# Drug safety and discovery with Human iPSC-Neuron and Artificial Intelligence

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# Neuroscience and Drug Discovery

## MEA assessment system and applications with ;

- **iPS cell-neuron, human**
- **MEA** : Microelectrode array for detection of extracellular action potential
- **AI** : Proprietary Artificial intelligence and multivariate analysis for toxicity and pharmacology

## (1) Drug phenotypic screening

- Toxicity and efficacy
- Phenotypic select ➡ Prioritization for lead compounds

## (2) Mechanism of action

- Ion channels and receptors for target molecule on neurons
- Assessment with AI and multivariate analysis
- Disease model assay (MEA, qPCR, Immunostaining)

## (3) Pain study and neuromuscular disease

- Human iPSC-sensory/motor neuron
- Ion channels and receptors assessment and diseases models

## (4) Relativity to animal study

- Solid and tangible assessment in vitro for the relativity
- Evidence for toxicity in human cells but no rodent

**Pharmaceuticals**
**Biotech**
**Academia**
**Research Institute ...**

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# Platform Technology (Selected)

## ■CNS : Seizure, Addiction

- Principal Component Analysis to Distinguish Seizure Liability of Drugs in Human iPSCell-Derived Neurons (Toxicological Sciences, 184:265, 2021)
- Can we panelize seizure? (Toxicological Sciences, 179:3, 2021)
- Toxicological evaluation of convulsant and anticonvulsant drugs in human induced pluripotent stem cell-derived cortical neuronal networks using an MEA system (Scientific Reports, 8:10416, 2018)
- Evaluation of drug addiction using human iPSC-dopamine neuron (Japanese Society of Toxicology, 2022)

## ■Sensory neuron: Pain assessment

- In vitro pain assay using human iPSC-derived sensory neurons and microelectrode array (Toxicological Sciences, 188:131, 2022)

## ■Motor neuron: Neuromuscular disease (In preparation for publication)

- ALS and related diseases models with human iPSC-motor neurons
- Efficacy for mutated neurons by gene-editing of a disease gene
- Inhibition effect for accumulation of mutated proteins in patient motor neurons

## ■Axon tracking : Conduction velocity, synaptic plasticity

Versatile live-cell activity analysis platform for characterization of neuronal dynamics at single-cell and network level (Nature Communications, 11:4854, 2020)

## ■Artificial intelligence : Raster plots machine learning to predict the seizure liability of drugs and to identify drugs (Scientific Reports, 12:2281, 2022)

## ■Drug response : Physiological maturation and drug responses of human induced pluripotent stem cell-derived cortical neuronal networks in long-term culture (Scientific Reports, 6:26181, 2016)

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# ■Analysis(primary): Artificial Intelligence

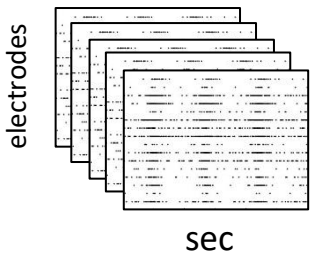

**【Deep learning】**
- Image recognition with raster plot of positive controls
- Weighted pattern recognition extracting feature value
- The AI is created to pile up multi-layers of algorithm.

**【Identification】**

The AI identifies/classifies feature value between control and test compounds to toxicity risk and efficacy.

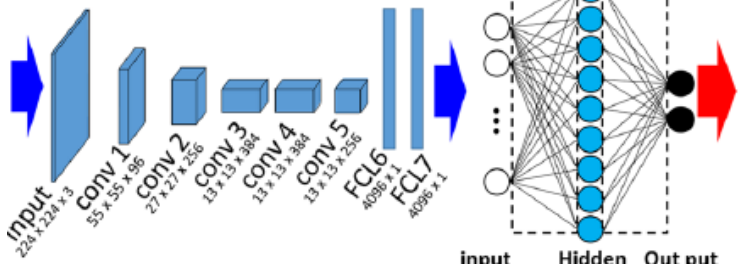
**【Advantages】**
- A wide range of accurate identification with 4000+ parameters.
- Hi-sensitive evaluation in weak neural firing.

**1. Separated spike stamp table**



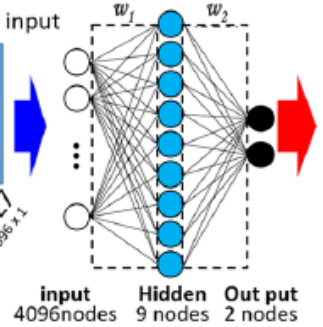

**2. Image Recognition**

(image recognition)

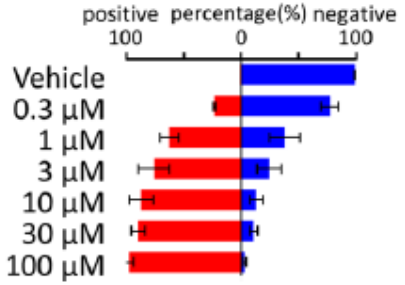



**3. Pattern Recognition**

Neural network (pattern recognition)

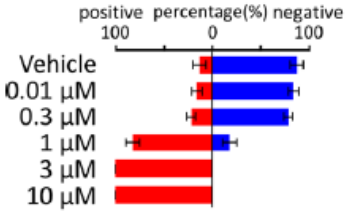



Pilocarpine, muscarinic R agonist




**4. Identification**

Kainic acid, glutamate R activator

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