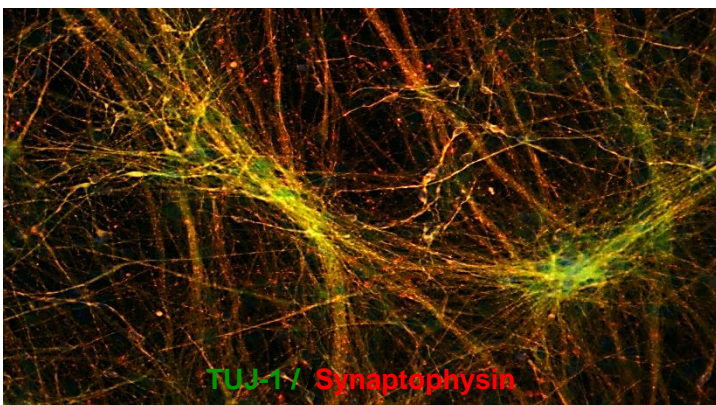
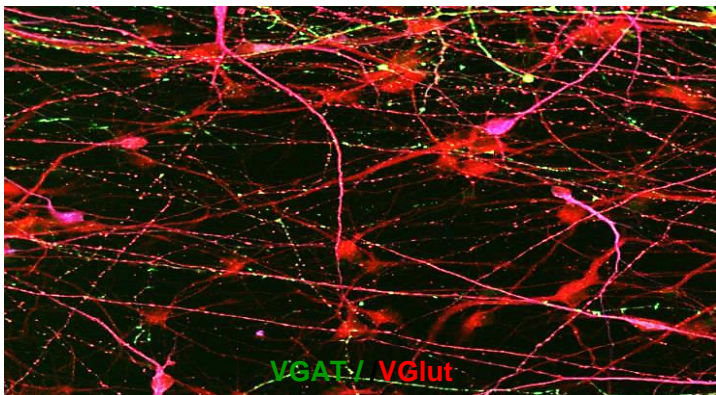




Scalable Neural Stem Cells Differentiate Into Mature Human Neurons With Excitatory and Inhibitory Synaptic activity

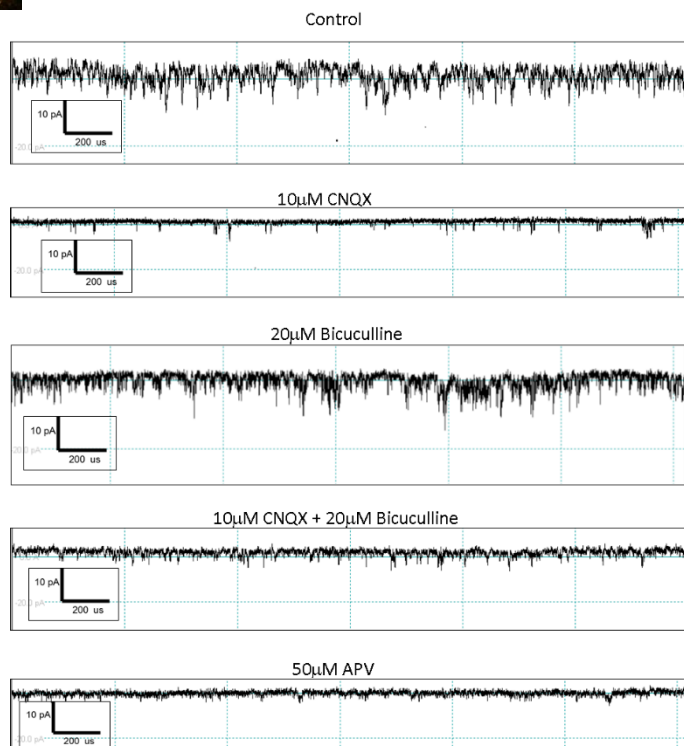


- Human HIP-009 neural stem cells isolated from human brain tissue
- Differentiates into multiple neural sub-types, astrocytes and oligodendrocytes
- Scale $>10^9$ cells with consistent reproducible results
- Proprietary media formulated for growth, transition and directed differentiation to enrich for specific neural sub-types
- Functional human neurons measured by electrophysiology patch clamp and on multi-electrode arrays (MEAs)
- Compatible with High Throughput Screening (HTS) Platforms

- Pan-neural model
- Spontaneous action potentials.
- Spontaneous network activity with Glutamatergic and GABAergic characteristics.
- Correlates well with High-Content endpoints

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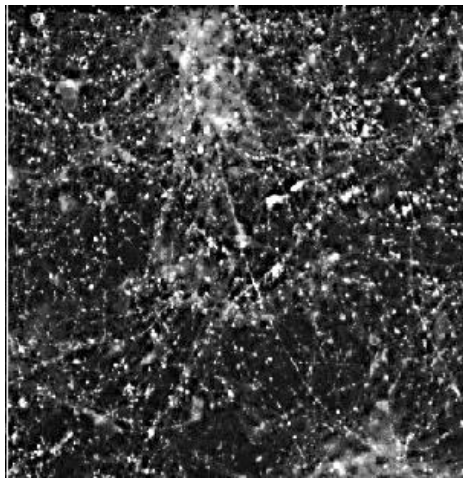
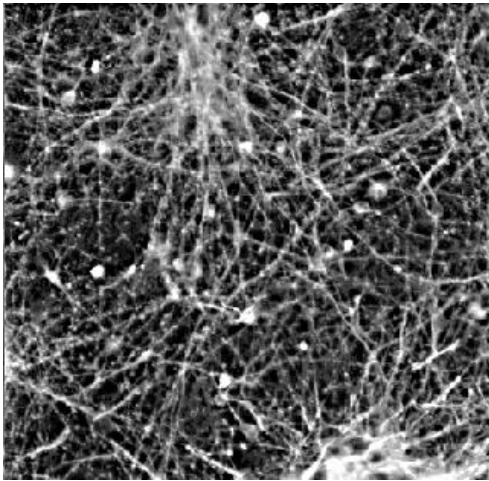


Alzheimer's Disease Model

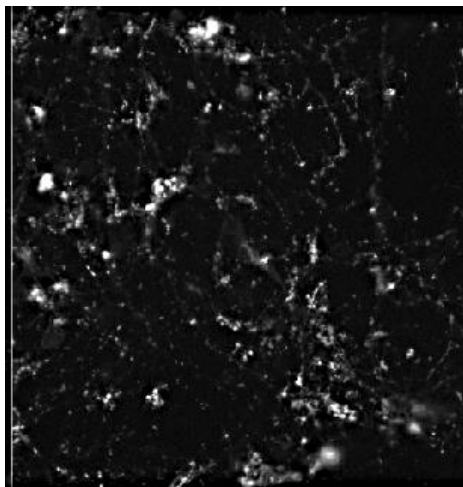
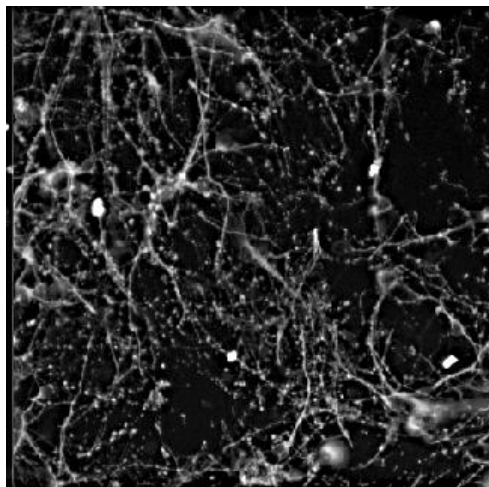


Tuj1

Synaptophysin

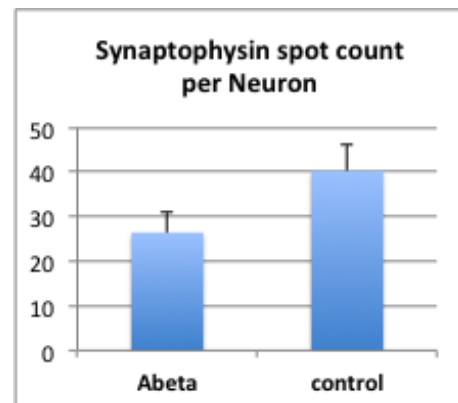
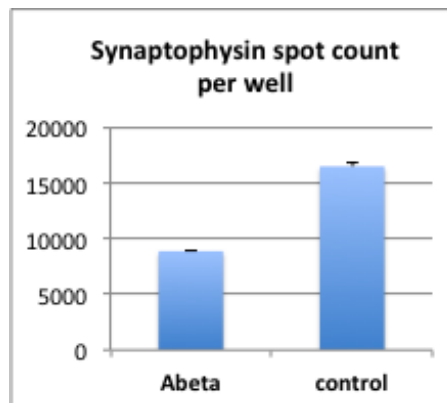
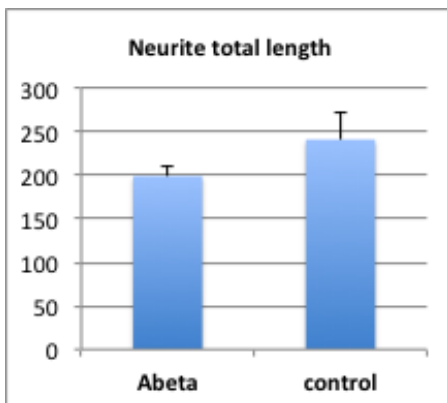


Control



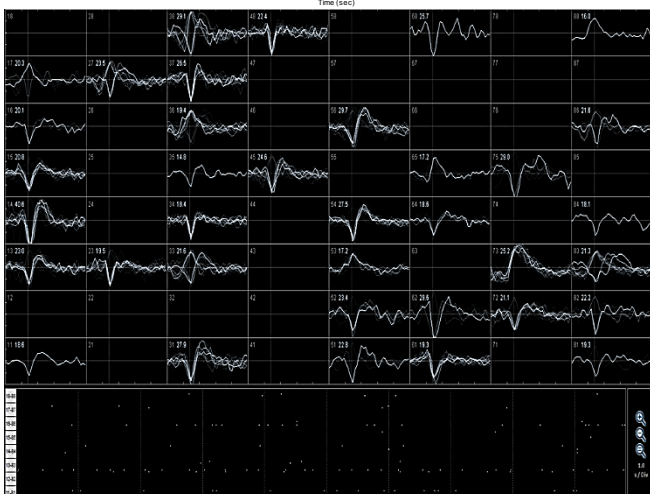
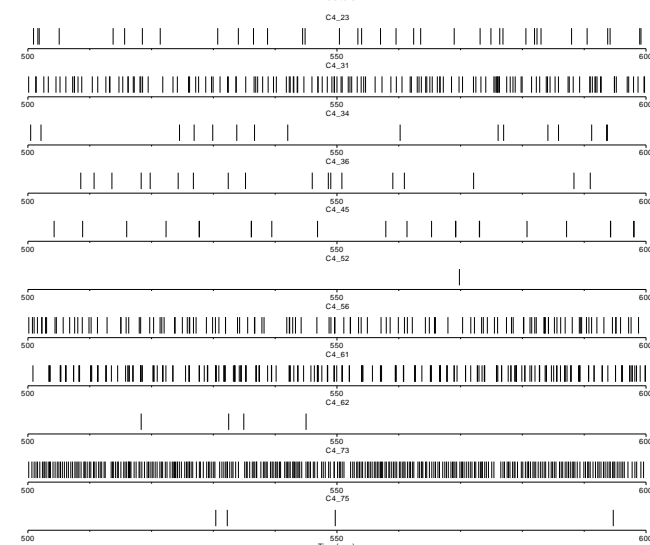
Ab 1-42

- HIP-009 NSCs were differentiated into mature functional pan-neurons
- Following 28 days neural cells were treated with 10 μ M A-Beta (Ab) oligomer 1-42 for 24 hours then fixed and immunostained for Tuj1, GFAP and Synaptophysin
- Image analysis was performed on Cellomics VTI
- High-Content analysis demonstrates significant synaptic deficit induced by Ab 42 oligomers.
- This model is being used to screen for drugs to prevent/treat Alzheimer's Disease

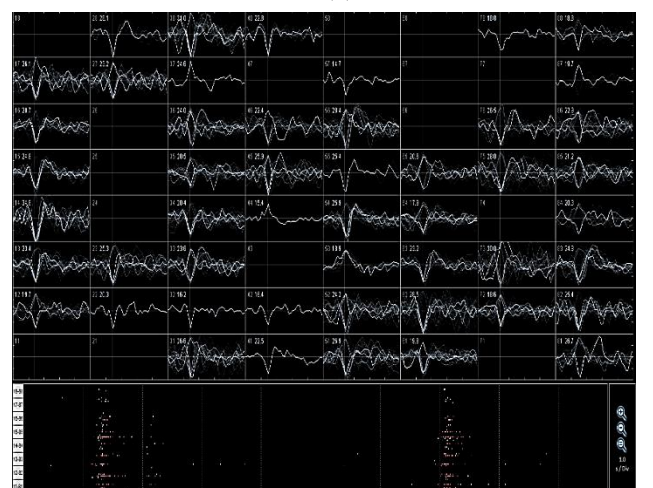
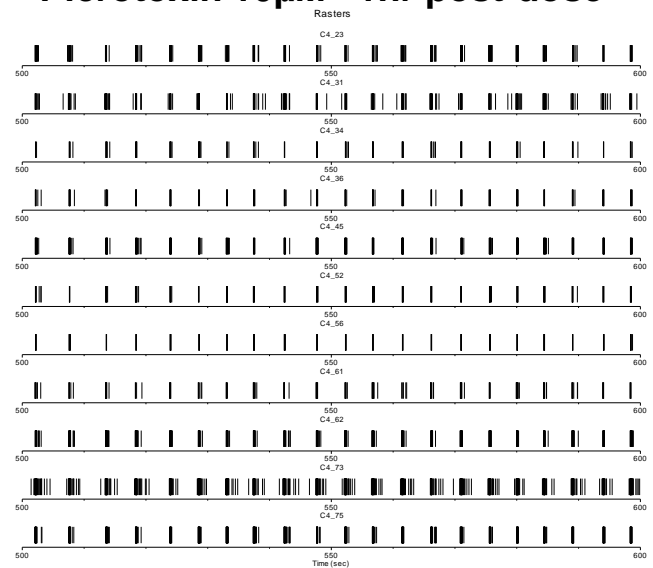


- HIP-009 NSCs differentiated into pan-neurons on MEAs and maintained in culture beyond 70 days
- Typical response to Picrotoxin ($10\mu\text{M}$) observed in HIP-009 human neurons was comparable to rat primary neurons
- Vehicle control (DMSO 0.2%) – data not shown
- Representative electrodes for each well were chosen for raster plot images
- Raster plots show increased
 - Firing rate
 - Burst rate
 - Burst length
 - Synchrony
 - Number of active electrodes

Baseline



Picrotoxin $10\mu\text{M}$ 1hr post-dose

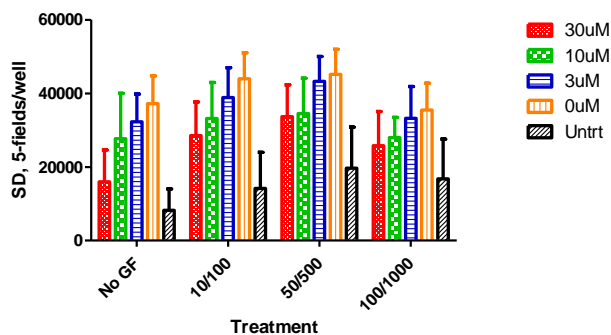


Parkinson's Disease Model

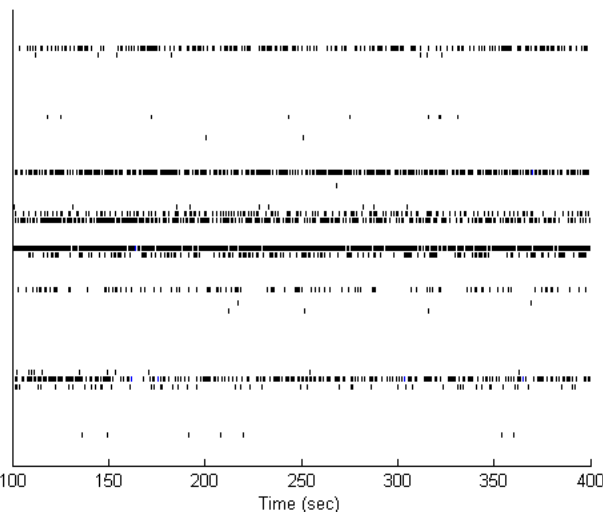


- DA-H9 NSCs differentiated into dopaminergic neurons on MEAs
- 70% of the neurons were TH+
- Developed neural networks with spikes and bursts
- Responded to MPP+ in a dose response curve
- This model was used to screen for drugs to treat/prevent Parkinson's Disease

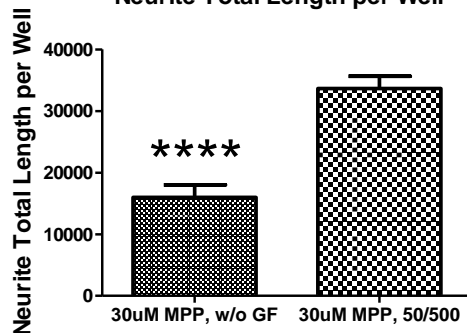
DA-H9-Cryo_MPP+ 27-IVD_Growth Factors
Neurite Total Length per Well



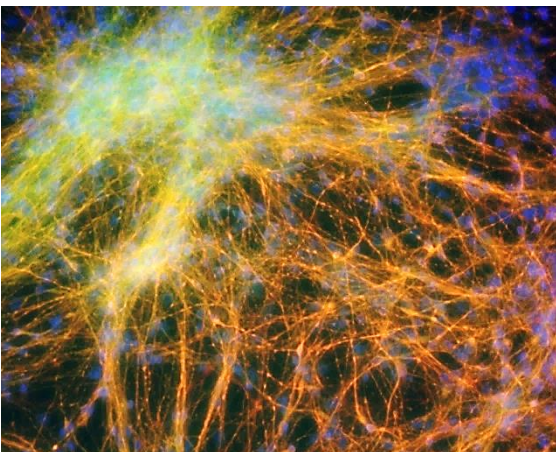
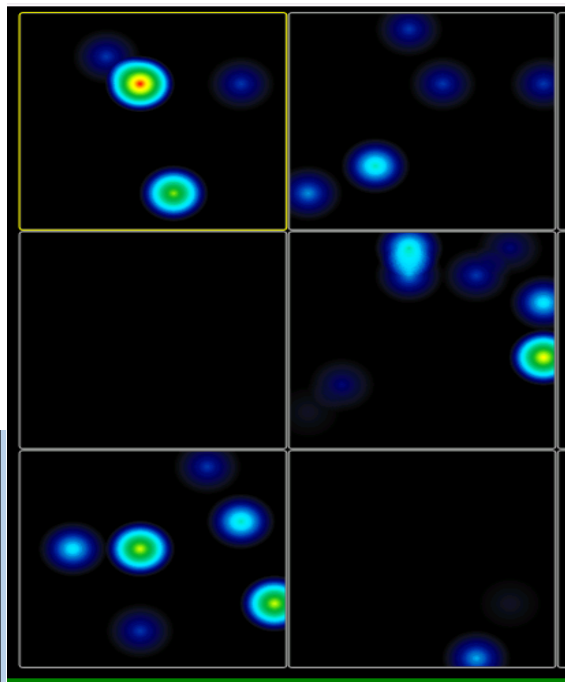
Well-A1



DA-H9-Cryo_MPP+ 27-IVD_Growth Factors
Neurite Total Length per Well



Unpaired t test	
P value	< 0.0001
P value summary	****
Are means signif. different? (P < 0.05)	Yes
One- or two-tailed P value?	Two-tailed
t, df	t=6.214 df=35



TH / MAP2

