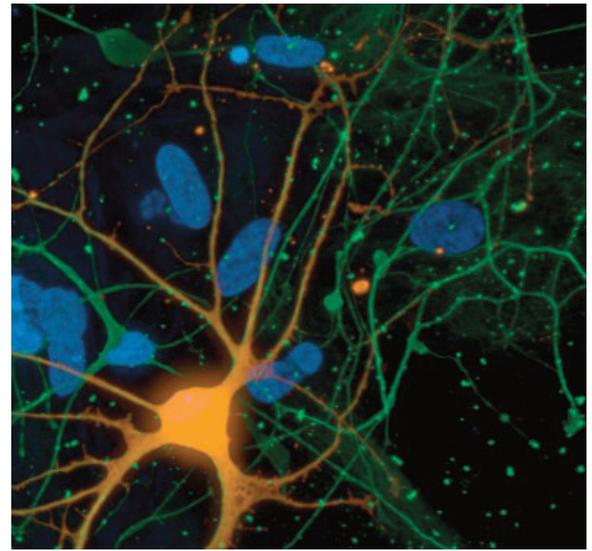# SynFire® Induced Neurons

Human iPSC Derived GABA and Glutamatergic Induced Neurons (iNs)

NeuCyte

REPROCELL Product Provider

Translatable Neuroscience

The high attrition rate of CNS drugs during clinical development is a major challenge to the pharmaceutical industry. High rates of drug failure have been largely attributed to the lack of biologically relevant models available to study the functional links between target and phenotype.

NeuCyte's mission is to accelerate and optimize CNS drug discovery by developing more predictive assays and platforms for phenotypic screening. SynFire® technology is at the forefront of this vision — a unique differentiation method that generates functional, human neurons.

SynFire® Neural Cells

- ✓ **Demonstrate** real human biology
- ✓ **Show** rapid and homogeneous maturation
- ✓ **Represent** a flexible modular system
- ✓ **Display** low batch-to-batch variation
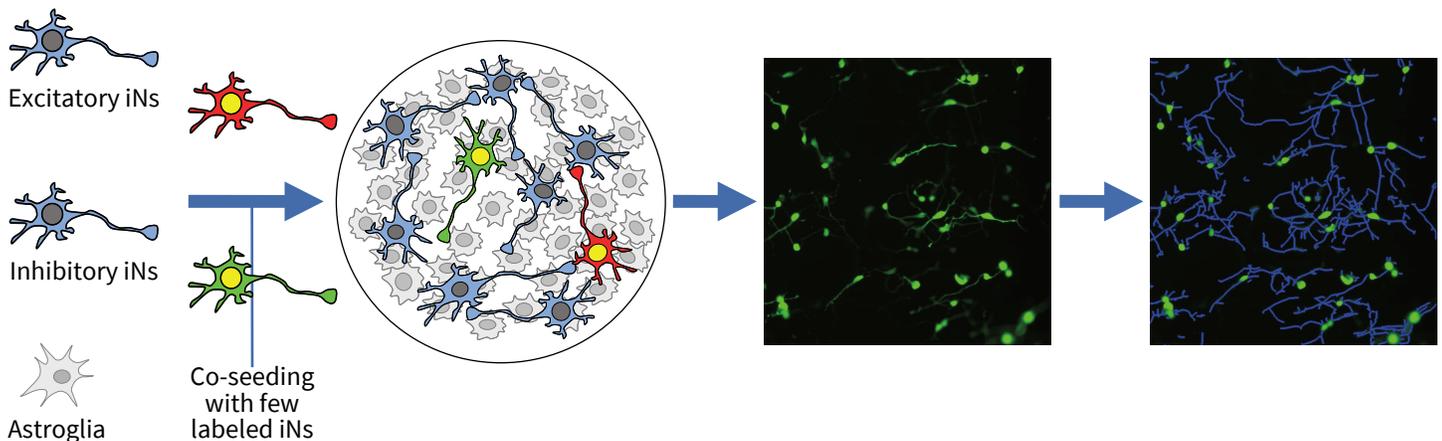- ✓ **Contain** pure populations of neural cells

Excitatory iNs

Inhibitory iNs

Astroglia

Co-seeding with few labeled iNs

Figure 1: SynFire® iNs can provide morphology-based readouts using live-imaging techniques

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SynFire® iNs exhibit mature neuronal characteristics

SynFire® iNs express pan-neuronal and subtype specific markers, rapidly mature to form complex networks and cellular morphologies. The modular aspect of SynFire® neural cells allow for defined co-culture conditions and specific ratios of mixed neuronal subtypes, includingexcitatory Glutamatergic and inhibitory GABAergic neurons.
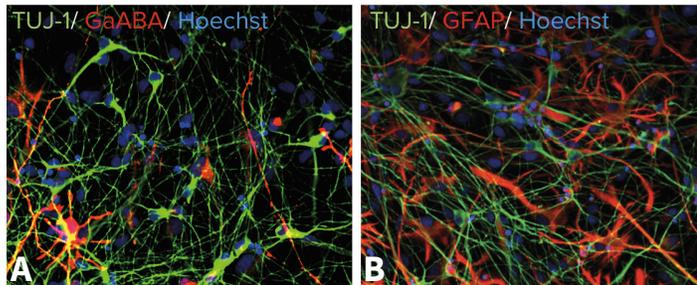
Pan-Neuronal and Subtype Specific Markers

Figure 2: Immunocytochemistry reveals mature markers in SynFire® Neurons (A) Mixed neural cultures: Pan-neuronal marker β3-Tubb (Tuj1)/Inhibitory neuron GABA neurotransmittor, α1/Nuclear staining Hoeschst. (B) Co-culture system: Pan-neuronal marker Tuj1/Astroglia marker GFAP/Nuclear staining Hoechst. The co-cultures exhibit complex neuronal networks, morphologies and show mature synaptic markers. (C) Synaptic competent cultures: Pan-neuronal marker Map2/Synaptic marker Synapsin1. (D) Ideally suited for network assays: Pan-neuronal marker Tuj1/Nuclear staining Dapi.

Elaborate Networks
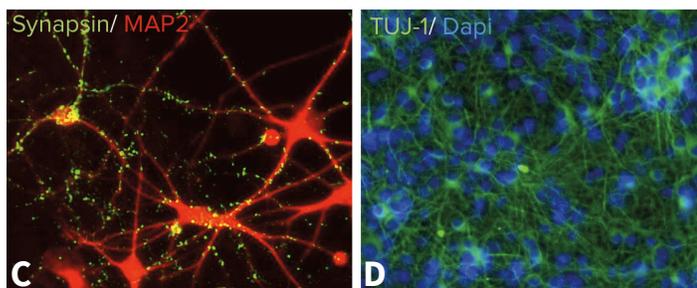
SynFire® iNs exhibit mature neuronal functionality

SynFire® iNs not only express neuronal markers on a phenotypical level — they also display the functionality of mature neurons from as early as two weeks post-plating.
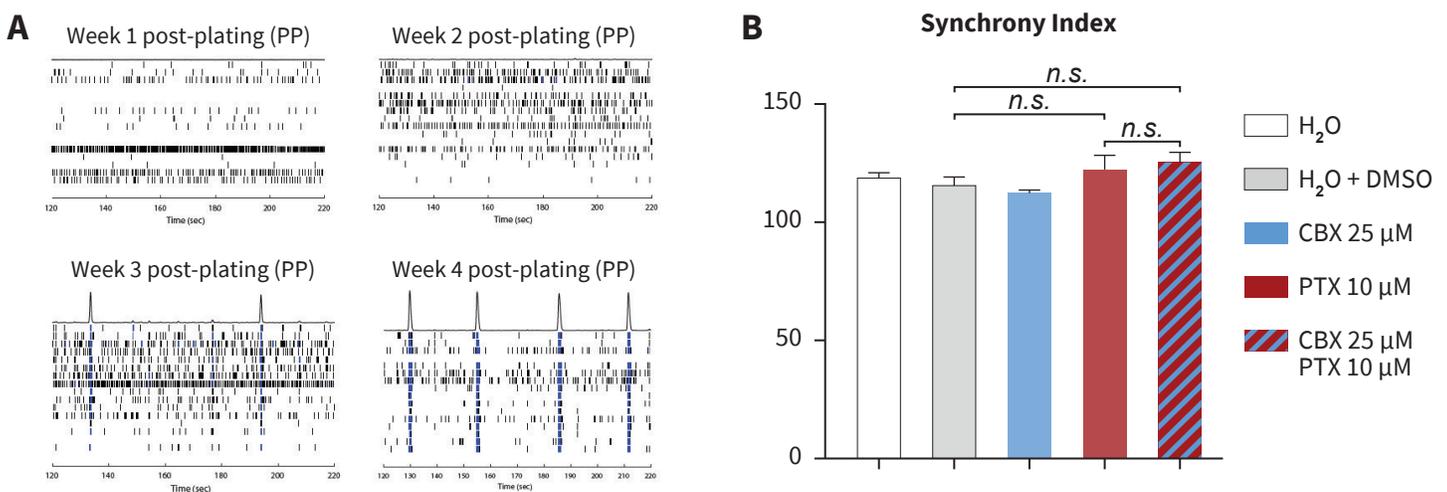

Figure 3. Synfire® neurons express mature neuronal functionality *(A) Ontogeny of neural network activity maturation of SynFire® co-cultures. These co-cultures contain 70% Glutamatergic, 30% GABAergic neurons and human astrocytes. Representative raster plots from Microelectrode arrays (MEA's) recordings at weeks 1-4. Axion 48 well MEA plates were used to assess activity. (B) SynFire® iNs transmit signals via synapses and not gap junctions. When treated with the connexin blocker CBX, SynFire® iNs still showed functionality. These results suggest that the neuronal activity observed is a result of synaptic transmission rather than gap-junction transmission.*

SynFire® iNs mimic primary cortical neuron activity

Neurons made with SynFire® technology demonstrate functional activity that resembles rat cortical neurons. Below shows an independent study of Mean Firing Rate (MFR) across various companies, provided by a NeuCyte customer. Results of this study showed that SynFire® co-cultures mimic the MFR of primary cell cultures more closely than any other commercially available neurons.
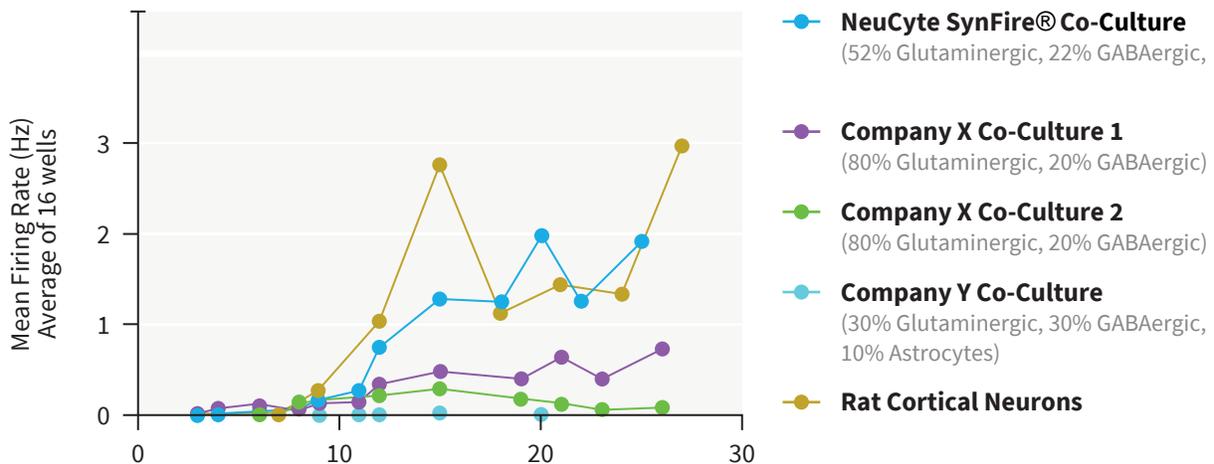

Figure 4. Independent comparison of NeuCyte's SynFire® neural cells to other iPSC derived neurons. Plot shows the mean firing rate (MFR) of SynFire® induced neural co-cultures and other commercially available neurons. MFR was assessed using Axion MEA plates. Axion Maestro Axis software Default setting for spontaneous neuron firing was used.

SynFire® iNs respond in a predictable manner to drugs

SynFire® iNs respond in a predictable manner to drugs, therefore demonstrating increased clinical relevance compared with inferior technologies. NeuCyte posses a documented pharmacological profile for each model, allowing comparison of your test articles to compounds with a known mechanism of action.
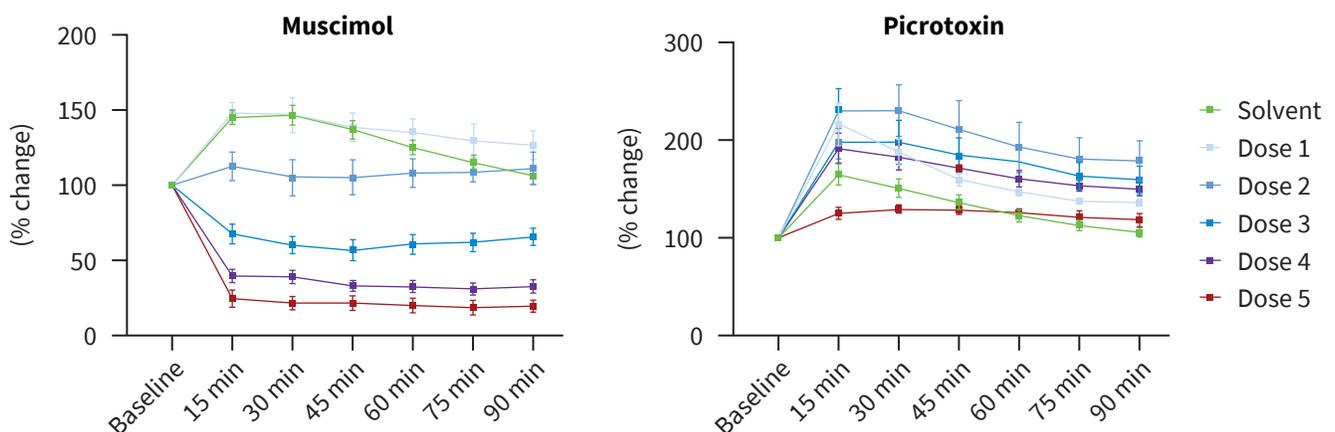

Figure 5. SynFire® Neurons respond in a predictable manner to licensed drugs. (A) Neurons respond in a dose-dependant manner to Muscimol, a GABA agonist which reduces neuronal activity, and (B) Picrotoxin, a GABA antagonist that prevents inhibition of neuronal activity.

Bridging the drug discovery path

Based on the advantageous SynFire® technology for generating human iPSC-derived induced neuronal cells, NeuCyte has developed a proprietary in vitro human neural platform for complex electrophysiological and morphological readouts suited for target identification and validation, efficacy testing and neurotoxicity assessment.

Applications of SynFire® iNs

- **Neural toxicity** testing
- **Chemically induced** disease models
- **Target identity** testing
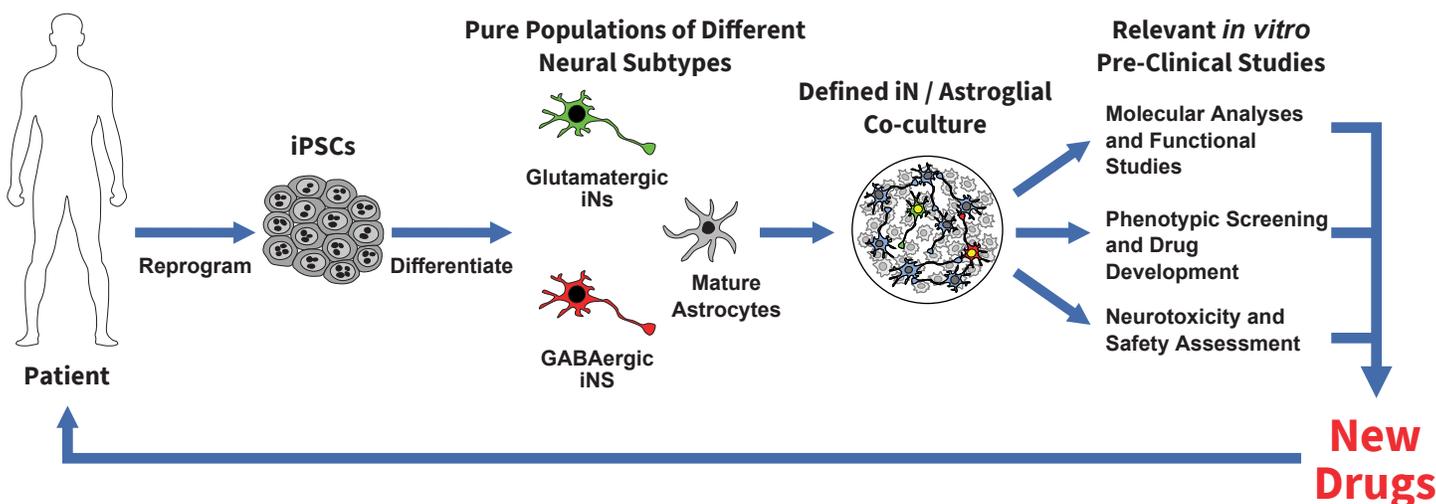- **Gene-edited** disease models
- **Drug efficacy** testing

Figure 6: SynFire® iNs can support your neurological research in drug discovery and non-clinical studies.

SynFire® Line	Catalog Numbers	Pack Size
SynFire® Co-culture Kit	NC1010-1.5 NC1010-7.5	
SynFire® GABAergic iN Kit	NC1002-10 NC1002-20 NC1002-40 NC1002-50	Various sizes and Custom packaging available
SynFire® Glutamatergic iN Kit	NC1001-10 NC1001-20 NC1001-50 NC1001-60	
SynFire® Media Kit	NC2010-10 NC2010-20 NC2003-1	

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