iPSC_PGNM core facility

Institut NeuroMyoGene - Pathophysiology and Genetics of Neuron and Muscle (INMG-PGNM)
UCBL - CNRS UMR5261 - INSERM U1315, 8 avenue Rockefeller 69008 **Lyon – France**

Scientific coordinators: G. Boncompain, A. Jacquier, V. Risson
Operational managers: L. Coudert and A. Hennick

contact: ips-pgnm@univ-lyon1.fr

OUR GOALS AND ACTIVITIES

- to be open to both internal and external researchers and to academic and industrial partners
- to provide expertise and technical assistance in hiPSC quality control
- to help for strategy and design of genome editing of hiPSC
- to offer comprehensive guidance on the differentiation of hiPSC into diverse structures, such as neurons, cardiomyocytes, spheroids, organoids, and co-culture systems.
- to store, maintain and validate hiPSC lines
- to provide and bank the control cell line AG08C5, hPSCreg #PGNMi001-A

OUR TRAININGS

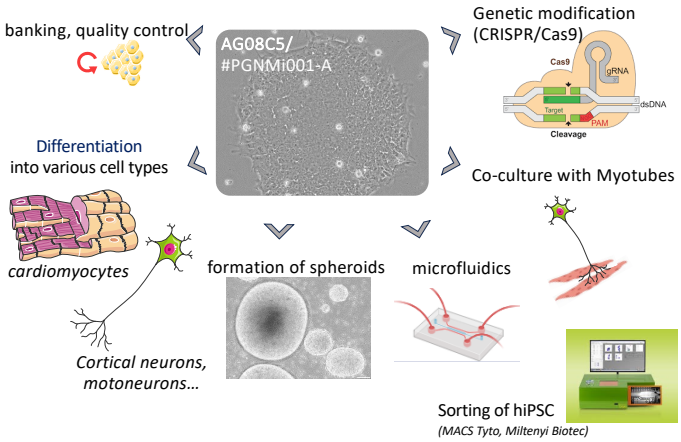
✓ Training of internal hiPSC users

✓ CNRS Formation Entreprises

- hiPSC ciulture, genome editing, quality control and differentiation
  https://cnrsformation.cnrs.fr/pdf/25221.pdf
- 3D cell culture from hiPSC: spheroids and organoids of neuronal, muscular and cardiac systems
  https://cnrsformation.cnrs.fr/pdf/25378.pdf

OUR CONTROL CELL LINE, AG08C5/ hPSCreg #PGNMi001-A

from a male donor , 1 year old



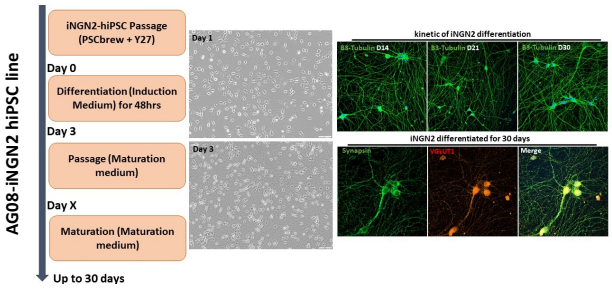
OUR DISEASE FOCUS

Neuro-muscular diseases
Spinal muscular dystrophy
Neurodegenerative diseases
Cardiac disorders

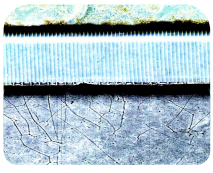
OUR HIPSC-DERIVED CELLS

Cortical neurons
Motoneurons
Sensitive neurons (DRG)
Cardiomyocytes
Chondrocytes

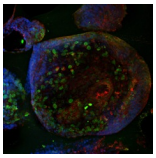
EXAMPLES



DIRECT CONVERSION of AG08-iNGN2 hiPSC line into cortical neurons
© L. COUDERT, Team: L. SCHAEFFER
AG08-iNGN2: genetic-inducible line where inducible neurogenin2 (NGN2) gene coding for key transcription factors in neurogenesis were introduced.
hiPSC are induced to differentiate at day 0 to day 3 by adding a medium containing doxycycline and allowing the transcription of NGN2. Cells rapidly transform into cortical neurons and on day 3 formed axons. On days 14, 21, and 30, cells were stained with an antibody targeting the neuron-specific structural protein beta-3-tubulin (in green) and showed growing neural arborescence. On day 30, cells were stained with an antibody targeting synapsin to visualize synapse and VGLUT1 to validate the glutamatergic nature of iNGN2

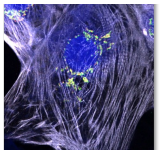


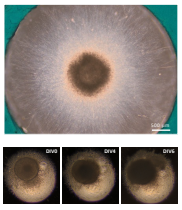
MICROFLUIDICS Pattern for Sensory Neurons *:*
© S. ROUBILLE , Team: P. LOMONTE
The loss of Survival Motor Neuron (SMN) gene causes Spinal Muscular Atrophy (SMA). We use human SMA patient derived iPSC to generate motoneurons as a cellular model to investigate the role of SMN in the SMA pathology.
Herpes Simplex Virus 1 is a neurotropic virus responsible for neurons decay. We differentiate hiPSC into sensory neurons and adapt them in microfluidic devices as a model to investigate HSV-1 viral infection



CARDIOMYOCYTE derived from iPSC:
©T. DARGAR, Team: V. GACHE
Cardiovascular diseases cover a wide spectrum of pathologies including dilated and hypertrophic cardiomyopathies and cardiac arrhythmias. In the perspective of identifying new pathological mutations leading to CVDs, we focus on variants of unknown significance (VUS). We are using patients derived hiPSC cells and/or CRISPR-Cas9 edited hiPSC. We differentiate them into ventricular cardiomyocytes (vCM) and track for functional implication of putative pathological mutations.

©G. BONCOMPAIN, Team: V. GACHE
Secretory protein transport is necessary to fulfil essential cellular functions. Cells from different tissues display distinct secretion needs. At the centre of the secretory pathway, the Golgi complex has to handle the correct processing and sorting of the cargo. The molecular players involved in specific Golgi-dependent secretory routes are not well characterized. We use hiPSC-derived cardiomyocyte to explore Golgi organization, proteome and secretory functions.





DORSAL ROOT GANGLIA Organoid (DRG):
© V. MOSBACH, A. HENNICK, Team: H. PUCCIO
Friedreich Ataxia (FA) and CANVAS syndrom are both recessive ataxias due to biallelic intronic expansion in FXN and RFC1 gene respectively that cause dorsal root ganglia (DRG) degeneration. hiPSCs were differentiated into 3D DRG organoids to investigate pathophysiological mechanisms. A two steps small-molecules based procedure allowed to generate in 40 days DRG organoids that recapitulate the 3D spatial organization and contain the principal sensory neural subtypes and glial cells found in *in vivo* DRG. Brightfield picture of DRG organoids.

WE ARE MEMBERS OF

AURA Stem Auvergne Rhône Alpes Stem Cell Network
FSSCR French Society for Stem Cell Research
CorEuStem