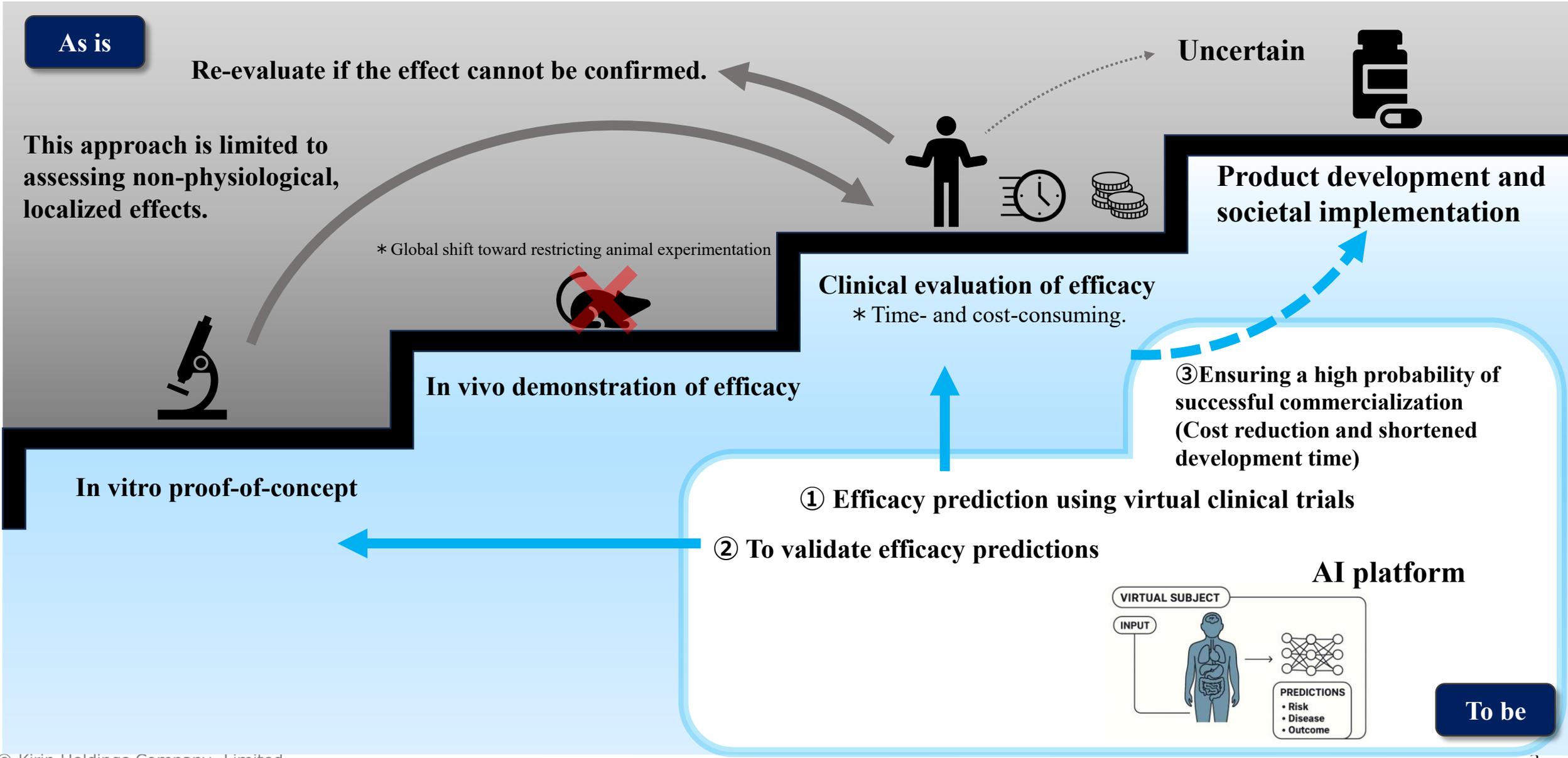# AI-driven functional simulation leveraging a drug-based DX platform

KIRIN R&D DAY 2025
Kirin Holdings Company, Limited
Institute of Health Sciences
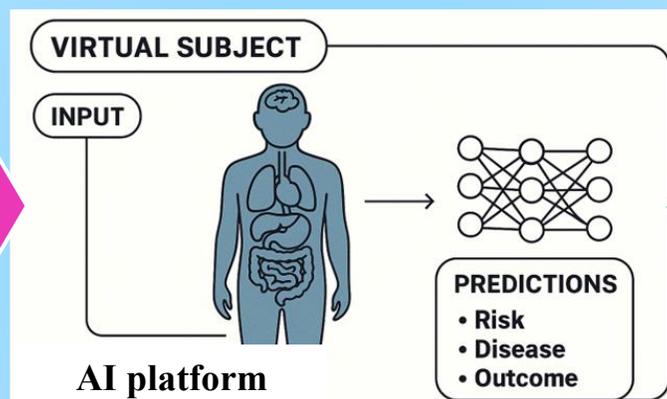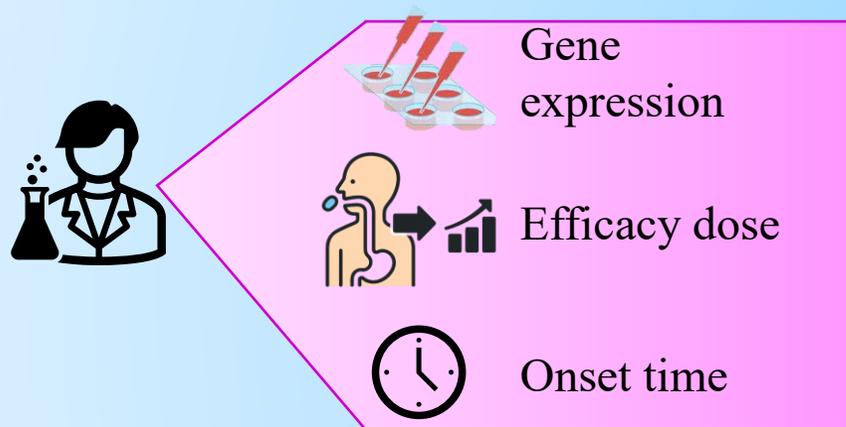
Dai Nogimura

Applying AI-driven clinical trial simulations for pharmaceuticals (QSP: Quantitative Systems Pharmacology) to functional food research
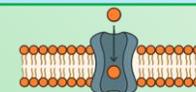

As is

Re-evaluate if the effect cannot be confirmed.

Uncertain

This approach is limited to assessing non-physiological, localized effects.

＊Global shift toward restricting animal experimentation

Product development and societal implementation

Clinical evaluation of efficacy
＊Time- and cost-consuming.

In vivo demonstration of efficacy

③Ensuring a high probability of successful commercialization (Cost reduction and shortened development time)

In vitro proof-of-concept

① Efficacy prediction using virtual clinical trials

② To validate efficacy predictions

AI platform

VIRTUAL SUBJECT
INPUT
PREDICTIONS
• Risk
• Disease
• Outcome

To be

Establishing QSP technology in functional food research

Proprietary data demonstrated by Kirin

- Gene expression
- Efficacy dose
- Onset time

VIRTUAL SUBJECT

INPUT

PREDICTIONS
- Risk
- Disease
- Outcome

AI platform

Co-creative collaboration for higher predictive accuracy

Material Information

Enzymatic characteristics involved in absorption and metabolism

Subject selection

Collaborative research: Fujitsu Limited / Nova In Silico SAS

Functional-prediction simulations for virtual subjects

The platform was operated using citicoline to validate its practical applicability

# Focus on citicoline as the first target

WHY

Kirin Group's citicoline

Cognizin® For the evolution of your mind®

Currently developing business as a B2B ingredient for overseas markets, such as dietary supplements for brain health
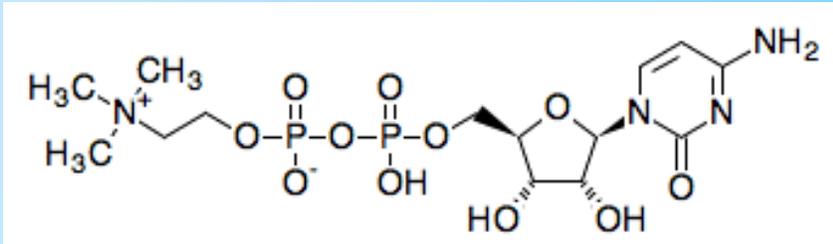**→We plan to expand the countries of deployment as a global B2C (APAC) product going forward**

KIRIN 小岩井 協和発酵バイオ コーポレート機能研究開発基盤

BLACKMORES BioCeuticals®

FANCL
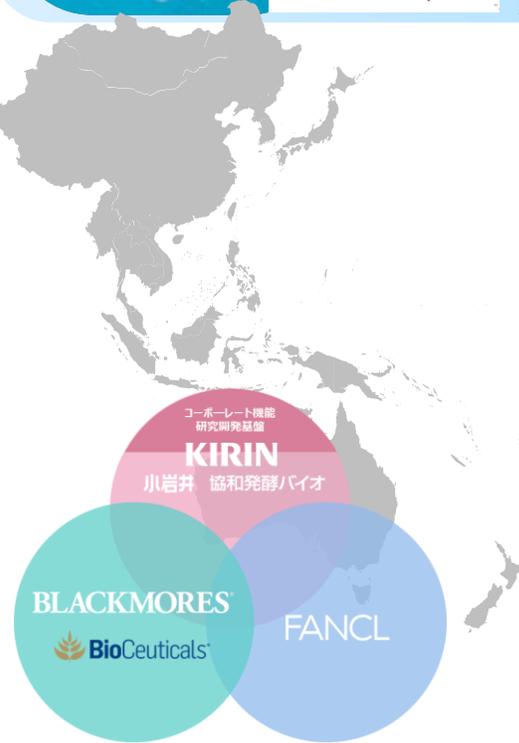
The development of new functionality is important for business expansion, and this was a good example of R&D that applies cutting-edge technology.

※At present in Japan, the use of citicoline is permitted only for pharmaceutical (medicinal) purposes.

Functions and Market Size of Citicoline

What

Citicoline is essential for brain function

Current target areas

- Enhanced Cognitive Function
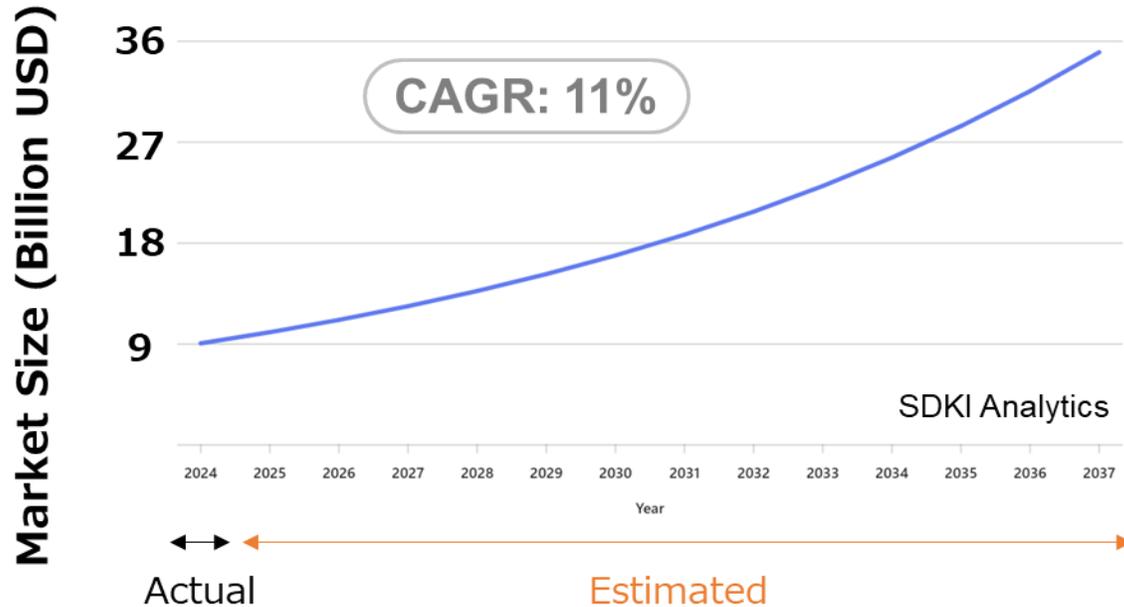- Better Emotional Regulation
- Improved Mood
- Reduced Anxiety and Depression
- Stress Reduction
- Improved Sleep

■ **The global market for brain-function supplements is very large — approximately ¥5 trillion**

CAGR: 11%

Market Size (Billion USD)

36
27
18
9

2024 2025 2026 2027 2028 2029 2030 2031 2032 2033 2034 2035 2036 2037

Year

SDKI Analytics

Actual Estimated

The expansion of new functions that are not limited to cognitive function will result in the simultaneous creation of social and economic value

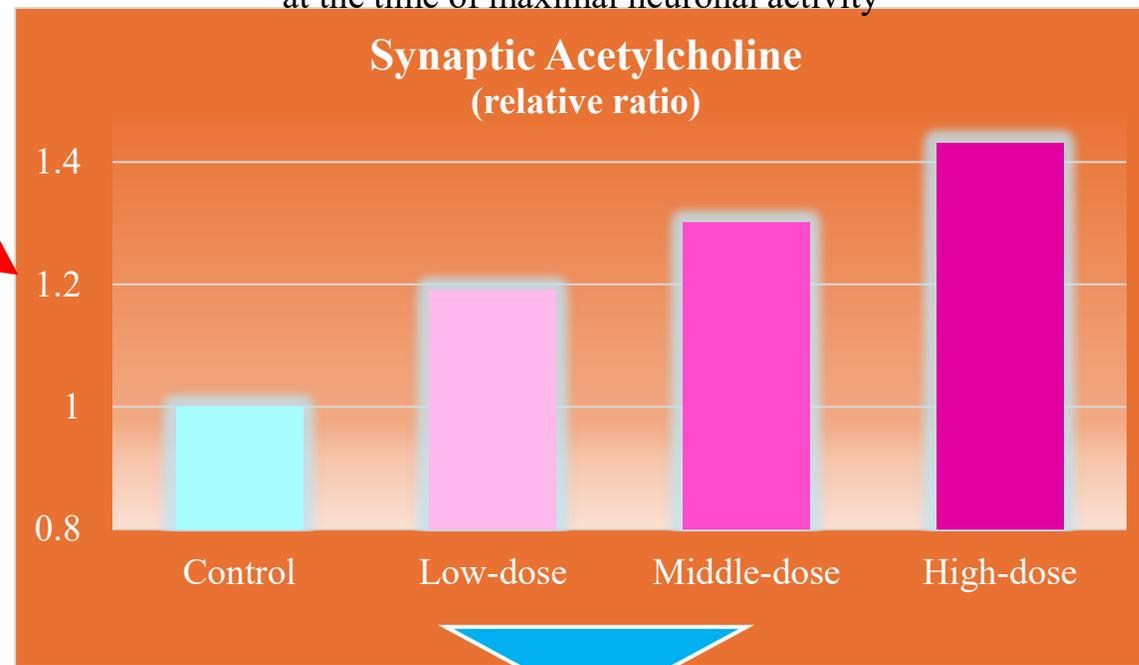よろこびがつなぐ世界へ
KIRIN

Predictive simulation of gut–nerve signal activity
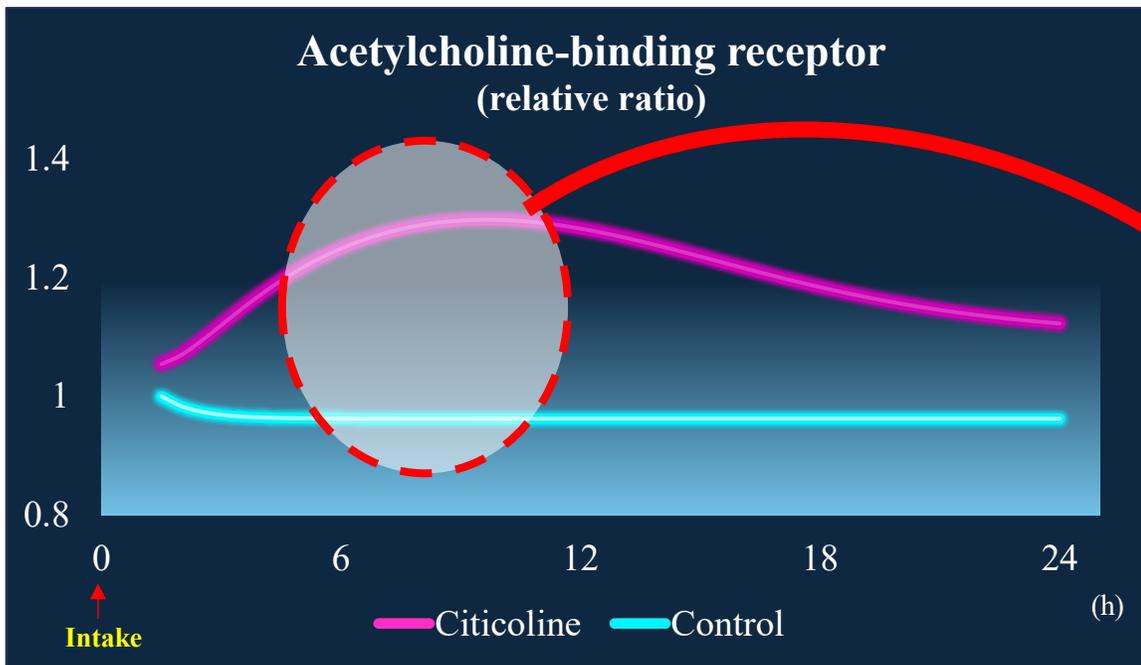
Predictive simulation of synaptic acetylcholine concentrations at the time of maximal neuronal activity

Acetylcholine-binding receptor
(relative ratio)

1.4

1.2

1

0.8

0   6   12   18   24
(h)
Intake

━━ Citicoline ━━ Control

Synaptic Acetylcholine
(relative ratio)

1.4

1.2

1

0.8

Control   Low-dose   Middle-dose   High-dose

$$\frac{dACh_{IE}}{dt} = \frac{(-k_{release}) \cdot Vmax_{AChRelease}}{Km_{AChRelease} + ACh_{IE}} \cdot ACh_{IE} + \frac{Vmax_{AChsyn} \cdot Ch}{Km_{AChsyn} + Ch}$$

$$\frac{dACh_S}{dt} = k_{prodAChneuron} + koff \cdot R_{bound} - (kon \cdot R_{free} \cdot ACh_S) + \frac{k_{release} \cdot Vmax_{AChRelease}}{Km_{AChRelease} + ACh_{IE}} \cdot ACh_{IE} - \left(\frac{Vmax_{AChE} \cdot ACh_S}{Km_{AChE} + ACh_S}\right)$$
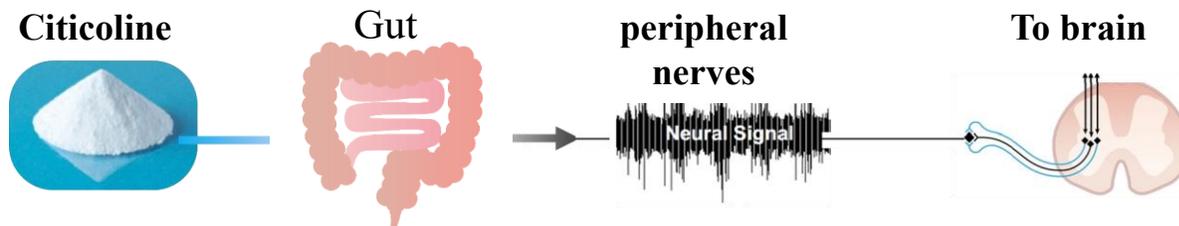
$$\frac{dCh}{dt} = k_{prodbasal} + citicoline_{breakdown} - \left(\frac{Vmax_{AChsyn} \cdot Ch}{Km_{AChayn} + Ch}\right) - (k_{lossCh} \cdot Ch)$$

$$\frac{dR_{bound}}{dt} = kon \cdot ACh_S \cdot R_{free} - (koff \cdot R_{bound})$$

$$\frac{dR_{free}}{dt} = (-kon) \cdot ACh_S \cdot R_{free} + koff \cdot R_{bound}$$

Computational Model

Newly discovered gut–nerve activating effect suggesting a gut–brain correlation
(difficult to detect by conventional methods)

Citicoline   Gut   peripheral nerves   To brain

Neural Signal

The predictive results were confirmed in vitro

②Supporting evidence for efficacy prediction results

In vitro

Transwell co-culture system

Culture well with embedded electrodes
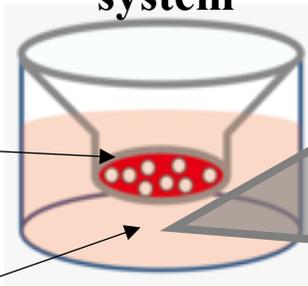
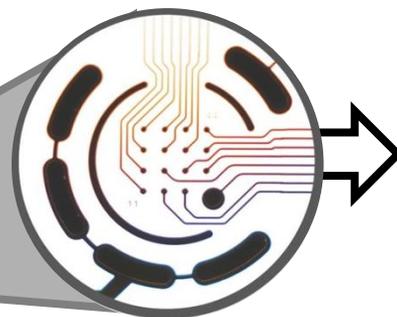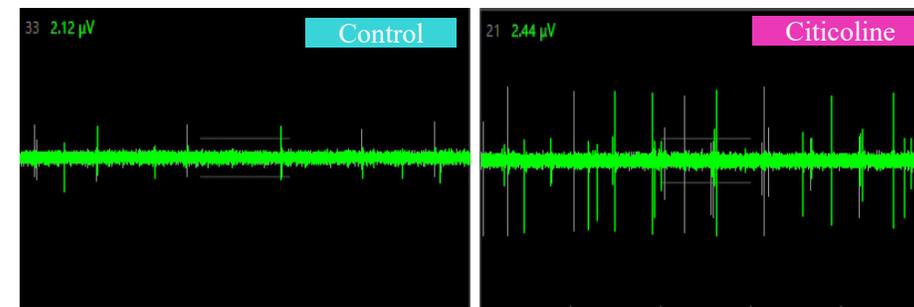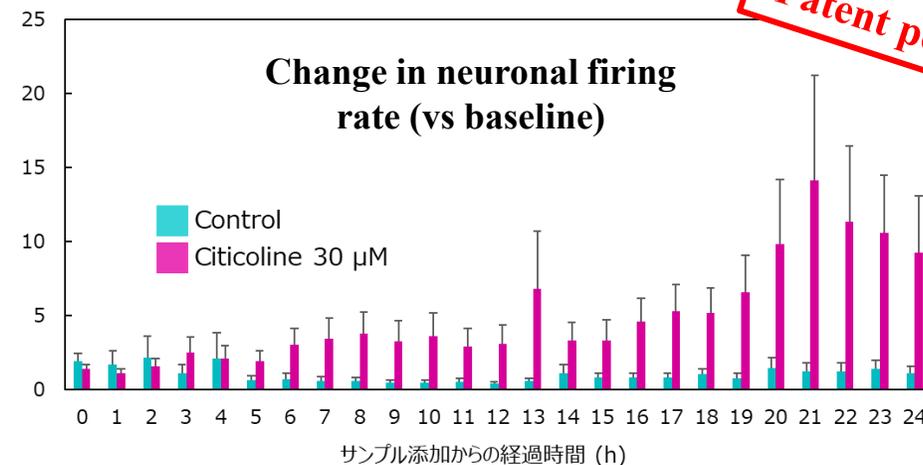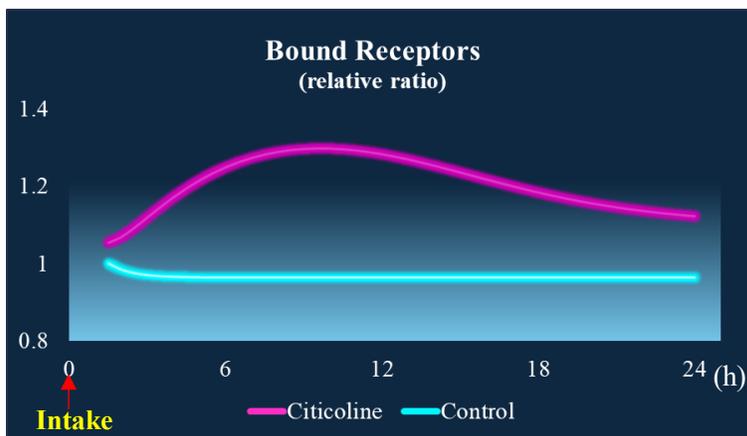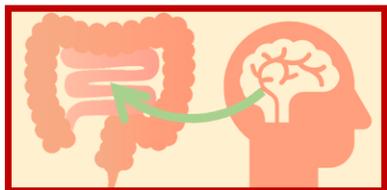**Assessment of neuronal activity (neuronal firing)**

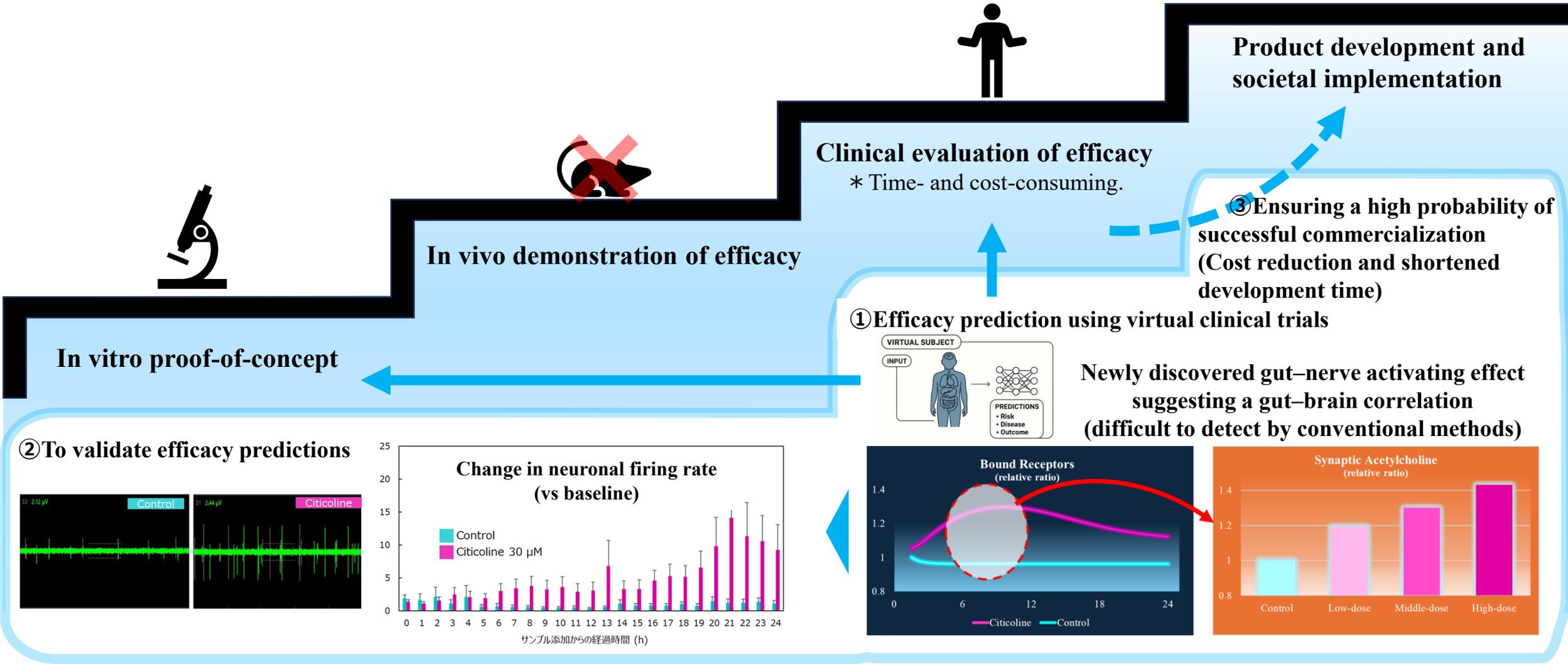**microelectrode array (MEA)**

Human iPSC-derived intestinal epithelial cells

Human iPSC-derived sensory (afferent) neurons

Gut – Brain interaction
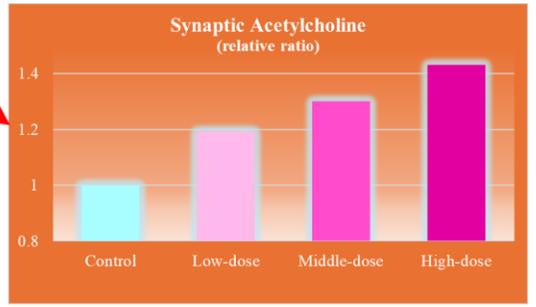
Bound Receptors (relative ratio)

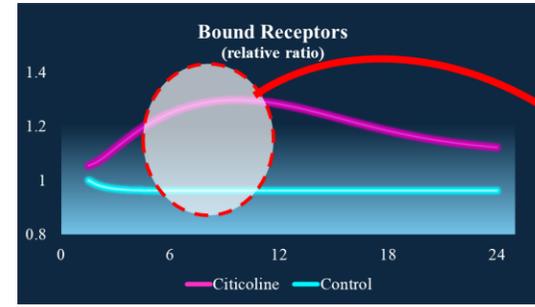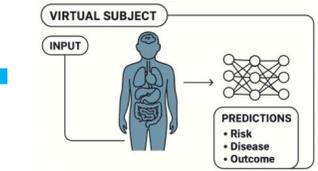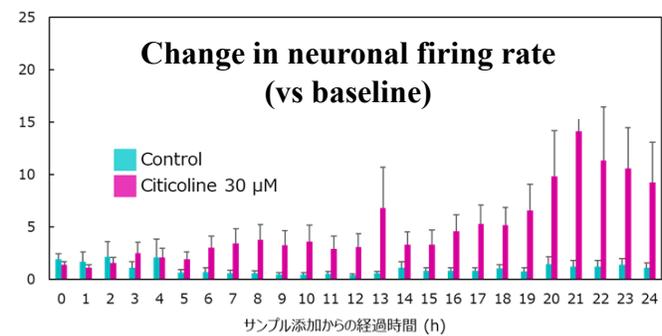Change in neuronal firing rate (vs baseline)

Patent pending

The results corroborating the efficacy predictions have revealed new potential for Citicoline

Applying AI-driven clinical trial simulations (QSP: Quantitative Systems Pharmacology) to functional food research
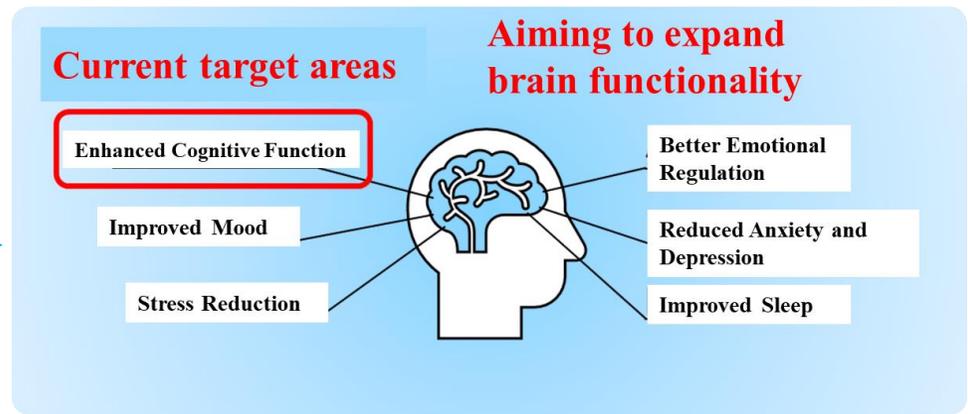

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②To validate efficacy predictions

Change in neuronal firing rate (vs baseline)

Control
Citicoline 30 μM

サンプル添加からの経過時間 (h)

Bound Receptors (relative ratio)

Citicoline — Control

Synaptic Acetylcholine (relative ratio)

Control Low-dose Middle-dose High-dose

③ Towards high-confidence product launch: Research timeline