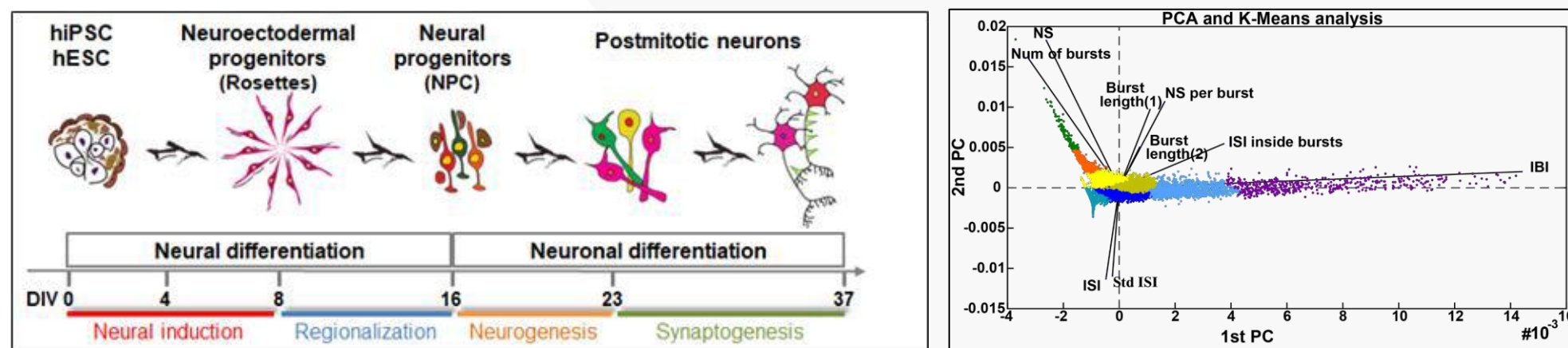


# NEUROTOXICOLOGICAL AND NEURODEVELOPMENTAL STUDIES USING HUMAN MODELS



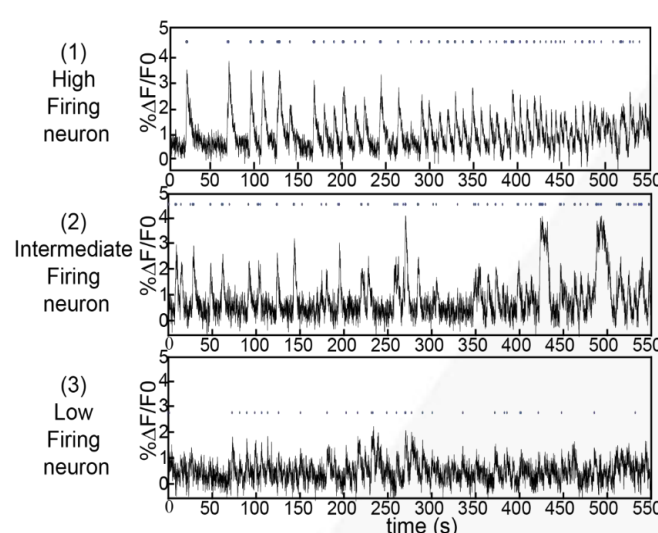
## Standardized cell culture

Built on more than 20 years of experience in the expansion and differentiation of human pluripotent stem cells (hPSCs), our protocol for neuronal differentiation has been reproduced more than 500 times with the strictest quality controls:

- ✓ **Karyotype stability:** we establish regular controls on genome abnormalities, testing chromosomal alterations by Q-band analysis every 10 passages and before starting each differentiation process, and by CGH array 20–30 passages.
- ✓ **Reproducibility:** we have tested our protocol in more than 10 different hPSC lines, including embryonic and induced hPSCs, obtaining a protocol reproducibility above 95% consistency.
- ✓ **Traceability:** we operate under ISO 9001:2015 and the Creatio Quality System, guaranteeing the traceability of all stem cell passages, the products used, and the results obtained.

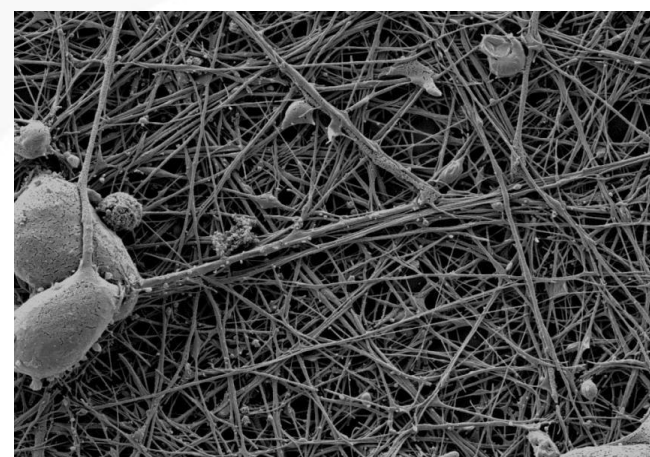


## High-throughput analysis



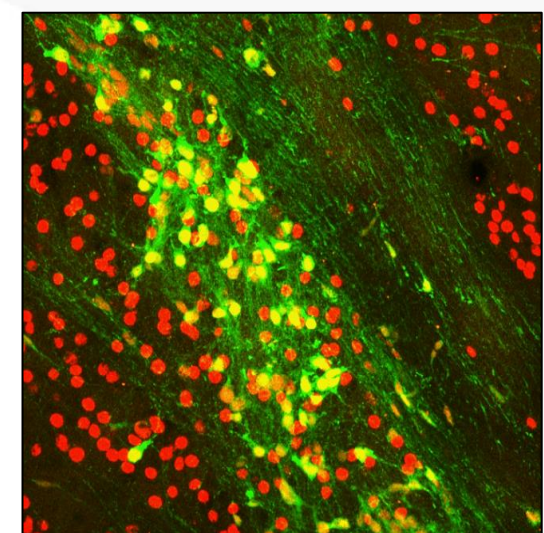
- ✓ **Gene expression profiles:** our OpenArray QPCR-based platform analyzes the expression of (I) 110 key genes at different developmental stages and (II) 160 genes associated with synaptic functionality (synaptic receptors, neuronal channels, and second messengers).
- ✓ **High-content analysis:** a wide range of specific markers for each developmental stage, from pluripotency to mature neurons and neurotransmitters.
- ✓ **Calcium imaging:** spontaneous and evoked neuronal response to chemicals or optical stimulation that allows the classification of neurons based on activity.

## Connectivity analysis



- ✓ **Electron microscopy:** analysis of connectivity formation by scanning electron microscopy at different development stages.
- ✓ **SNARE analysis:** we perform SNARE characterization by semi-quantitative western blot.
- ✓ **Immunocytochemistry of synaptic proteins:** fine colocalization of synaptic proteins permits the analysis of disturbances of regular function.
- ✓ **Extracellular vesicle characterization:** we investigate the morphological alteration of subcellular organelles.

## Chimeric human-mouse model



- ✓ **Cell transplantation:** transplantation of hNPCs from control and Huntington's Disease patients into the striatum of new-born mice.
- ✓ **Cell integration, differentiation and axonal projection:** transplanted hNPCs differentiate into striatal neurons and send axonal projections towards and establish synaptic connections within the host basal ganglia circuitry.

## Drug testing and toxicology

- ✓ **Drug testing:** efficacy testing of new drugs along the neurodevelopmental process. New drugs can be tested at all developmental stages in control or disease-derived human cells.
- ✓ **Developmental toxicology:** drug toxicity analysis in different neuronal developmental stages. High-throughput analysis of neuronal development and its response to new drugs.



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