

BRAIN-C LAB

COMPENSATION SYSTEMS IN NEURODEGENERATIVE DISEASES AND AGING

OUR TEAM

(حیک) STAFF SCIENTISTS

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UNDERSTANDING THE DYNAMICS OF CELLULAR RESILIENCE TO FOSTER THE PRECISION MEDICINE FOR NEURODEGENERATIVE DEVELOPMENT OF **DISEASES AND AGING-ASSOCIATED DISORDERS**

THE BRAIN-C LAB IS A MULTIDISCIPLINARY RESEARCH TEAM THAT INCLUDES NEUROBIOLOGISTS, CELL AND MOLECULAR BIOLOGISTS, MATHEMATICIANS, BIOINFORMATICIANS AND PHYSICISTS. OUR KNOWLEDGE DISCOVERY MODEL IS BASED ON THE COMBINED USE OF SYSTEMS MODELING, CELL BIOLOGY AND CLINICAL RESEARCH, AND WE WORK AT THE **CROSSROADS OF THESE FIELDS.**

WE PROMOTE A STRATEGIC MODEL BASED ON A MULTI-DISCIPLINARY AND TRANS-SECTORIAL APPROACH TO ADDRESS THE FOLLOWING QUESTIONS:

• What are the most important <u>compensatory mechanisms</u> that are <u>lost in</u> the course of <u>neurodegenerative disease</u> processes?

(حي) Post-Doctoral fellows

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• CELL AND MOLECULAR BIOLOGY OF

- How to reinstate these mechanisms to <u>prolong compensation</u> and <u>delay</u> the progression of <u>neurodegenerative diseases</u>?
- What are the factors allowing to predict the individual capacity for biological resilience in neurodegenerative disease and age-related stress?
- What are the molecular diagnosis and precision medicine markers allowing to predict the most likely course of neurodegenerative disease **PROGRESSION RATE?**

We study these questions in the context of <u>Huntington's disease</u> (HD), a genetic neurodegenerative disease for which well-characterized models and HIGHLY DIMENSIONAL DATASETS ARE AVAILABLE ACROSS SPECIES, AND IN ALZHEIMER'S DISEASE (AD). WE ALSO HAVE AN INTEREST IN THE PROCESS OF AGING AND ALTERED HOMEOSTASIS. WE TAKE ADVANTAGE OF THE MOST COMPREHENSIVE DATASETS TO UNDERSTAND HOW NEURODEGENERATIVE DISEASES MAY WORK ON A SYSTEMS LEVEL, PARTICULARLY IN TERMS OF AGING & COMPENSATION.

HUMAN NEURAL STEM CELLS

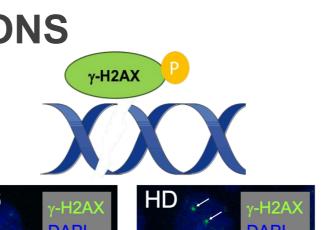
PANELS OF ISOGENIC AND NON-ISOGENIC LINES:

- HUMAN IPSC-DERIVED ISOGENIC CELLS HD 72Q/19Q AND C116 21Q/19Q (L. ELLERBY, BUCK INSTITUTE, CA)
- 2 NON-ISOGENIC HD (60Q AND 109Q) AND 2 CONTROL LINES (18Q AND 20Q) (CEDARS-SINAI)

DISSECTING THE DNA DAMAGE & REPAIR MECHANISMS IN NSCs AND IPSC-DERIVED NEURONS

Comet Assay Alkaline: SSB + DSB **Neutral: DSB** C116 C116 HD

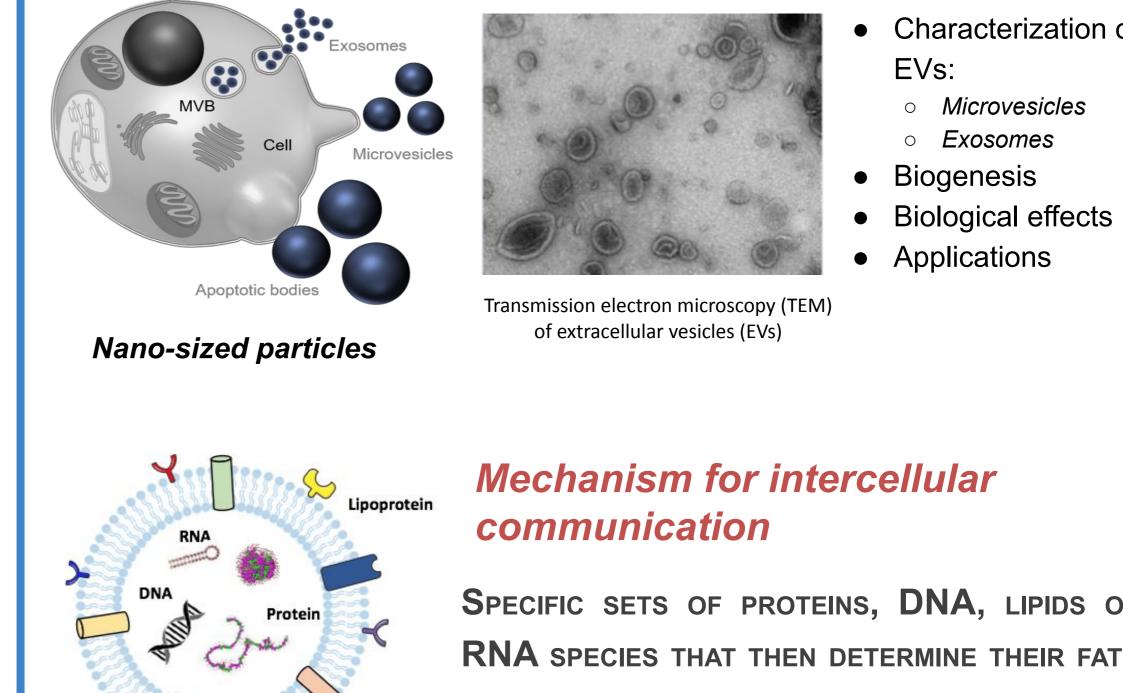
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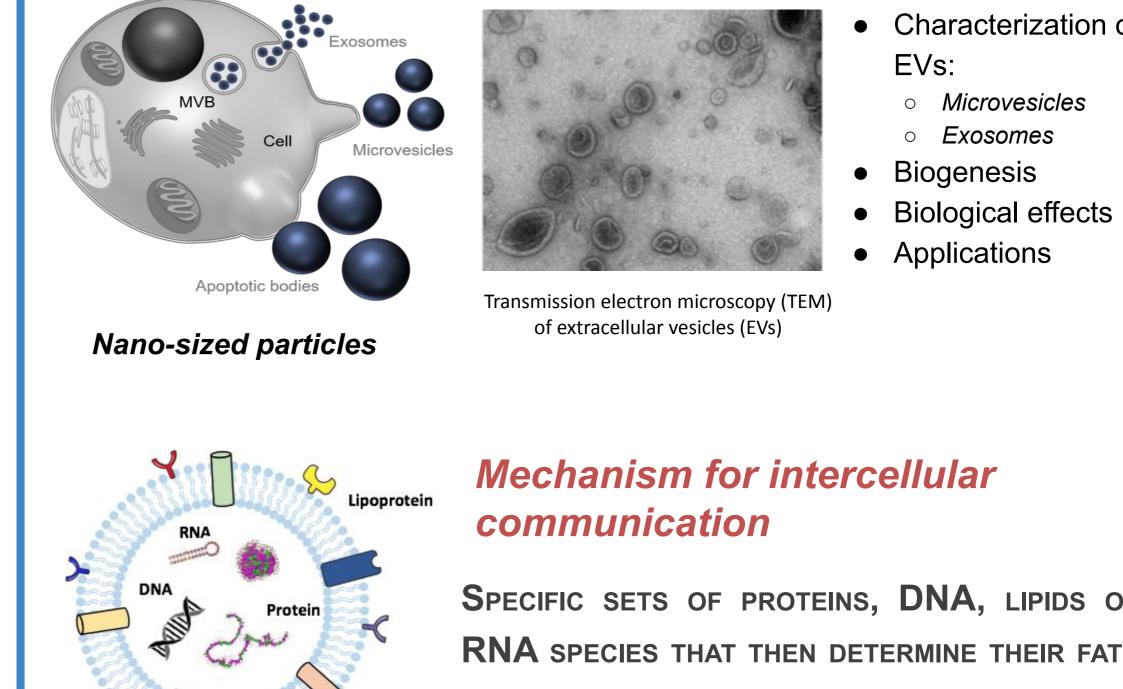




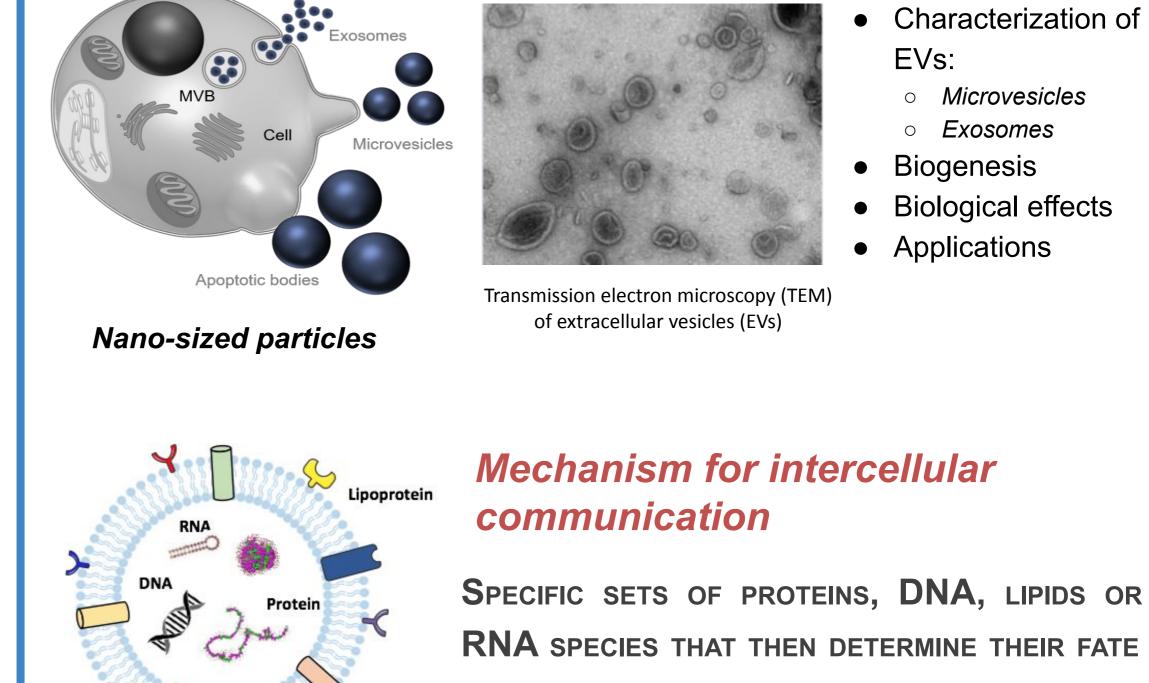
EXTRACELLULAR VESICLES (EVS) ARE CELL-DERIVED MEMBRANOUS STRUCTURES WITH EITHER ENDOSOMAL ORIGIN OR ARE SHED FROM THE PLASMA MEMBRANE.

WE ARE ISOLATING SMALL EV (EXOSOMES) FROM HUMAN HD IPSC-DERIVED **NSC**S AND **CAG-**CORRECTED CELLS AND INVESTIGATING THEIR ROLE IN THE RESPONSE TO PROTEOTOXIC STRESS AND NEURONAL SURVIVAL IN HD.





AND FUNCTIONS.



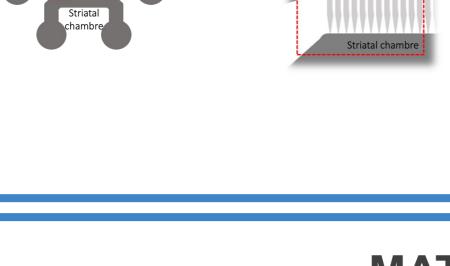
STRESS RESPONSE

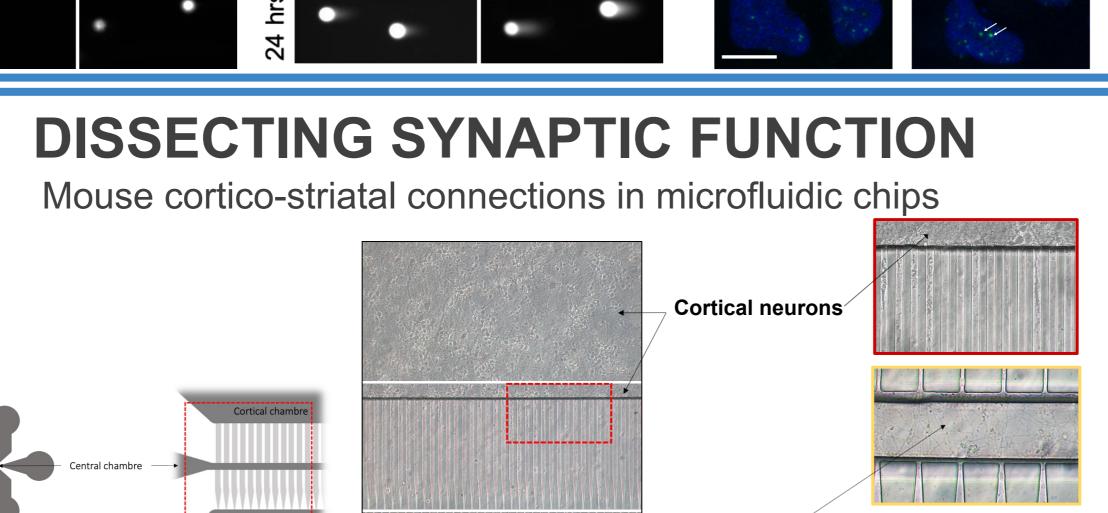
- **N**EURODEGENERATIVE DISEASES
- **A**GING
- INTERCELLULAR COMMUNICATION
- EXTRACELLULAR VESICLES

BIOINFORMATICS (حري)

- RNA-SEQ ANALYSIS
- STATISTICAL ANALYSIS
- NETWORK ANALYSIS & GRAPH THEORY
- SHAPE DEFORMATION ANALYSIS
- MACHINE LEARNING (RANDOM TREE FOREST, FEATURE SELECTION)
- WEB DEVELOPMENT
- DATABASE CURATION & MANAGEMENT

LATEST





MATHEMATICAL MODELING, BIOINFORMATICS AND MACHINE LEARNING

To understand how neurodegenerative diseases and aging may work on a systems level, we developed BioGemix — a data integration framework BASED ON INNOVATIVE MACHINE LEARNING APPROACHES FOR BIOLOGICAL PRECISION IN THE ANALYSIS OF DIMENSIONAL DATA — AND WE USE IT FOR BASIC RESEARCH AND CLINICAL DISCOVERY PURPOSES. BIOGEMIX INCLUDES DIFFERENT PIPELINES AND IS CONTINUOUSLY BEING DEVELOPED TO INCORPORATE NEW DATASETS AND TOOLS THAT WE CONTINUE TO DEVELOP.

GEOMIC - SHAPE ANALYSIS

WEIGHTED EDGE NETWORK ANALYSIS

• MEGRET ET AL., *ELIFE* [JUNE 2021]

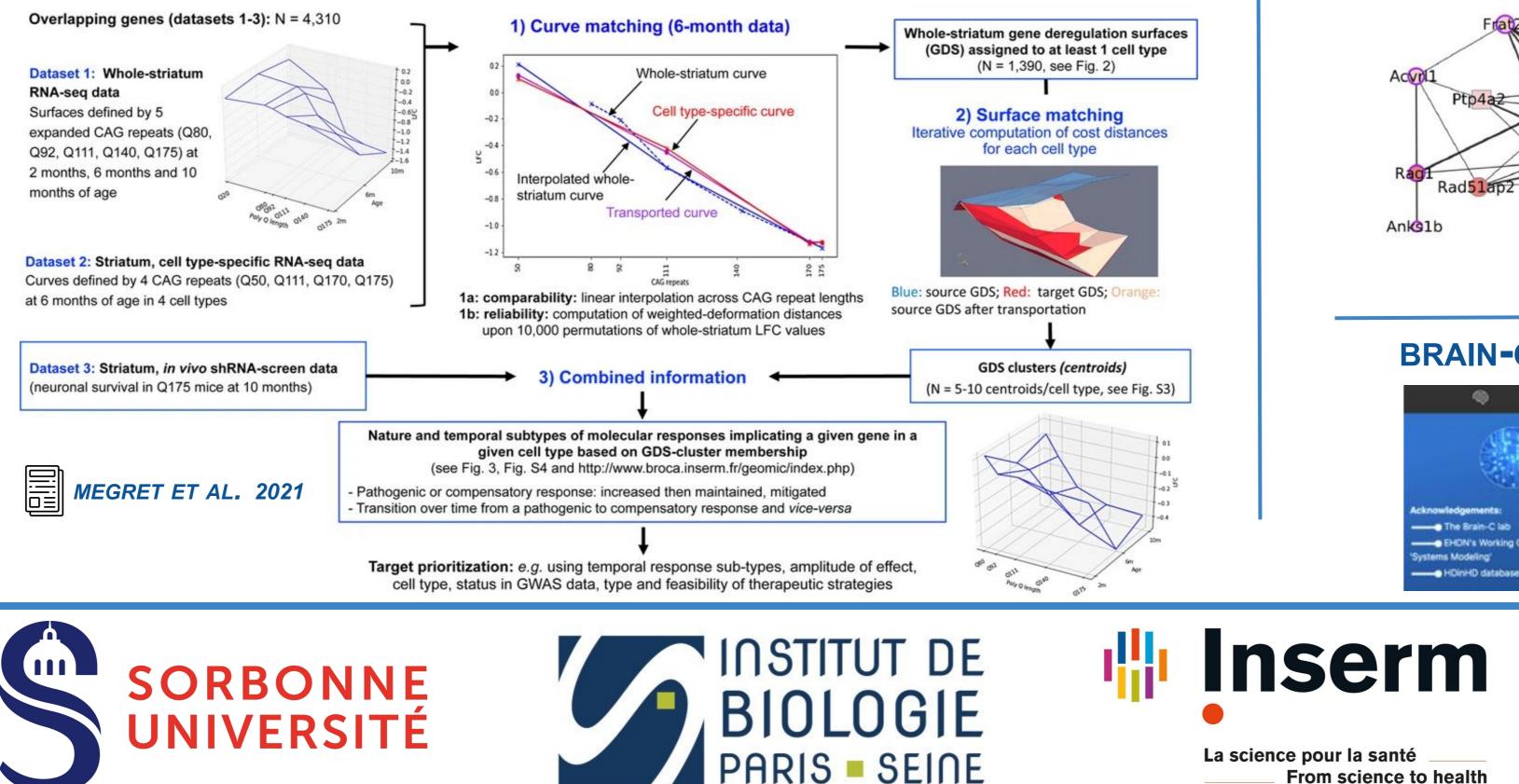
PUBLICATIONS

- VOISIN ET AL., AGING CELL JUNE 2020]
- MEGRET ET AL., BMC **BIOINFORMATICS** [FEBRUARY 2020]
- HAMPEL ET AL., PROGRESS IN **NEUROBIOLOGY** [JULY 2019]
- **BIGAN ET AL., BIOINFORMATICS** [JUNE 2019]



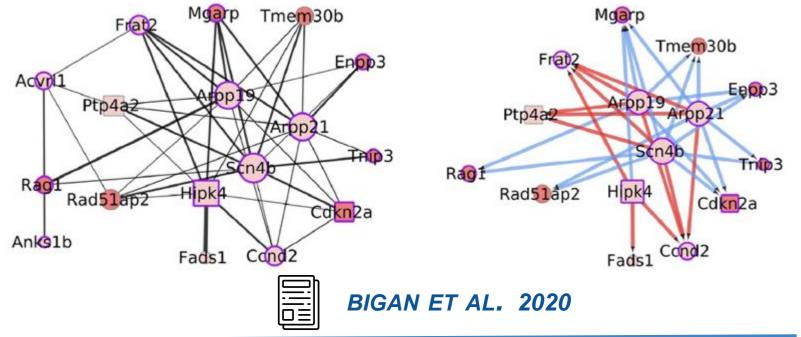
CASSAN BUILDING **B** 6TH FLOOR CASSAN BUILDING A 5TH FLOOR





Synapses

Striatal neurons



BRAIN-C LAB HD KNOWLEDGE DATABASE

