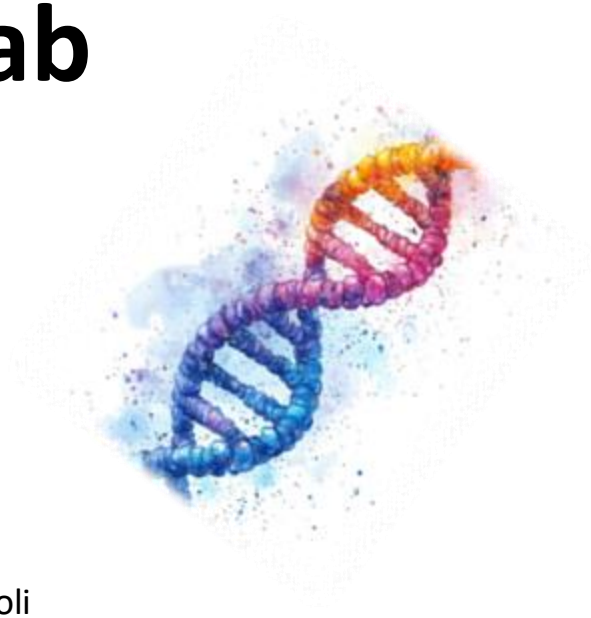
Department of Life Sciences
International Master's Degree in Neuroscience
Corso di Laurea Magistrale in Neuroscienze

LAB PRESENTATIONS

Pharmacogenomics and Molecular Pharmacology Lab



University of Trieste
Marianna Lucafò
mlucafo@units.it

Speakers: Dr. Giulia Zudeh, Dr. Paola Rispoli

Pharmacogenomics and Molecular Pharmacology Lab

UNIVERSITÀ DEGLI STUDI DI TRIESTE

DIPARTIMENTO DI SCIENZE DELLA VITA

Biomarker Identification

Discovery of pharmacogenomic indicators that predict drug response.

Patient-specific Cellular Model Development

Establishing 2D and 3D patient-derived models to simulate in vivo conditions.

Drug Discovery

Screening potential therapeutic compounds on personalized cellular models.

REGIONE AUTONOMA FRIULI VENEZIA GIULIA

ISTITUTO DI RICOVERO E CURA A CARATTERE SCIENTIFICO

Burlo Garofolo di Trieste

BURLO

Pharmacogenomics laboratory

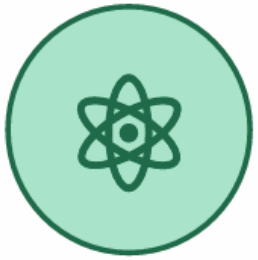
Projects related to **neuroscience**:

- Pharmacoepigenomics of ketamine;
- Study of thalidomide-induced peripheral neuropathy;
- Induced pluripotent stem cell (iPSCs)- derived neurons as a model for pharmacological studies in primary immune deficiencies, such as Aicardi-Goutières Syndrome.

Study of the pharmacoepigenomics of ketamine

SEDATIVE, ANALGESIC AND ANESTHETIC AGENT

PROCEDURAL SEDATION IN EMERGENCY DEPARTMENT



N-METHYL-D-ASPARTATE (NMDA) GLUTAMATE RECEPTOR ANTAGONIST IN THE CENTRAL NERVOUS SYSTEM

VOMITING AND RECOVERY AGITATION

DOSE- AND AGE-DEPENDENT EFFECT

Predict the onset of **ketamine-induced adverse effects** in pediatric patients

SCAN ME

Study of the pharmacoepigenomics of ketamine

PATIENTS

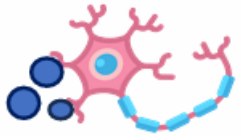
50 pediatric patients

ketamine

44% ADR

56% non-ADR

SAMPLES



neuron-derived extracellular vescicles (NDEVs)

ANALYSES

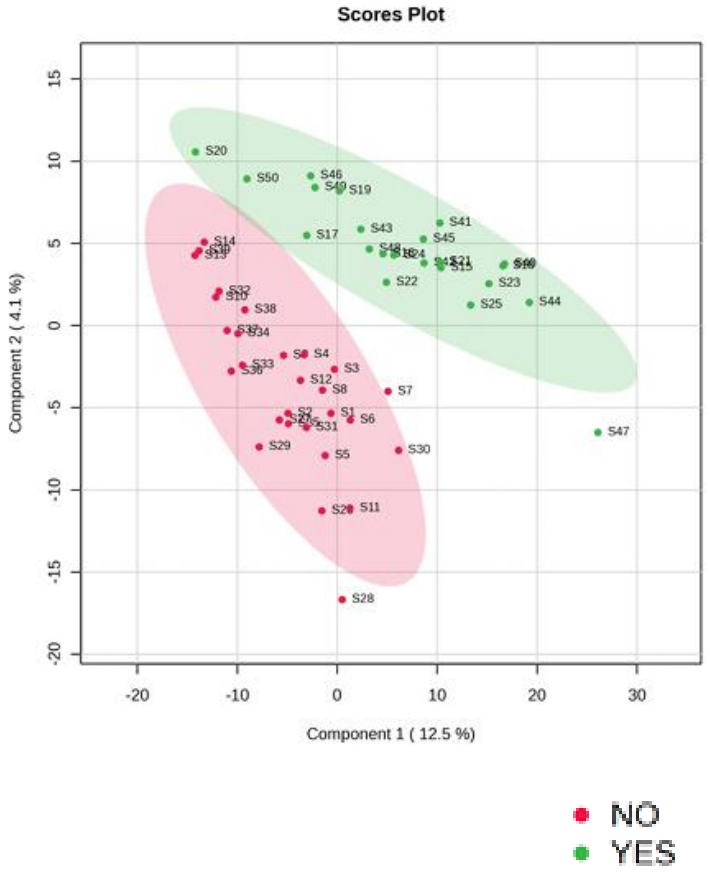
miRNA sequencing

predictive modelling (PLSDA)

differentially expressed miRNAs

gene target and functional analyses

Study of the pharmacoepigenomics of ketamine

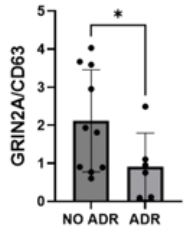


ADR ~ miR-18a-3p+ miR-484+ miR-548az-5p

up miRNA

- 1670 target genes ("inhibited")

GRIN2A, BDNF, MECP2 (**NMDAR-related genes**)



- Glutamatergic synapse
  Long-term potentiation (LTP)
  Neurotrophin signalling
  Dopaminergic synapse
  Cholinergic synapse

GRIN2A, encoding for the **glutamate ionotropic receptor NMDA** type subunit 2A, **is a target of miR-484**

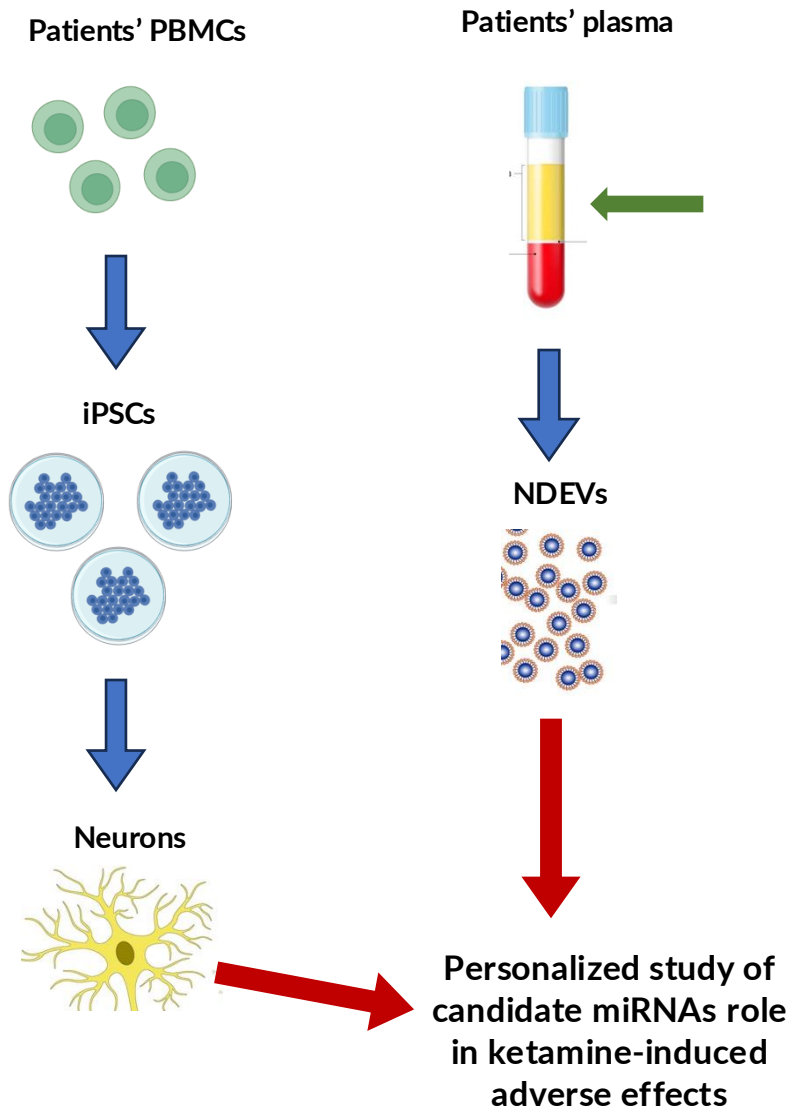
Study of the pharmacoepigenomics of ketamine

AIM OF THE PROJECT

To investigate the functional role of **neuron-derived extracellular vesicles (NDEVs) candidate miRNAs** to provide insights into the molecular mechanisms underlying **ketamine-induced recovery agitation and vomiting** by using **patient-derived iPSCs**.
Investigation of **GRIN2A role** in ketamine-induced side effects.

ANALYSES

- iPSCs generation and differentiation into excitatory neurons;
- Neuron-derived extracellular vesicles (NDEVs) isolation and characterization;
- Assessment of candidate miRNAs expression levels.



REGIONE AUTONOMA FRIULI VENEZIA GIULIA
ISTITUTO DI RICOVERO E CURA A CARATTERE SCIENTIFICO
Burlo Garofolo di Trieste
BURLO
UNIVERSITÀ DEGLI STUDI DI TRIESTE

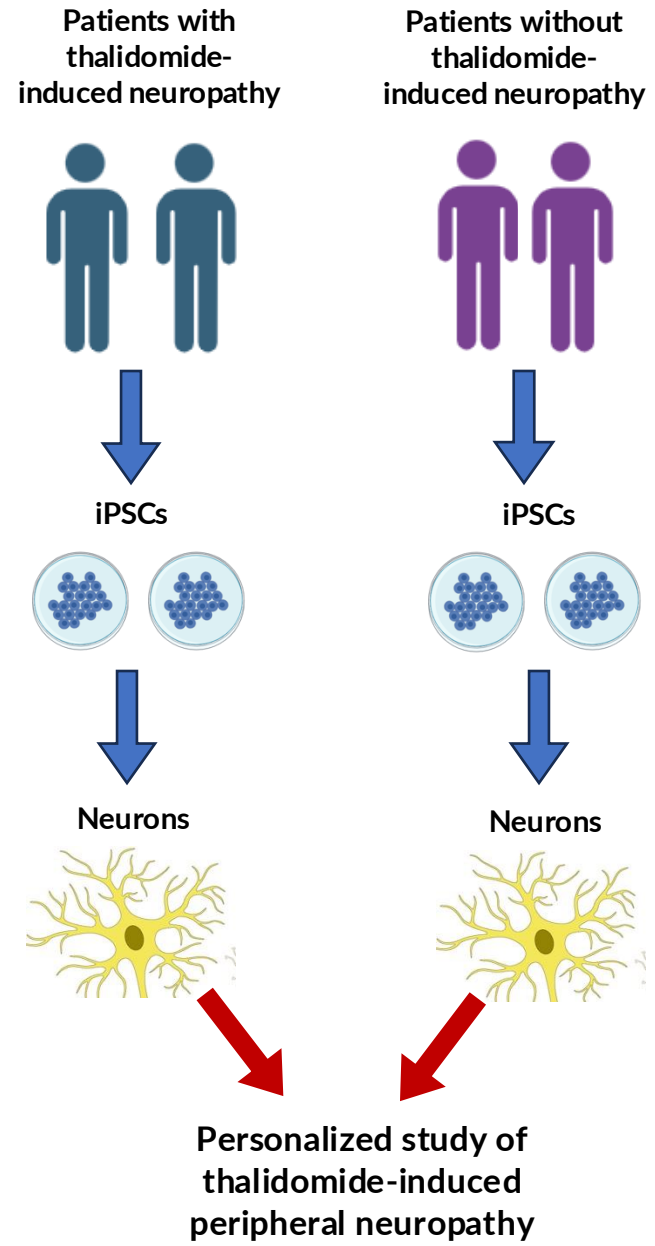
Study of thalidomide-induced peripheral neuropathy

AIM OF THE PROJECT

To investigate *in vitro* **the mechanisms underlying thalidomide-induced peripheral neuropathy** by using **patient-specific iPSCs and neuronal models**.
To assess **miRNAs role** in thalidomide-induced toxicity.

ANALYSES

- Cytotoxicity assays;
- Evaluation of calcium levels;
- Reactive oxygen species (ROS) evaluation;
- Evaluation of the protective role of different substances against thalidomide-induced peripheral neuropathy.

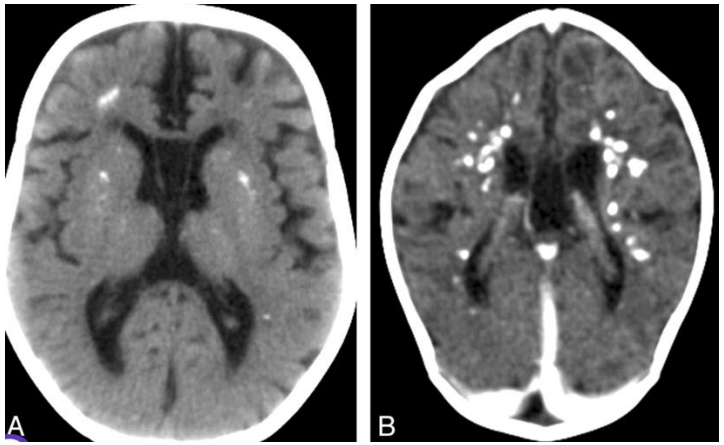


REGIONE AUTONOMA FRIULI VENEZIA GIULIA
ISTITUTO DI RICOVERO E CURA A CARATTERE SCIENTIFICO
Burlo Garofolo di Trieste
BURLO

UNIVERSITÀ DEGLI STUDI DI TRIESTE

Precision therapy of innovative drugs for pediatric Aicardi-Goutières syndrome using iPSCs cells

Aicardi-Goutières syndrome

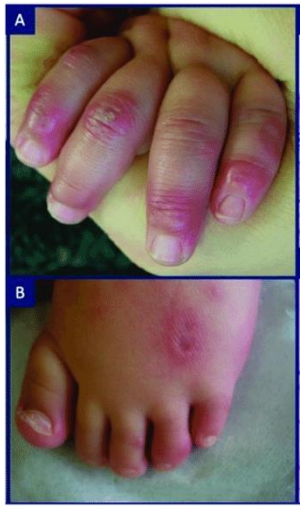


-Calcifications in the basal ganglia and the cerebral white matter
-Atrophy
-Microcephaly
-Abnormal myelination

CLINICAL FEAUTURES OF THE DISEASE:

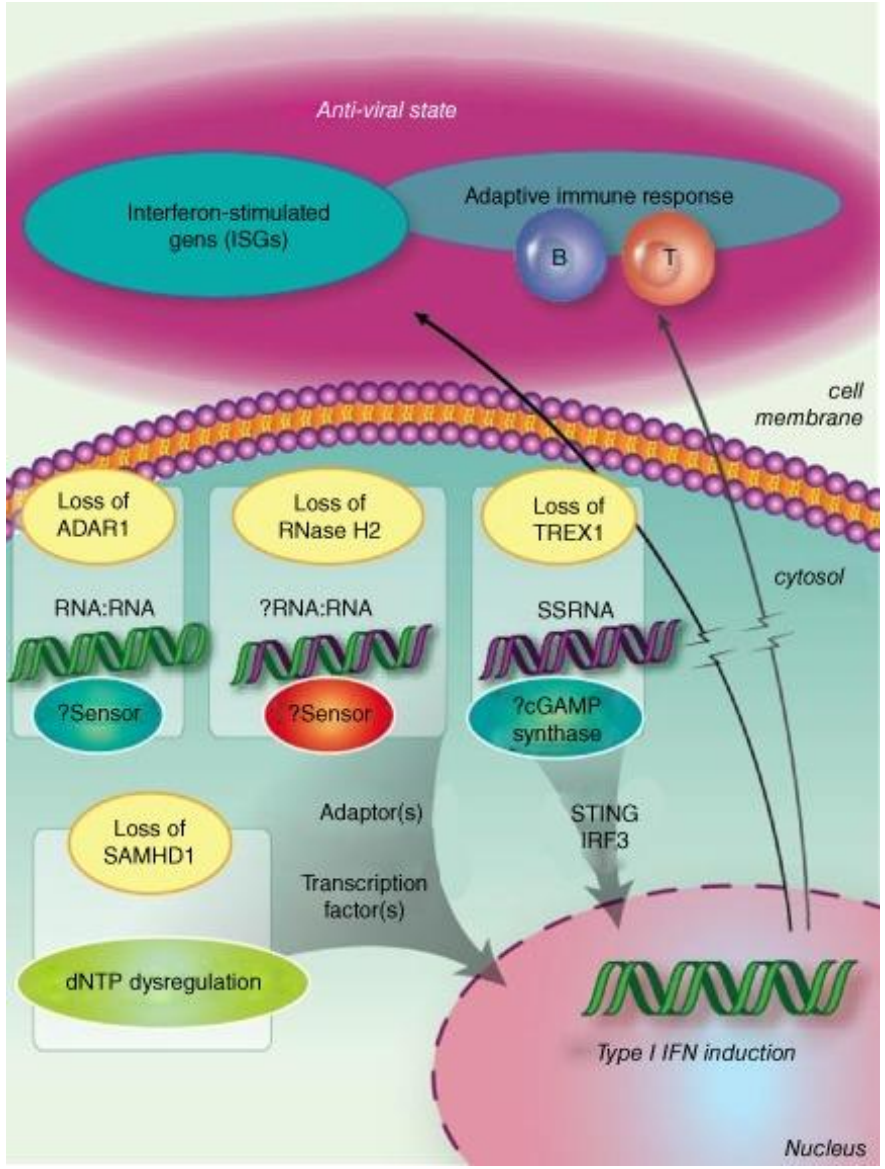
- Neurodevelopmental degeneration
- Microcephaly
- Mental delay
- Dystonia
- Tetraparesis
- Skin lesions

- Poor life expectation



Autosomal recessive inherited rare diseases

Precision therapy of innovative drugs for pediatric Aicardi-Goutières syndrome using iPSCs cells



Aicardi-Goutières syndrome

- mutations of at least one out of multiple genes involved in nucleic acid metabolism or sensing leading to an altered interferon signaling → **neural chronic inflammation**

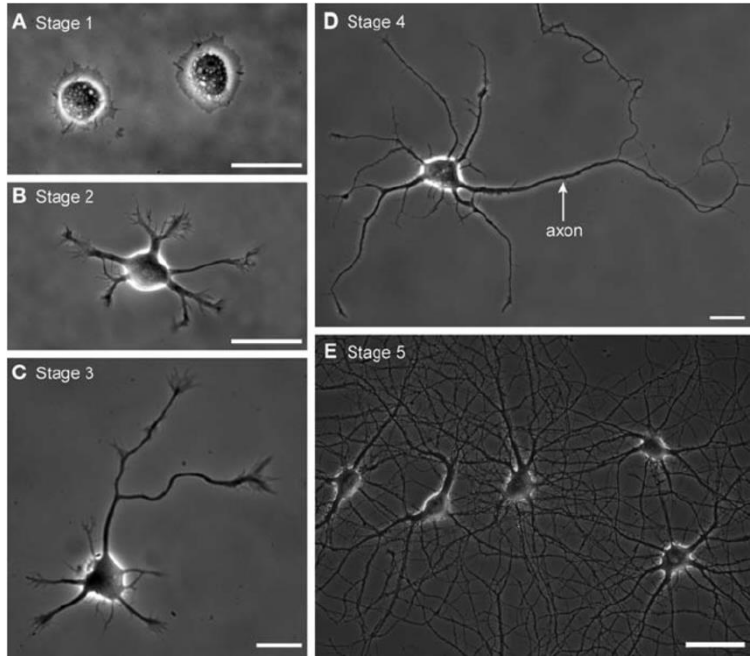
- elevated levels of IFN I and abnormal myelination

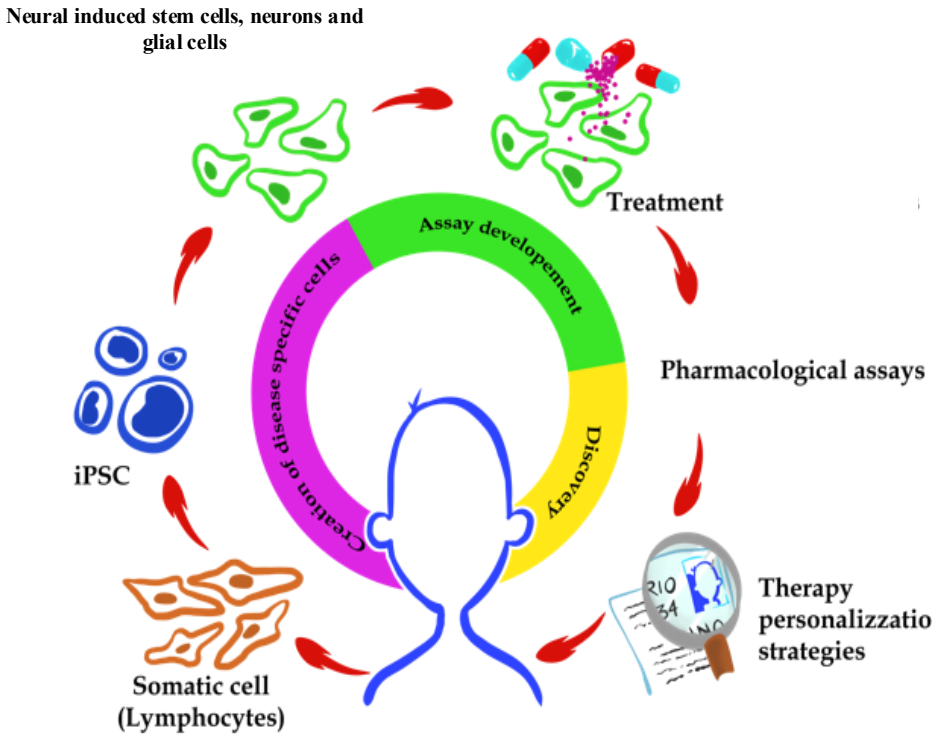
Type	Gene
AGS1	*TREX1*
AGS2	*RNASEH2B*
AGS3	*RNASEH2C*
AGS4	*RNASEH2A*
AGS5	*SAMHD1*
AGS6	*ADAR1*
AGS7	*IFIH1*

Precision therapy of innovative drugs for pediatric Aicardi-Goutières syndrome using iPSCs cells

AIM OF THE PROJECT

To evaluate the **safety and efficacy of innovative drugs** potentially acting directly on the pathogenic mechanism of **AGS** on **patient-specific *in vitro* model of neural induced pluripotent stem cells, differentiated neural and glial cells**





ANALYSES

- Cells culture and differentiation
- Cytotoxicity and proliferation analyses
- Gene and protein expression analyses
- Cytokines evaluation
- Morphology analyses

UNIVERSITÀ DEGLI STUDI DI TRIESTE

UNIVERSITÀ DEGLI STUDI DI BRESCIA

REGIONE AUTONOMA FRIULI VENEZIA GIULIA
ISTITUTO DI RICOVERO E CURA A CARATTERE SCIENTIFICO
Burlo Garofolo di Trieste

Contact: Prof. Marianna Lucafò, mlucafo@units.it