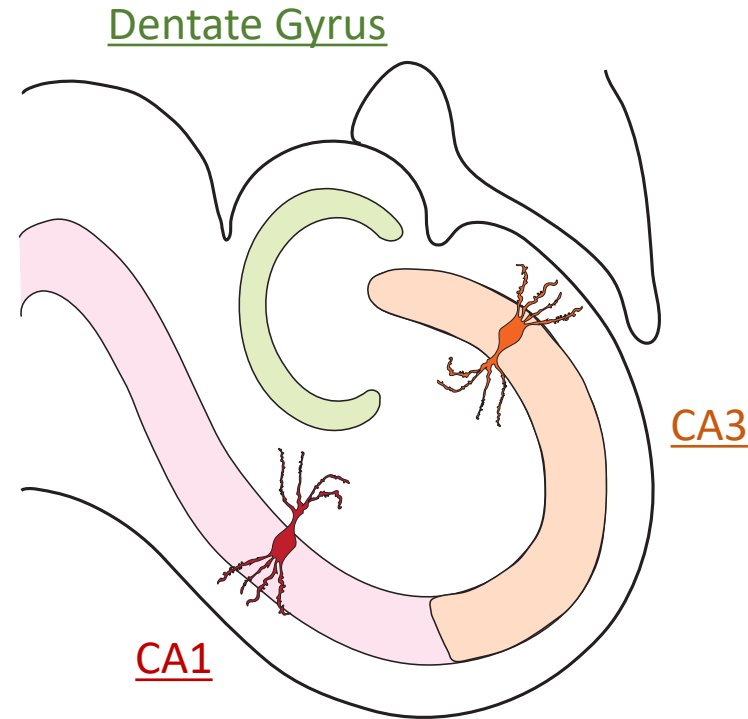
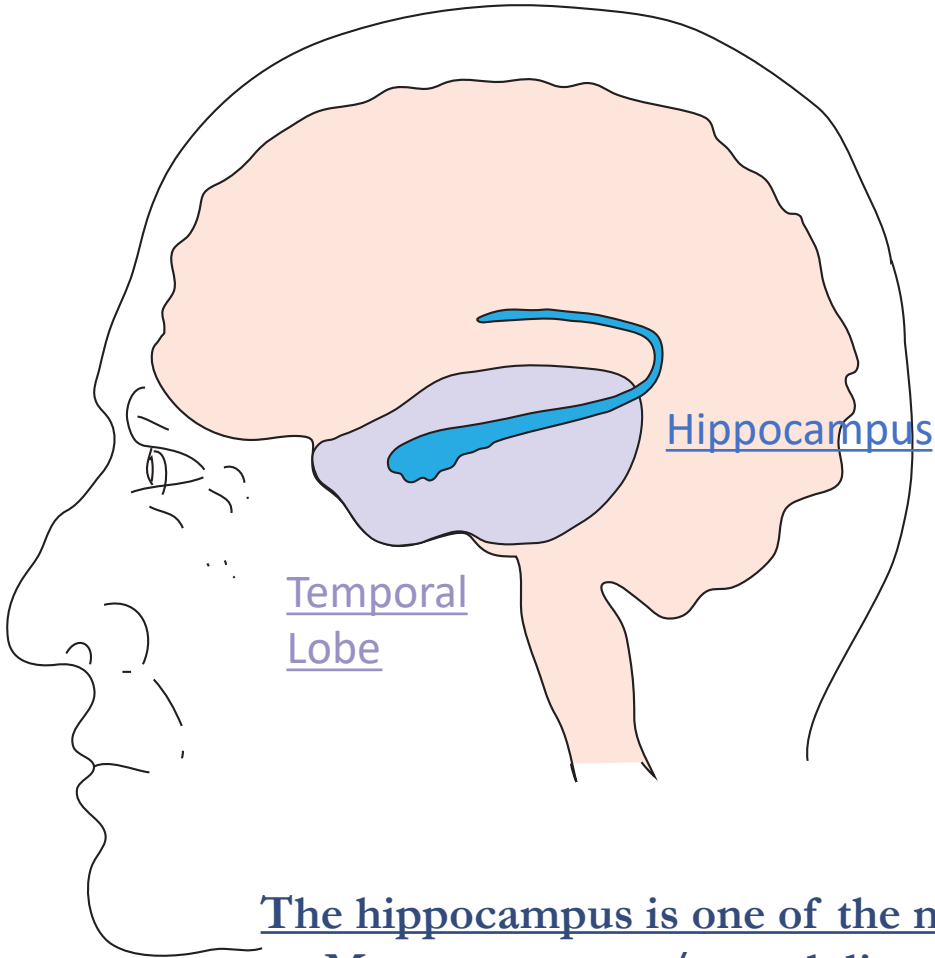


Working Hypothesis 1:

Some glial cells usually protective, become toxic in AD and impact significantly the progression of Alzheimer's Disease/Dementia.

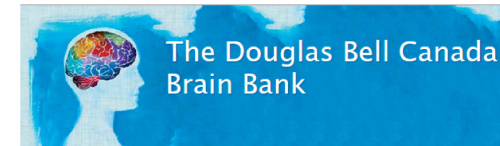


Glial cells are involved in the hippocampus deterioration



The hippocampus is one of the most vulnerable region to AD:

- Memory process/ mood disorder/epilepsy
- Severe atrophy of CA1 (30% initial volume)
- Hippocampal microglia: maladaptive responses? Toxic?
- Astrocytes: how do they cope with AD pathologies?



DH	cases	gender	age	PMD	Stage
DH 1725	AD	F	77	24,3	x (severe)
DH 1669	AD	M	87	21,75	A2B3C2
DH 1631	AD	M	87	10,8	x
DH 1565	AD	M	83	43,25	Braak III
DH 1523	AD	M	86	27,25	A2B3C2
DH 1504	AD	M	91	25	A2B3C2
DH 1501	AD	F	83	25	A2B3C2
DH 1494	AD	M	85	31,08	A2B3C3
DH 1352	AD	F	83	15	x
DH 1296	AD	M	80	15,5	Braak IV
DH 1251	LBD	M	89	17	x
DH 1158	LBD	M	70	24,5	x
DH 1157	AD	F	85	24,75	x (severe)
DH 1117	CTL	F	82	32,58	
DH 1073	AD	M	85	35,5	x
DH 1012	LBD	M	69	9,5	x
DH 975	LBD	F	77	19,5	x
DH 965	CTL	M	88	15,98	
DH 948	LBD	M	76	21,75	x
DH 881	CTL	M	85	5,67	
DH 808	CTL	F	80	17,5	
DH 488	CTI	F	86	5,75	
DH 378	PDD	F	76	26,75	x
DH 252	PDD	M	83	23,25	x
DH 246	PDD	M	77	11,5	x

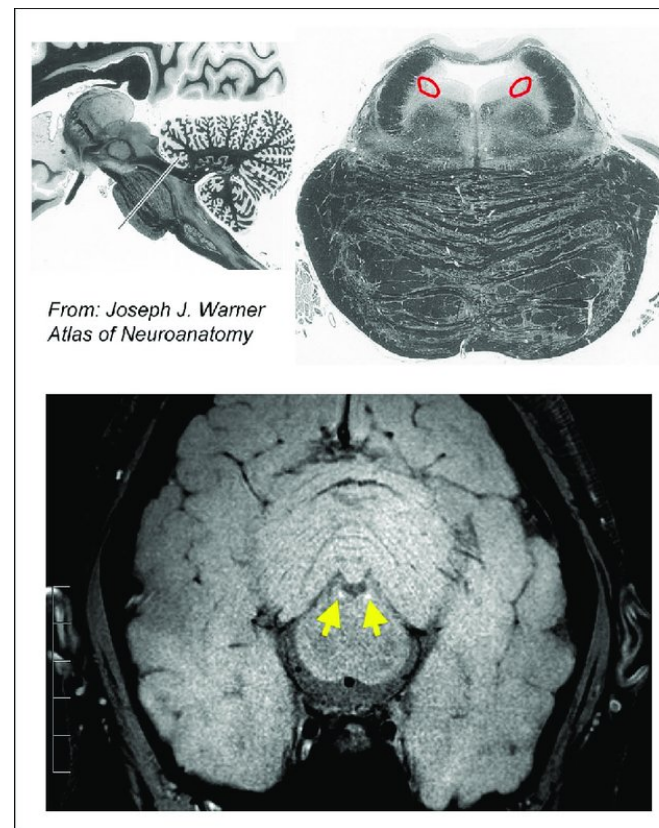
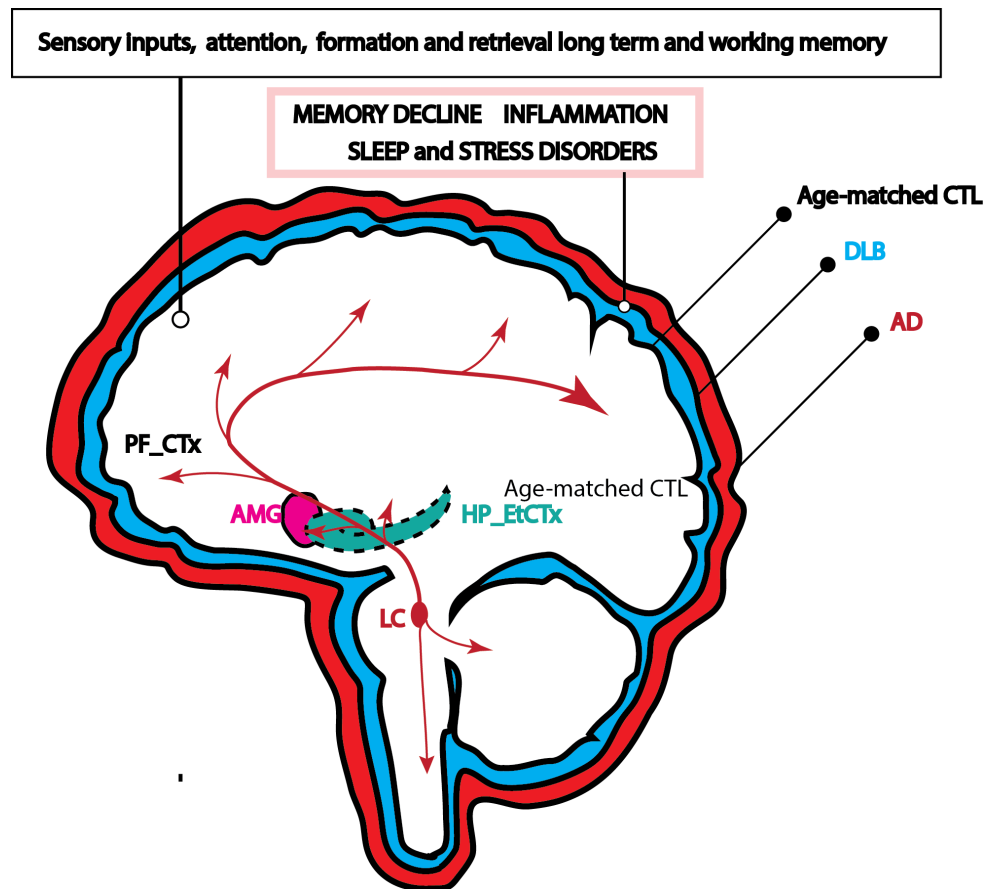
Working Hypothesis 2:

Brain Noradrenaline system alteration leads to the dysfunction of glial cells, ultimately to toxic states



Espoir en tête
Les Rotariens aident la recherche sur le cerveau

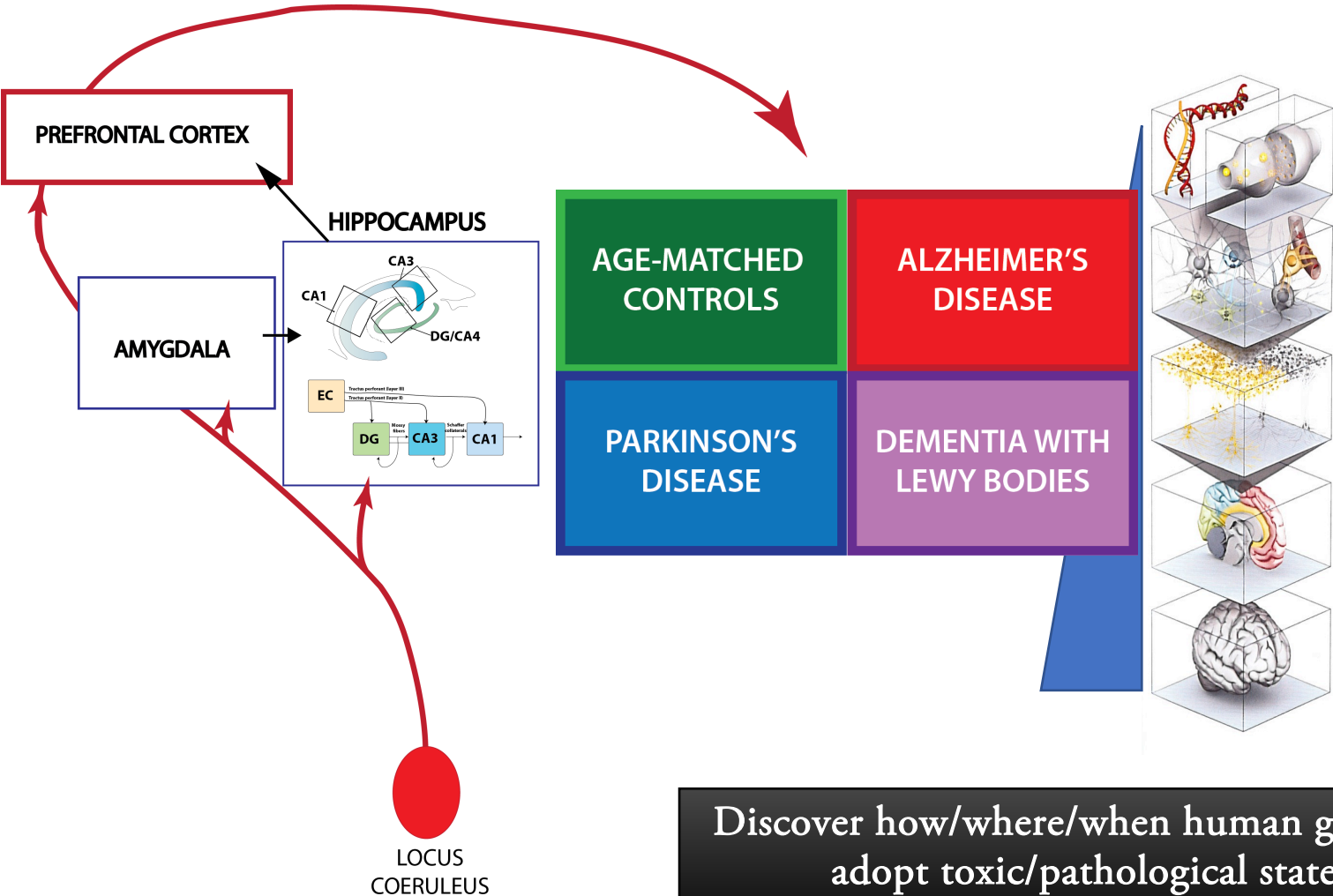
2021



Epigenetic, molecular, and structural Alterations in Noradrenaline modulated memory circuits in Alzheimer's and Parkinson's associated Dementia

Pilot project on 11 brains from AD patients with a strong clinical assessment (imaging+ cognitive tests)_4 brain regions (FFPE, fixed and frozen)

MULTI-SCALE EXPERIMENTAL APPROACH



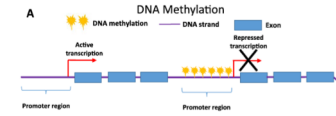
Noradrenaline Modulated circuits involved in Memory formation, consolidation and storage

Discover how/where/when human glial cells adopt toxic/pathological states

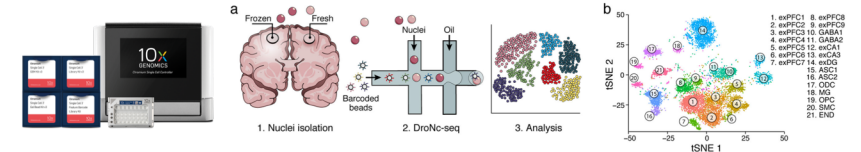
help to design new therapeutic strategies for personalized treatment

REVERSE ENGINEER RESCUE
PATHOLOGICAL MECHANISMS
CELLS/ Mouse Models

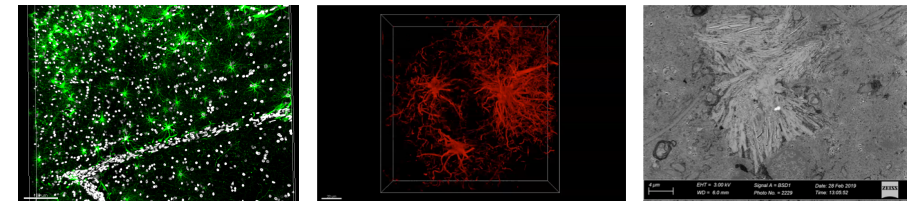
Genome-wide methylation profiling, ATAC-seq



Single Nuclei RNA-Seq (sNuc-Seq)



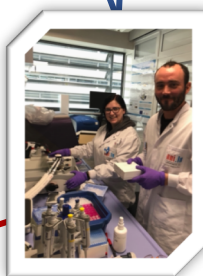
High-content Microscopy (confocal, STED, EM) and Analysis (MIC-MAC)



A team work!

Sonja Fixemer (Microglia and Alzheimer)
Corrado Ameli (MIC-MAC 2.0)
Dr. Luis Salamanca (MIC-MAC)
Simon Mangold (Astrocytes and Alzheimer)
Dr. Aymeric Fouquier d'Hérouël
(Microscopy platform)

Dr. Alexander Skupin et
Prof. Rudi Balling



Prof. Michel Mittelbronn
Luxembourg Centre of Neuropathology
Félicia Jeannelle
Dr Tony Heurtaux (LSRU)
Dr Gaël Hammer
Dr Felix Kleine-Borgmann
Lorraine Richart
Dr Ann-Christin Hau

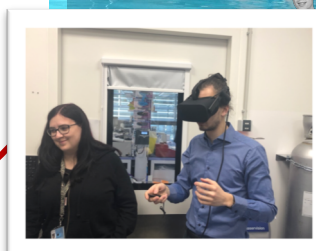
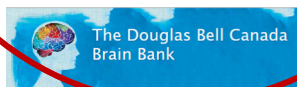


Centre universitaire de santé McGill | McGill University Health Centre

Prof. Keith Murai
Prof. Remi Quirion



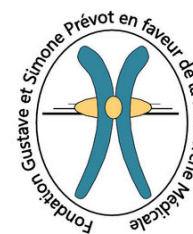
Prof. Naguib Mechawar



Luxembourg Brain Bank



Espoir en tête
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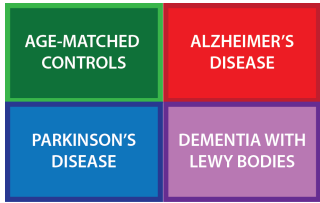


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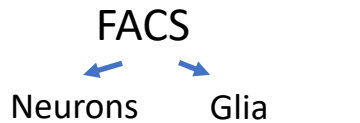
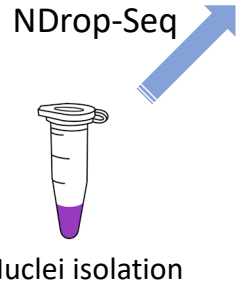
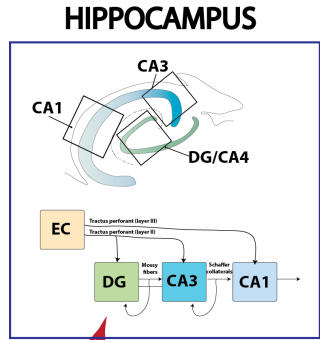


Fundraising: Dr. Philippe Lamesch
Annick Spellini





Frozen Samples



LOCUS COERULEUS

WP2: Neurons and glia transcriptomic signatures in LC and Hippocampus in AD and PD associated dementia



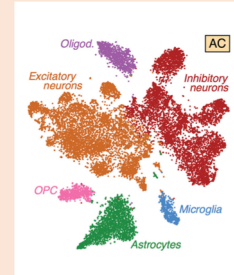
10x genomics

Illumina NextSeq
500

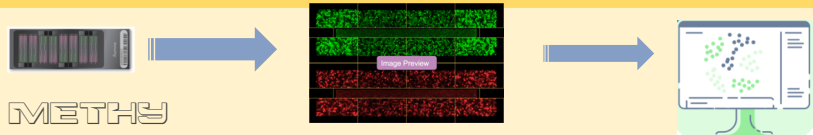
DEG

Cell type transcriptomic signatures across conditions

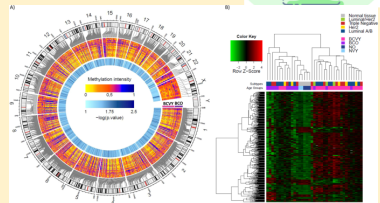
Specific Clusters



WP3: Neurons and glia transcriptomic signatures in LC and Hippocampus in AD and PD associated dementia



METHYLATION
EPIC
BEAD
DMG
BSOK



Methylation profiles for neurons and glia across conditions

WP4: Validations of signatures with multiplex assay, IHC

