Evaluation of Ready-to-Use Quick-Neuron™ Plate - MEA 48

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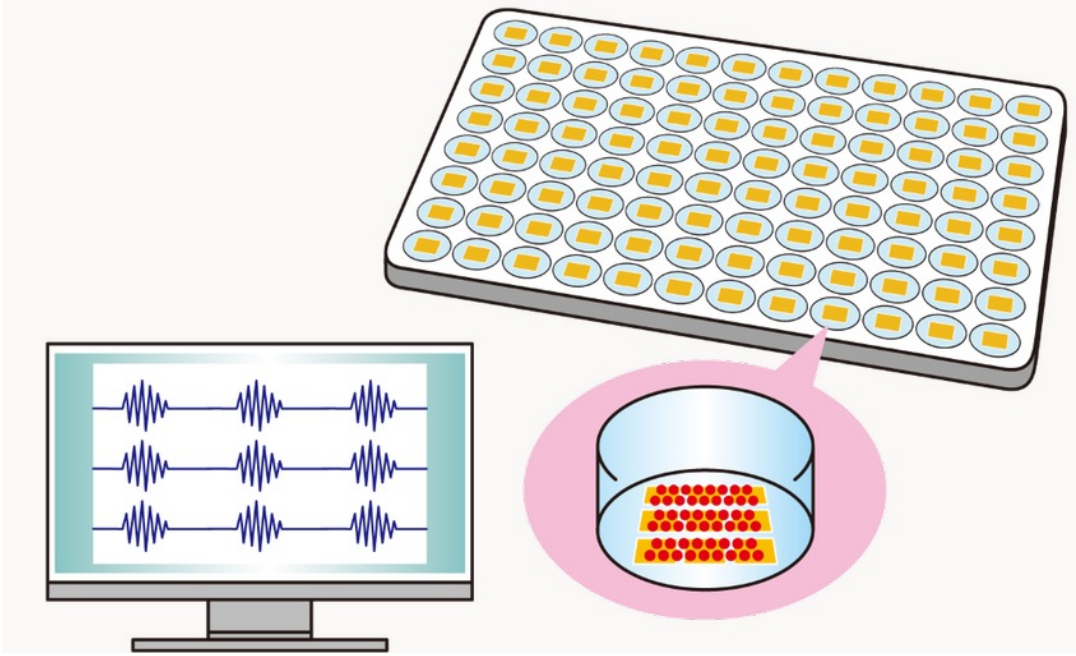

Society for Neuroscience 2021

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1.RICOH COMPANY, Ltd.

2.Elixirgen Scientific, Inc.

How can we evaluate neural activities?

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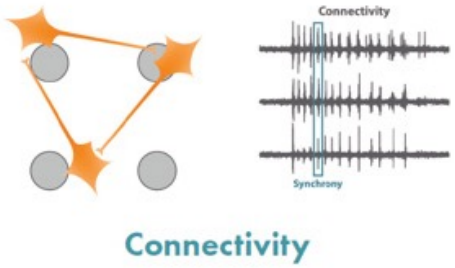
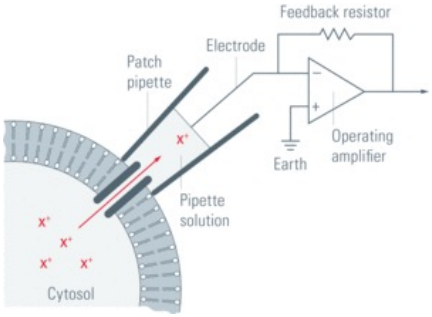
- **Detection methods**

Multi-electrode array



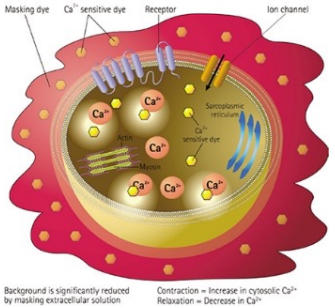
https://www.waisman.wisc.edu/cellular-and-molecular-neuroscience/axion-maestro-pro-mea-multi-electrode-array/

Patch-Clamp



https://www.leica-microsystems.com/science-lab/the-patch-clamp-technique/

Ca transient assay



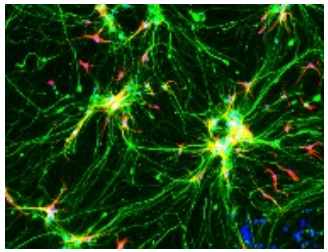
https://www.moleculardevices.com/en/assets/app-note/dd/flipr/compound-effects-upon-calcium-transients-in-beating-axiogenesis-cor.4u-human-ips-cell-derived-cardiomyocytes

- **Features of MEA(Multi-electrode Arrays)**

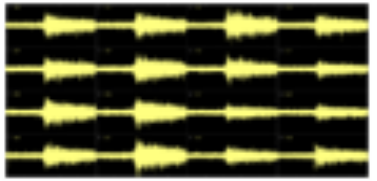
Detection :Extracellular electrode
Format :Well-plate format

Advantages
- ✓ Damageless for cells
- ✓ High time-resolution
- ✓ Easy to assay

Multi-electrode Array



iPSC-derived neuron



Neural activities measured with MEA

Challenge of MEA Assays with iPSC-derived neurons

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- Challenge

- The spontaneous firing rate is unstable.
- Cumbersome to prepare and culture cells for months.
- It's difficult to optimize culture conditions for obtaining good responsibility to pharmacological drugs.

- Our solution

Providing a Ready-to-use MEA plate!!

Users can evaluate drug efficacy and toxicity.
- Stable firing rate
- Assay immediately after receiving the plate
- Expected responses to typical compounds

What is Quick-Neuron™ Plate?

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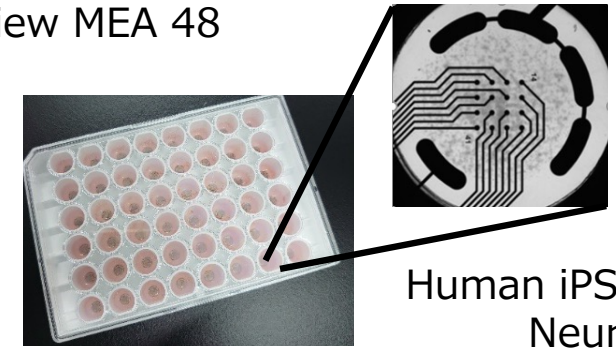
"Quick-Neuron™ Plate frees users
from experiment preparation!!"

CytoView MEA 48



Human iPSC–derived
Neurons

Product Specifications

Cell :
- Elixirgen Scientific
  Human iPSC-derived Neurons
- Thermo Fisher
  Human Astrocytes

Plate :
- Axion Biosystems
  CytoView MEA 48

Objective in this study

Evaluate Quick-Neuron™ Plate can be use as Ready-to-use

- Stability of firing rate
- Assay immediately after receiving the plate
- To show expected responses to typical compounds
  -Receptor agonist and antagonists
  -Anti-epileptic drugs

How stable is Quick-Neuron™ Plate?

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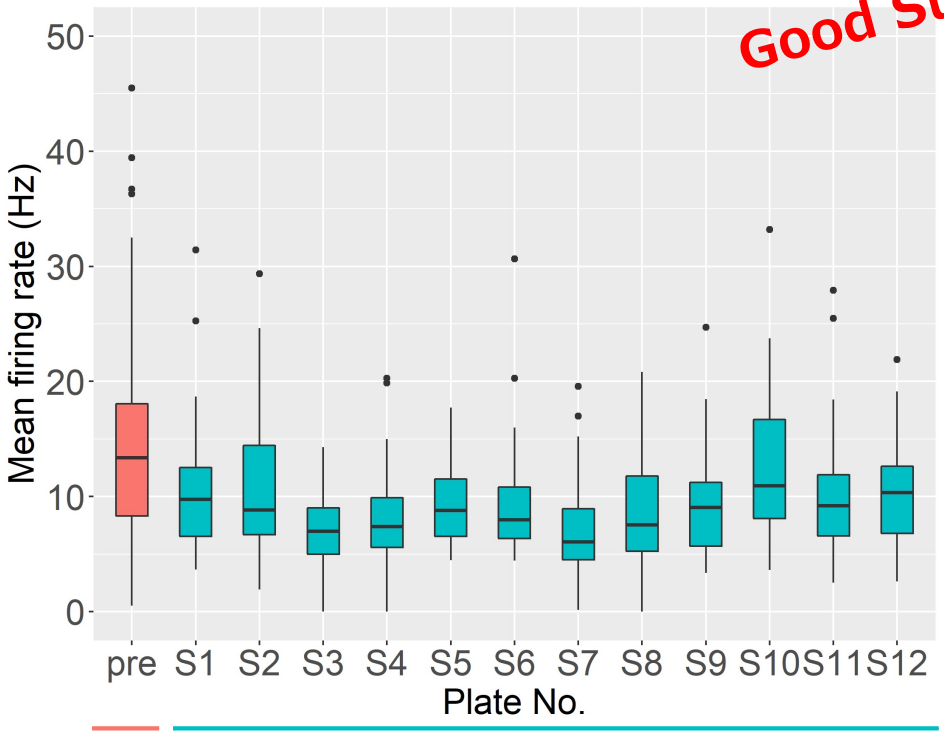
The spontaneous firing rate of Quick-Neuron™ Plate was more stable than the plate with non-optimized condition.

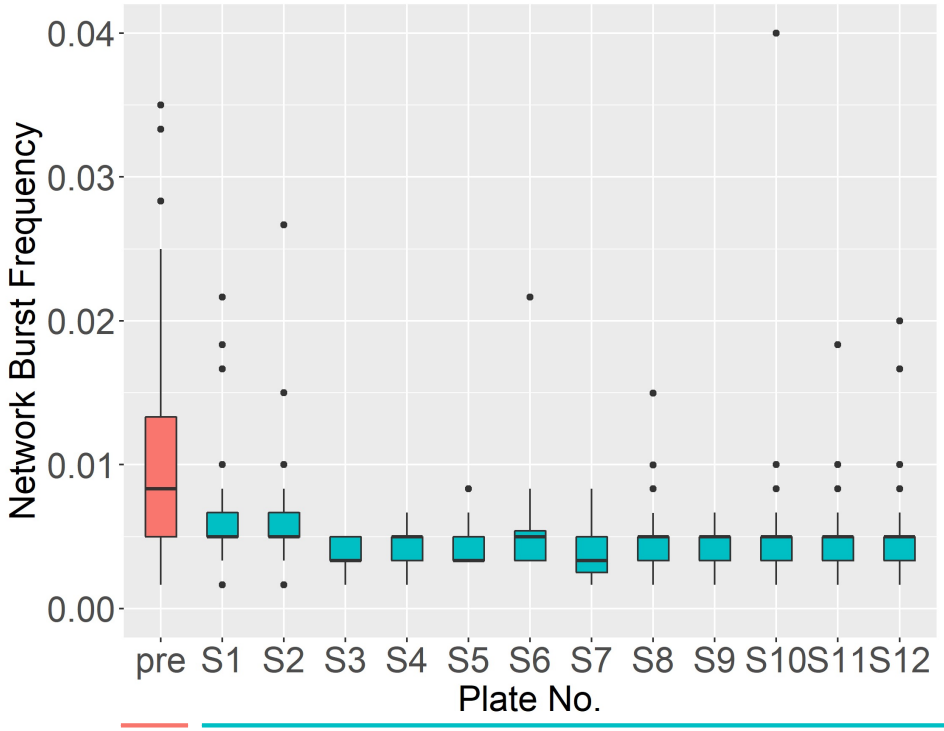
Mean firing rate



No optimization

Optimized culture method

Network burst frequency



No optimization

Optimized culture method

Are the plates functional after long-distance transportation?

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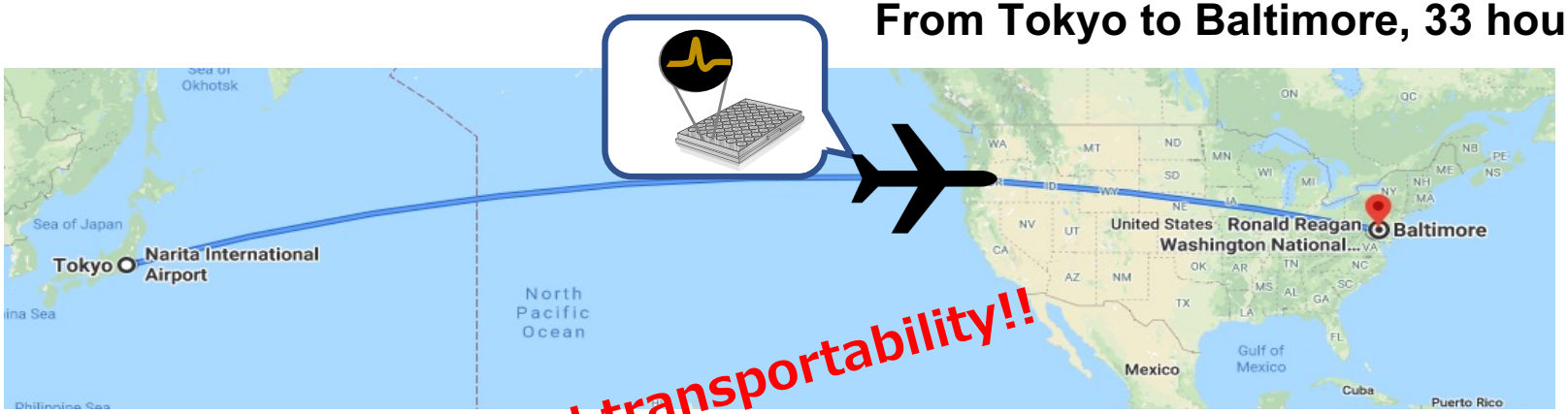
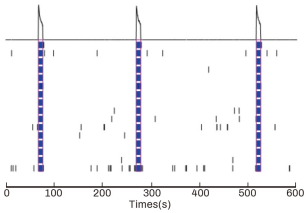
The plate transported from Tokyo to Baltimore showed the good response to 4AP, K^+ channel blocker.

From Tokyo to Baltimore, 33 hours

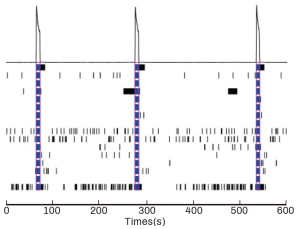


Good transportability!!

Before transportation
(In Japan)

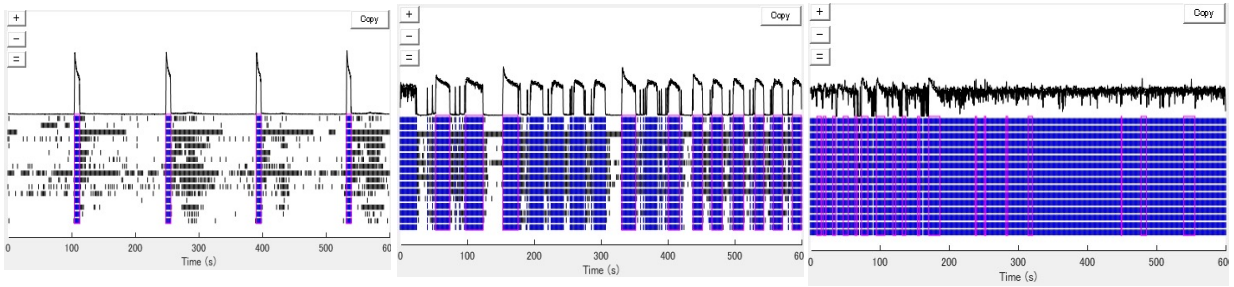


After transportation
(In America)



Drug response after transportation

Control (DMSO) **4AP (3 μM)** **4AP (30 μM)**



Can the plate be used for neuroscience research?

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The plate showed robust responses to compounds that affect major receptors

Good response!!

Mode	Receptors / Ion channels	Compounds	Testing density	Changes of spike number	Ref: IC50
Negative control	-	Acetaminophen	1-100 μM	No change	
Neuro Transmitter	Glutamate receptors	Glutamate	1-100 μM	↗↘	2.3 μM
	GABA receptors	GABA	0.1-10 μM	↘	2.8 μM
	Dopamine receptors	Dopamine	0.1-10 μM	↘↗	0.122 μM（D1) 2.76 μM (D2) 1.66 μM (D5)
	Muscarine receptors	Pilocarpine(HCl)	0.1-10 μM	↗	18 μM(M1,3) 4.5 μM(M2)
	Histamine receptors	Histamine	0.3-30 μM	↗	24 μM
Receptor Antagonist	AMPA, Kainate receptors	CNQX	0.5-50 μM	↘	0.92/6.1μM
	GABA(A) receptors	Gabazine	0.3-30 μM	↗	0.2 μM
	Dopamine D2 receptors	Chlorpromazine	0.1-10 μM	↗↘	0.363 μM
	NMDA receptors	D-AP5	0.5-50 μM	No change	4.1 μM
	GABA(A) receptors	Picrotoxin	0.1-10 μM	↗	2.4 μM
	Histamine H1 receptors	Ketotifen	0.1-10 μM	↗↘	-

The plate can be also used for anti-epileptic screening.

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Negative control

Anti-epileptic drugs

(Na^+ channel blocker)

Good response!!

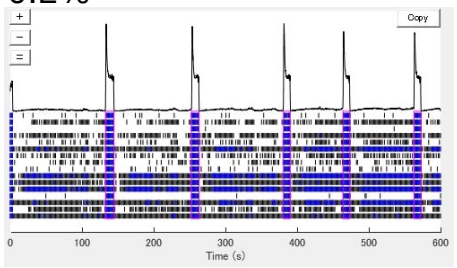
DMSO

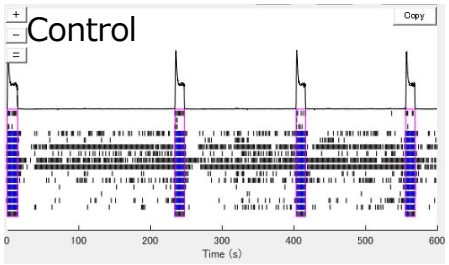
Acetaminophen

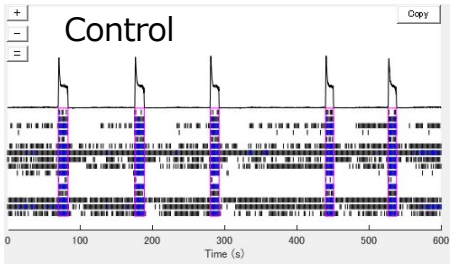
Phenytoin
(IC50:16.6 μM)

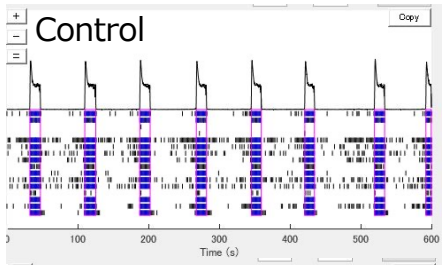
Carbamazepine
(IC50:131 μM)

0.2%









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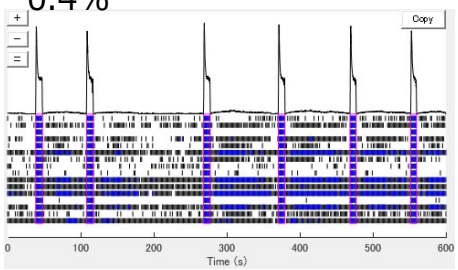
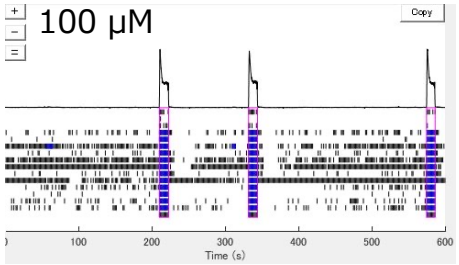
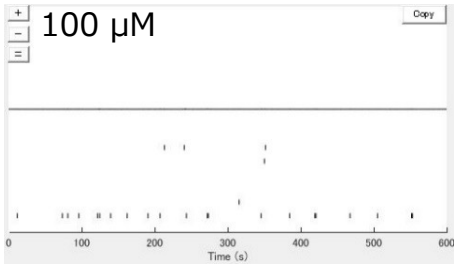
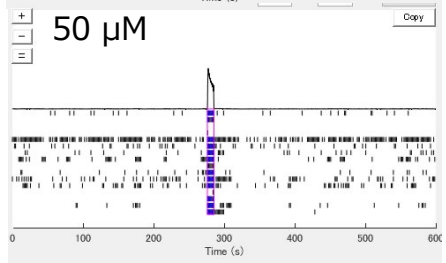
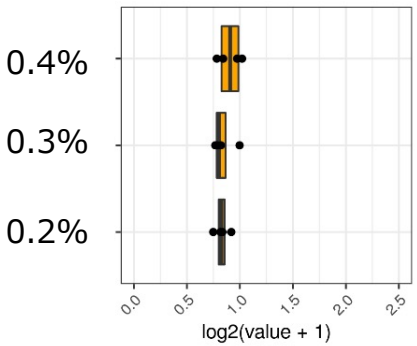


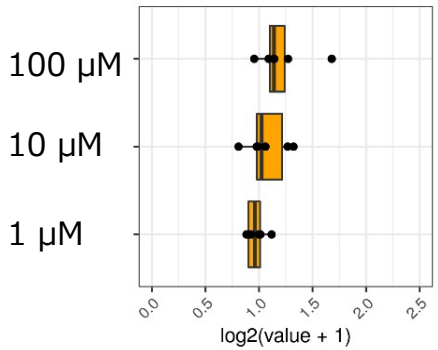


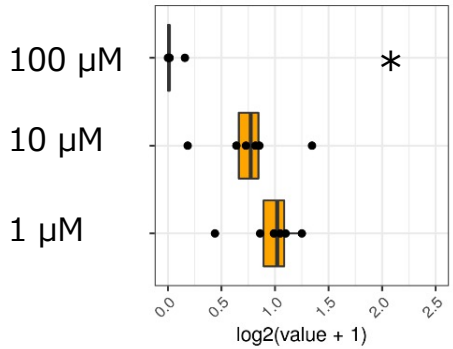




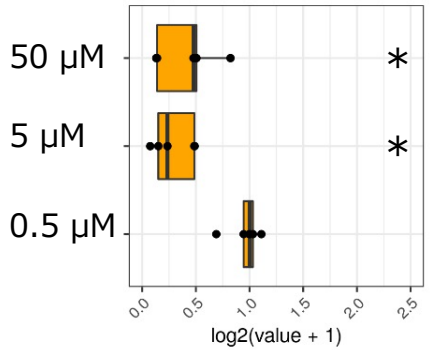
Relative change of MFR to Control







* : $p<0.05$



* : $p<0.05$

Conclusions

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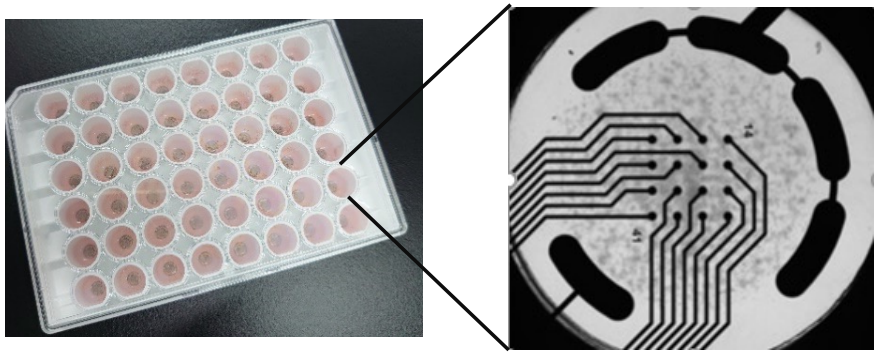
Quick-Neuron™ Plate is expected to be a useful tool for nervous system drug discovery.

- We developed Quick-Neuron™ Plate, which is Ready-to-use MEA plate for iPSC based neuronal assays
- Quick-Neuron™ Plate can be used for Ready-to-use plate.
  - Stable firing rate
  - Assay immediately after receiving the plate
  - Expected responses to typical compounds



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