

NIHS 150th Anniversary and Regulatory Science

Enhancing safety and quality of life
through scientific research



September 27, 2023
GSRS 2023



Masamitsu Honma, Ph.D.
Director General
National Institute of Health Sciences
JAPAN

NIHS is the oldest national institute in Japan since 1874



The Origin of the NIHS



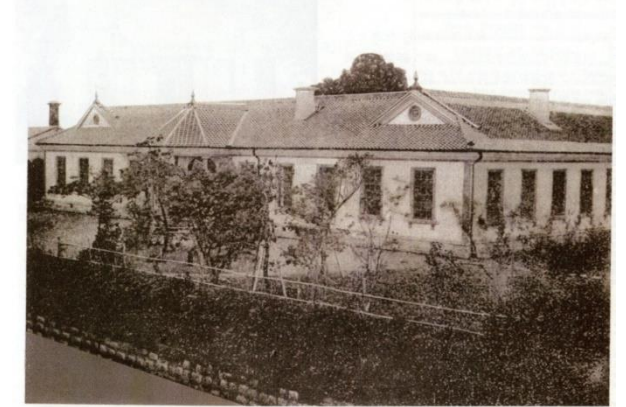
Dr. Anton J. C. Geerts
(1843-1883)



Mr. Sensai Nagayo
(1838-1902)

At the beginning of the Meiji Era (from 1868), many of the drugs imported from the Western countries were of poor quality, so Dr. Geerts, a pharmaceutical expert of Dutch proposed the establishment of a drug quality testing laboratory. In response to this suggestion, Dr. Nagayo, who was then working at the Meiji Government Medical Affairs Bureau, established “Tokyo Shiyaku-Jou” (Tokyo Drug Control Laboratory) in Year 7 of the Meiji Era (1874), which were the origin of NIHS.

東京司薬場和泉町庁舎へ移転 1874年8月29日



Tokyo Drug Control Laboratory (1874)



Monument honoring Dr. Geertz erected in 1891
(at the gate of the NIHS campus)

*Bij het Samenstellen van deze Pharmacopoea heeft de
Commissie, waaraan deze taak door het Ministerie van
Binnenlandse Zaken was opgedragen, gemeend alleen
die geneesmiddelen op te nemen, welke in de nieuwere
geneeskunde gebruikt worden, terwijl de talrijke oudere
geneesmiddelen, welke tegenwoordig meer en meer ongebruikt
blijven, daarin niet vermeld zijn.*

Draft of the Japanese Pharmacopoeia in Dutch written by Dr. Geerts
(Displaying on the wall of the lobby on the first floor of the NIHS building)

History of NIHS



Tokyo Drug Control Laboratory & Tokyo Institute of Hygienic Science(Kanda; 1874-1945)

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- 1874** Tokyo Drug Control Laboratory (Kanda, Tokyo)
 - 1887** Tokyo Institute of Hygienic Science
 - 1945** End of World War II
 - 1949** National Institute of Hygienic Sciences (Setagaya-ku, Tokyo)
 - 1997** National Institute of Health Sciences
 - 2017** Move to Kawasaki King SkyFront (Kawasaki, Kanagawa)
 - 2024** NIHS 150th Anniversary
-



National Institute of Hygienic Sciences & National Institute of Health Sciences (Setagaya; 1949-2017)



**National Institute of Health Sciences
(Tonomachi; 2017-)**

Tokyo bay

New NIHS Campus (2017-)

Haneda Tokyo
International Airport

Tamagawa Sky Bridge

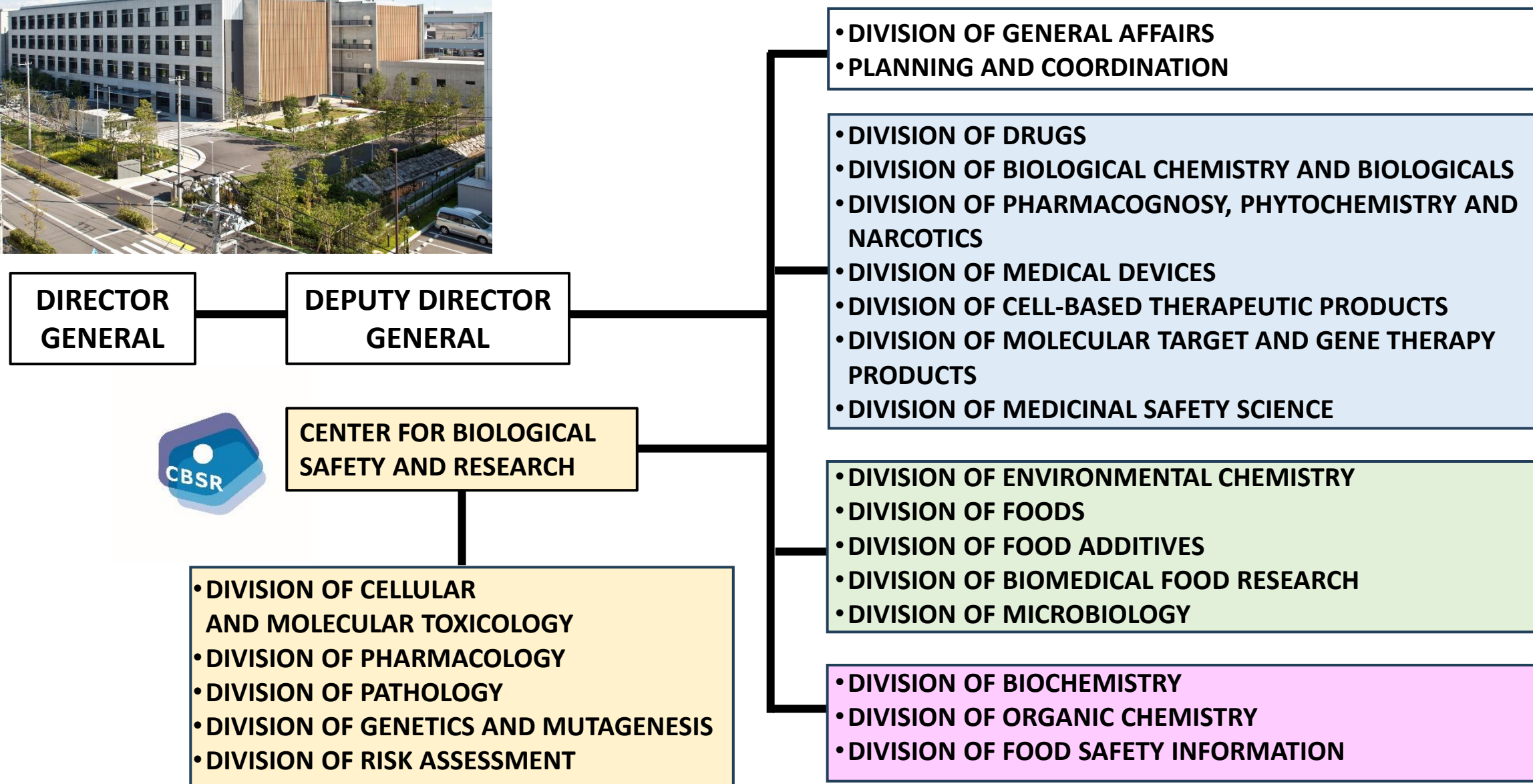
Tama River

NIHS

Tonomachi
KingSky Front
Area

Provided by: Kawasaki City Fire Department Air Corps

Organization of NIHS



Research Targets of NIHS

Drugs and medical devices

- Chemically synthesized drugs
- Biotechnological drugs
- Biopharmaceuticals
- Oligonucleotide drugs
- Peptide drugs
- Radiopharmaceuticals
- Cell-based therapeutic products
- Gene therapy products
- Natural medicines
- Illicit drugs
- Medical devices
- In vitro diagnostics
- Real-world data analysis etc.



Food, food-related substances, and others

- Residual pesticides
- Heavy metals
- Radioactive substances
- Veterinary drugs
- Allergenic substances
- Food additives
- Genetically modified foods
- Newly developed foods
- Food utensils, containers and packaging
- Food poisoning agents (microorganisms, viruses, molds, parasites, toxins produced by microorganisms, etc.) etc.



Chemical substances related to daily life

- Household products
- Sanitary supplies
- Drinking water
- Indoor air
- Cosmetics
- Quasi-drugs
- Industrial chemicals
- Substances of occupational exposure
- Pollutants etc.





Mission of NIHS

The National Institute of Health Sciences (NIHS) is an institution tasked with conducting tests, research, and surveys (regulatory science) to scientifically and accurately evaluate the quality, safety, and efficacy of pharmaceuticals, medical devices, regenerative medical products, as well as any chemical substance present in foods and our living environment. Our mission is to reflect the results in the health, labor and welfare administration.

Regulatory Science in Japan

“Regulatory science is a science that makes accurate predictions, assessments, and judgments based on evidence to adjust the outcomes of science and technology to the most desirable form in harmony with people and society.”



*By Dr. Mitsuru Uchiyama,
21st Director General NIHS, in 1987*

“Promotion of Regulatory Science” was approved in the Fourth Science and Technology Basic Plan in Japan (August 2011: Cabinet Decision)

Regulatory Science Researches in NIHS

1. Enhancing the development of advanced medical product

- Regenerative and cell medicine products, gene therapy products, highly modified antibody drugs, medium molecule peptide drugs, nucleic acid drugs, molecular target drugs, companion diagnostics, and radiopharmaceuticals
- New formulation/manufacturing technology and advanced quality control for continuous production, DDS, nanomedicine, and IoT
- Advancement of nonclinical test methods related to safety and efficacy evaluation for medical devices and medical materials
- Application of iPS cells for drug discovery and introduction to safety pharmacology
- Nonclinical and post-marketing evaluation method research corresponding to conditional early approval

2. Ensuring the safety of food, chemical, and living environment

- Assessing the safety of foods, food additives, food utensils, containers, and packaging in consideration of the increase in international food distribution
- Research on prediction/evaluation and management based on food risk analysis
- Food allergy research in which sensitization pathways are diversified
- Health risk assessment of chemical substances such as indoor air and household products and elucidation of the cause of pollution accidents
- Modernization of nonclinical safety test methods and development of animal replacement methods aiming at improving predictability in humans
- Enhancement and strengthening of various safety databases using ICT

3. Supporting indispensable tests and inspections for health crisis management

- Testing and inspection as an Official Medicines Control Laboratories (OMCL) accompanying the internationalization of pharmaceutical GMP
- Tests and inspections to ensure the quality of generic drugs
- International standardization of Kampo preparations
- Structural analysis, structural-activity correlation analysis, analysis method, and database creation for countermeasures against dangerous drugs and illegal pharmaceutical products
- Response to food terrorism
- Response to widespread food poisoning
- Monitoring of radioactive contamination of food
- Monitoring residual pesticides in food
- Development of the toxicity test method for the next generation

4. Integrated research in the fields of pharmaceuticals, foods, and chemicals

- Construction of the chemical safety big database and development of basic technology for predicting human safety using AI
- Research for social implementation of genome editing technology

Emerging Technologies Applied to Regulatory Science in NIHS

1. *Activities of the Japanese Center for the Validation of Alternative Methods (JaCVAM), NIHS (Dr. Hirabayashi)*
2. *In silico approaches for chemical risk assessment (Dr. Yamada)*
3. *Safety assessment of cell-based therapeutic products derived from iPS cells (Dr. Yasuda)*
4. *Structural analysis of therapeutic antibodies using CRYO EM (Dr. Kiyoshi)*
5. *Utilization of Cardiac MPS and activities for Industrial implementation and regulatory acceptance in Japan (Dr. Yamazaki)*
6. *Evaluation for developmental toxicity using human iPS cells (Dr. Ohkubo)*
7. *Identification of foreign particles in Moderna COVID-19 vaccine using SEM-EDX*



Activities of the Japanese Center for the Validation of Alternative Methods (JaCVAM), NIHS:

by HIRABAYASHI, Yoko, MD, PhD



International Cooperations

15th Anniversary of JaCVAM at 2020

(Founded 2005)

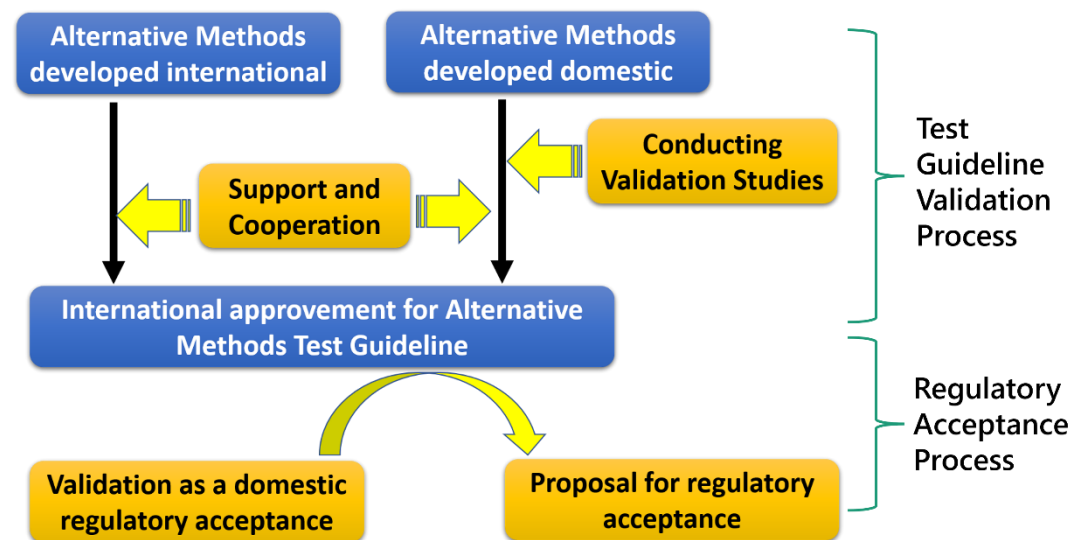


JRC
EURL ECVAM



ICATM

Flowchart of Activities



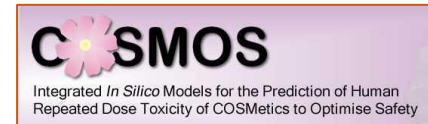
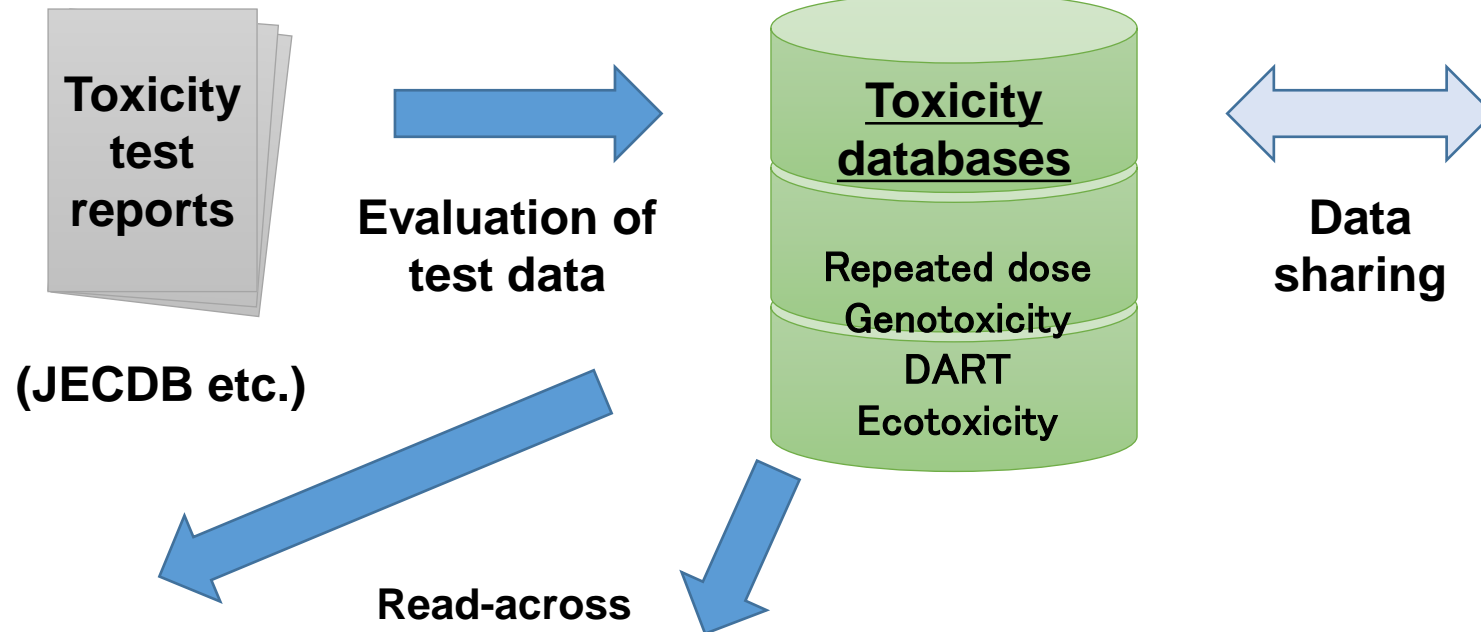
Toward the development of NAM...
a challenge with a particular focus on general toxicity

In silico approaches for chemical risk assessment

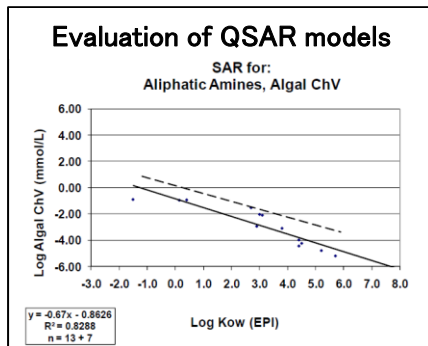
by Yamada, Takashi, Ph.D.



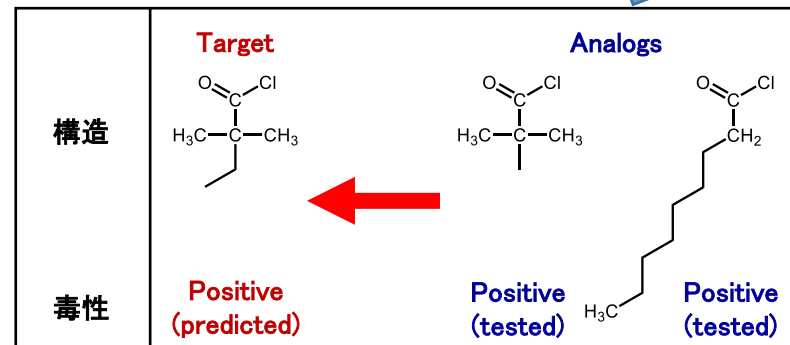
Constructing
and sharing
toxicity
databases



QSAR



Read-across



Evaluating
reliability of
prediction

Regulatory
decision
support

Developing *in silico* prediction methods

Safety assessment of cell-based therapeutic products derived from iPS cells

by Yasuda, Satoshi, Ph.D

- As undifferentiated pluripotent stem cells such as iPS cells intrinsically possess **tumorigenicity** property, potential risk of **residual undifferentiated iPS cells** intermingled with cell therapy products is concerned.

For the product development, testing methods to confirm removal of undifferentiated iPS cells are required.



CT-TRACS Committee-Tumorigenicity WG

ddPCR Team: International multisite evaluation of ddPCR assay to detect residual iPS cells in cell therapy products



Sumitomo Pharma

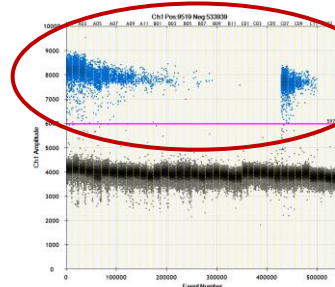
NOVARTIS



CATAPULT
Cell and Gene Therapy

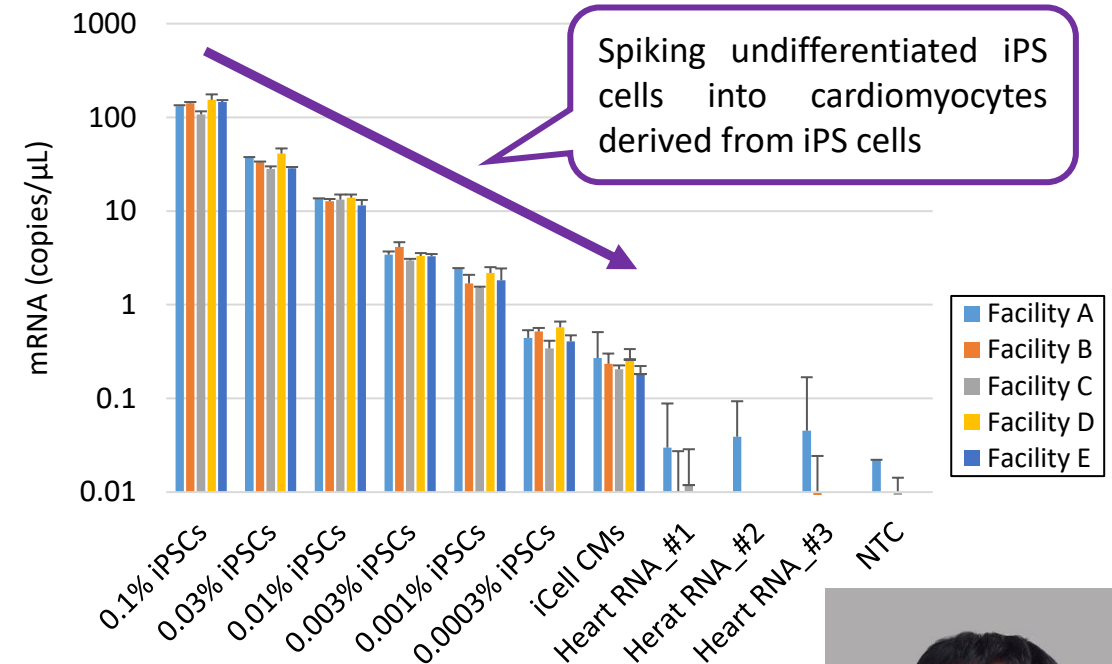


Droplet digital PCR (ddPCR)



Positive droplets
≈ copy number

mRNA copy number of iPS cell marker *LIN28A*



Precision of the ddPCR assay targeting iPS cell marker genes was evaluated at multiple sites for method validation.



Structural analysis of therapeutic antibodies using CRYO EM

by KIYOSHI, Masato, Ph.D.



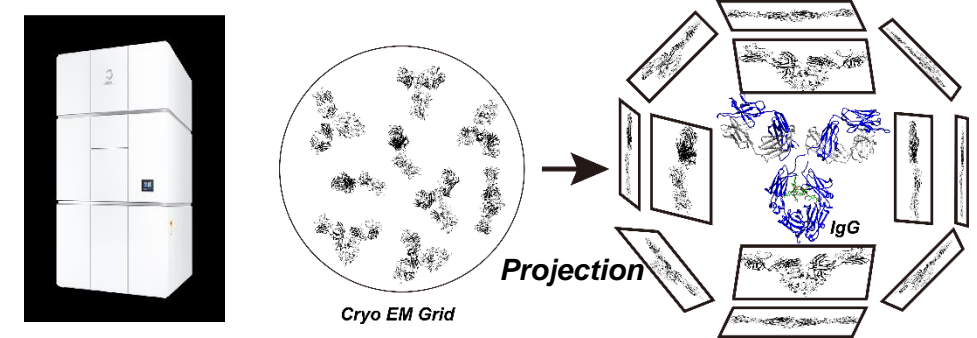
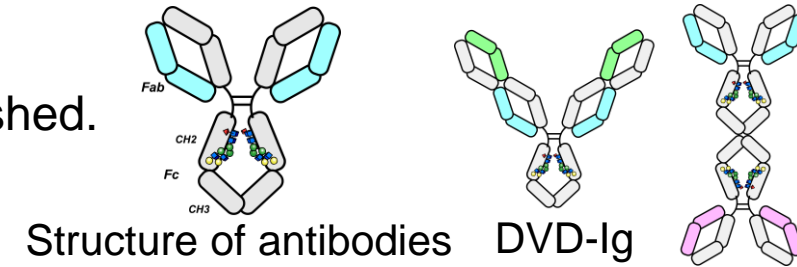
Background

Recently, Various engineered antibody drugs are developed.
However, structural characterization method is not well-established.

Aim

Our aim is to develop a characterization method using CRYO electron microscopy (EM) for structural analysis.

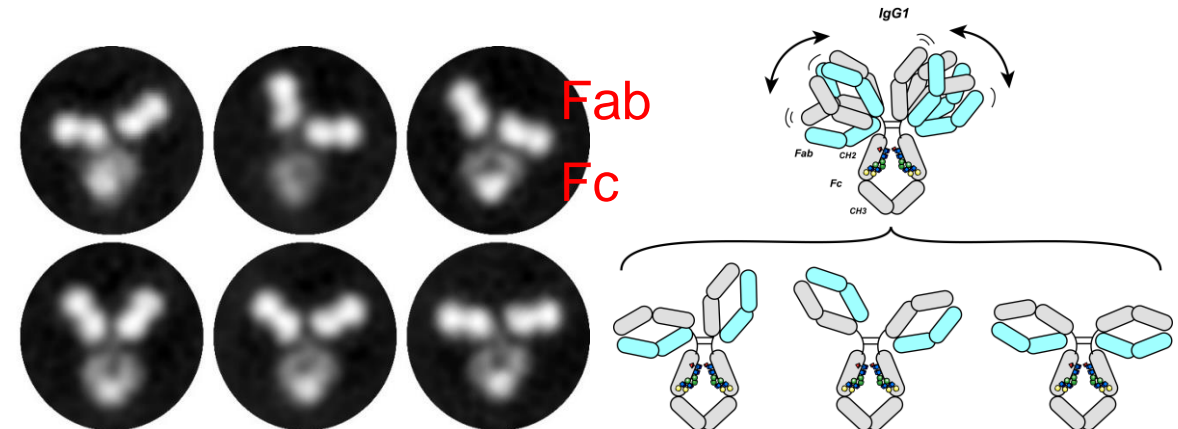
As a first step, we tried to perform structural analysis using three model antibodies.



Results

We successfully observed Fab and Fc domain clearly.

The results show that structural variations could be discussed from the negative staining data.



Utilization of Cardiac MPS and activities for Industrial implementation and regulatory acceptance in Japan

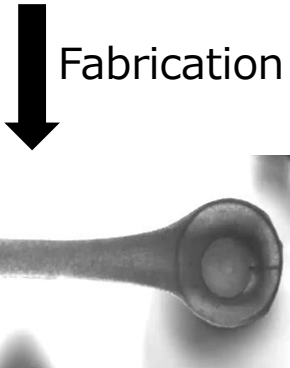
Utilization of Cardiac MPS

by Yamazaki, Daiju, Ph.D.

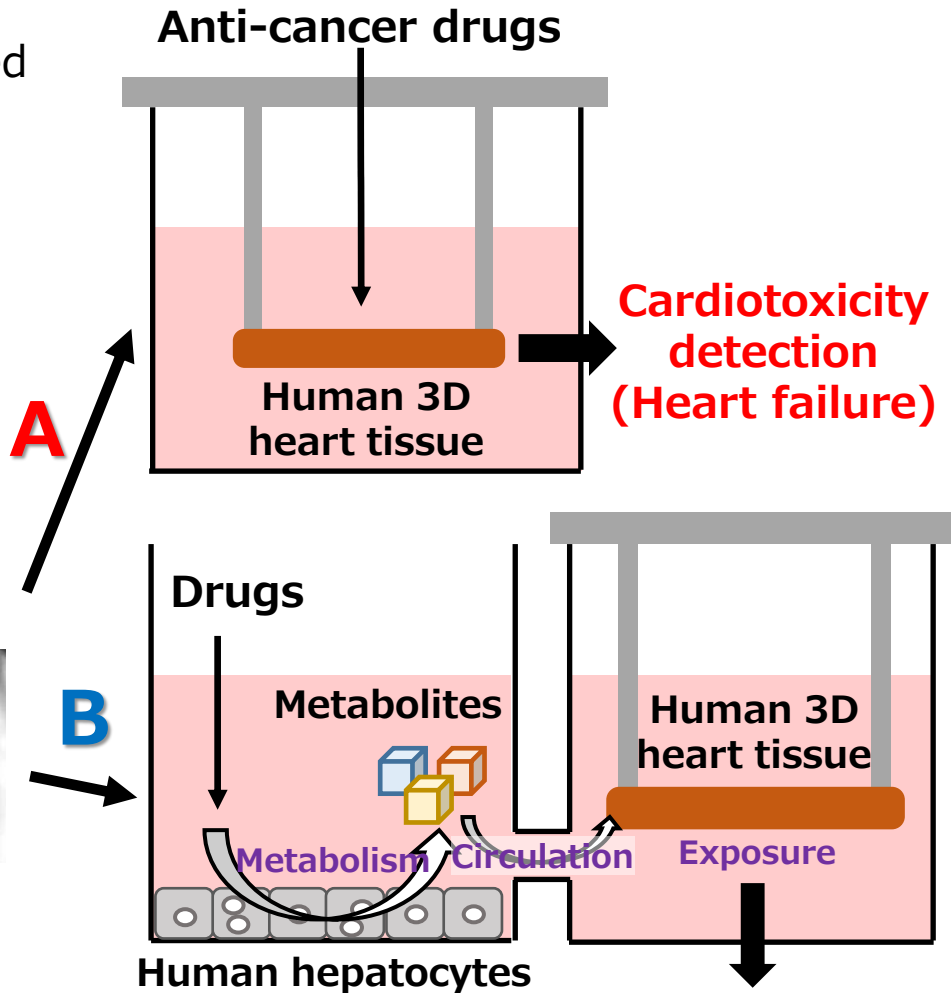
Human iPS cell-derived cardiomyocytes (hiPS-CM)



Fabrication



3D Heart tissue



- Stable autonomous beating
- Long-term culture (~6 month)

Activities in Japan

MPS Consortium



MPS実用化推進協議会

microphysiological systems



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おしらせ

2023年6月8日

6/7(水)に開催しました設立説明会には各方面から多数の方々にご参加いただき、ありがとうございました。8月にはキックオフシンポジウムを、2024年1月には第1回学術シンポジウムを計画しております。

2023年7月24日

8月21日(月)キックオフシンポジウムを開催いたします。

お問い合わせ

〒210-9501 神奈川県川崎市川崎区駅前3-25-26 国立医薬品食品衛生研究所 薬理部 内
MPS実用化推進協議会事務局 連絡先 mps-kyogikai@nihs.go.jp



※入会をご希望の方は、こちらから登録ください。
※入会の申込をいただいた方は、メーリングリストに登録させていただいております。
情報記憶先の変更や停止のご希望がございましたら、事務局までご連絡ください。

[ページ上部へ戻る](#)

最終更新日 2023年7月26日

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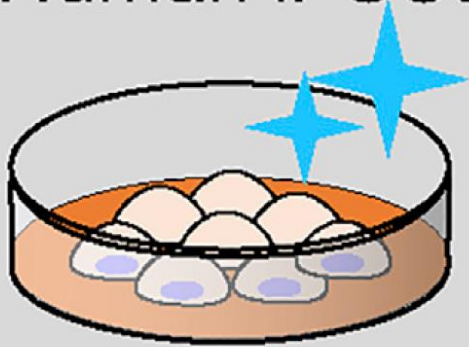
Just launched!!

(mps-kyogikai@nihs.go.jp)

Evaluation for developmental toxicity using human iPS cells

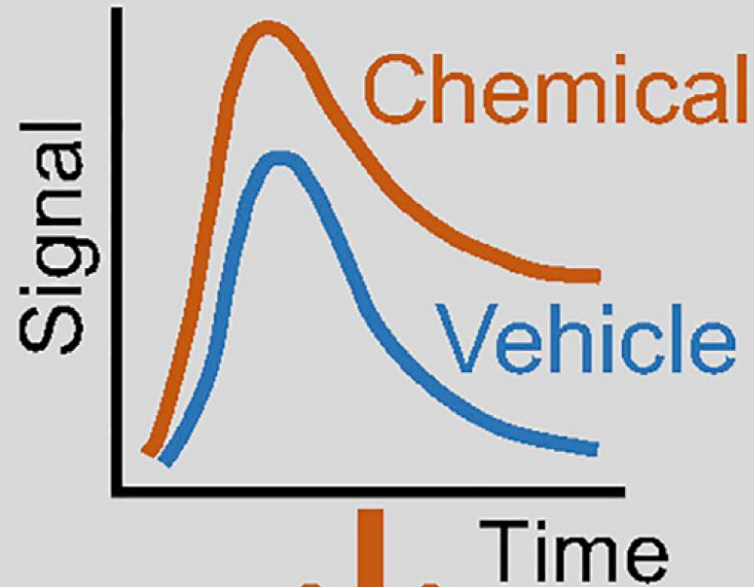
by Okubo, Yusuke, Ph.D.

FGF-SRF signal
reporter
(Human iPSCs)

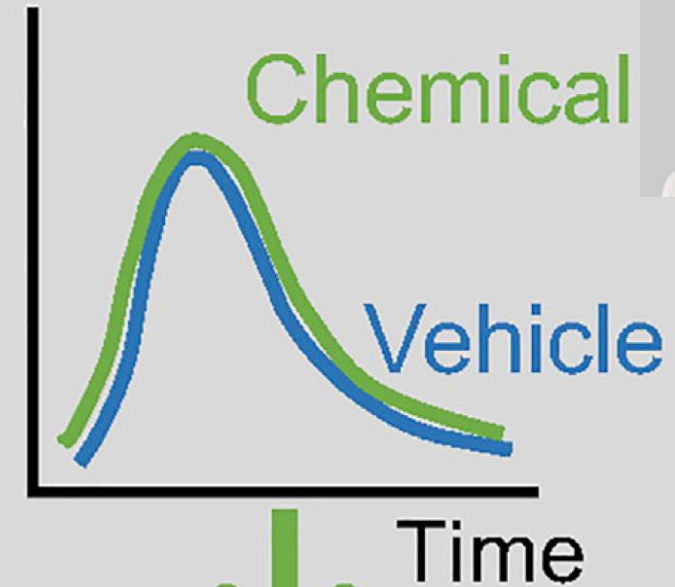


Prediction of
Developmental tox

Monitoring signal disruption



Toxicant



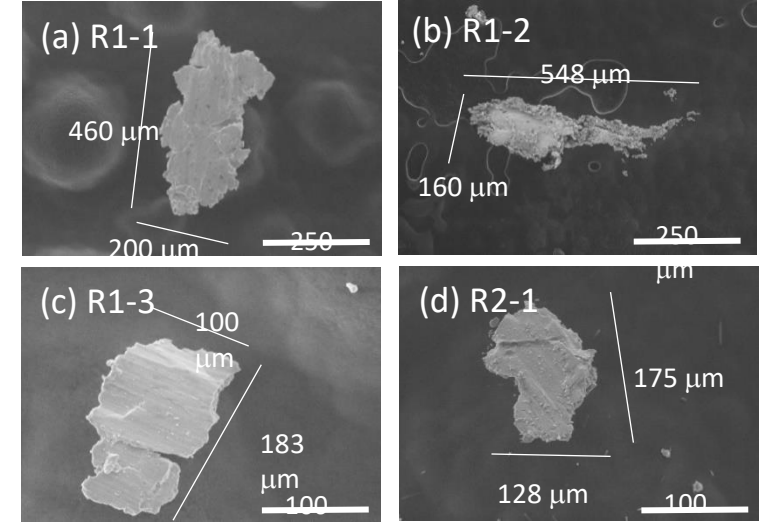
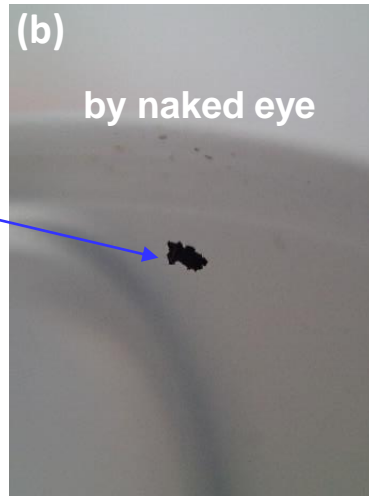
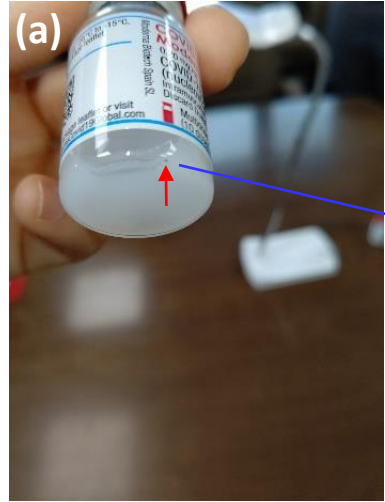
Non toxicant

Accuracy: 89% (21 toxicants, 14 negative chemicals)

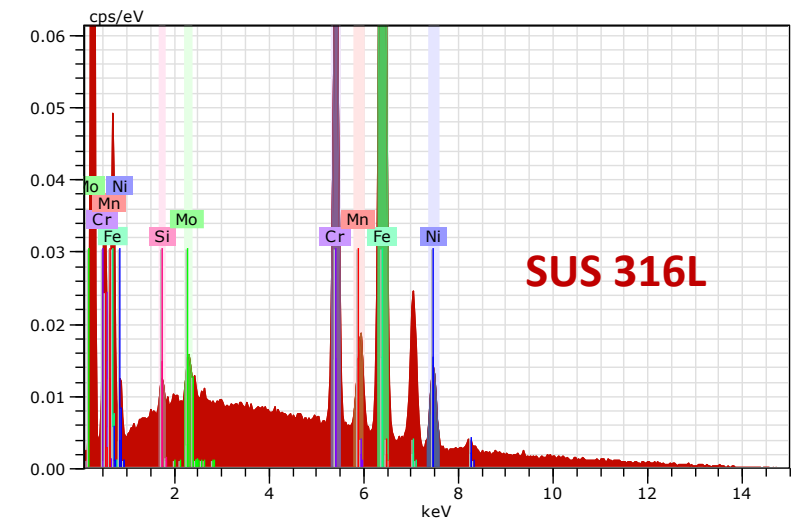
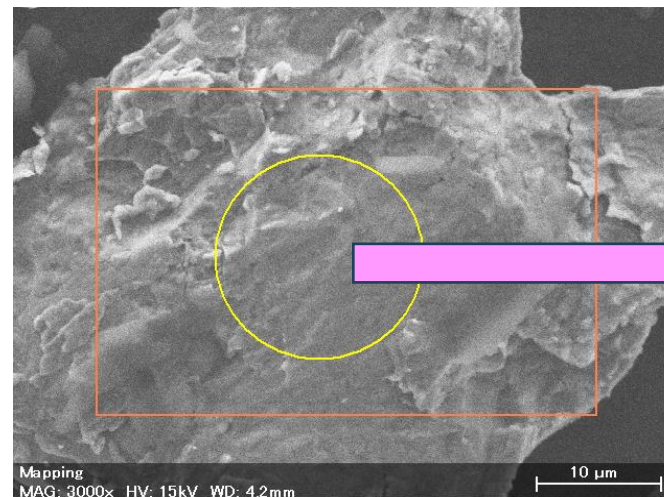


Identification of foreign particles in Moderna COVID-19 vaccine using SEM-EDX

by NIHS COVID-19 Team

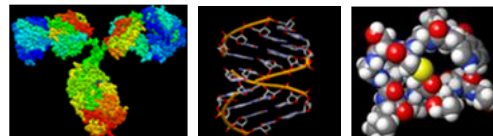
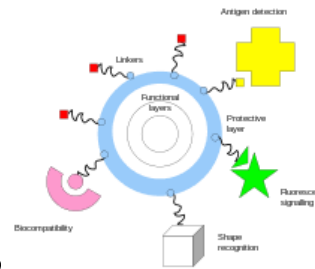
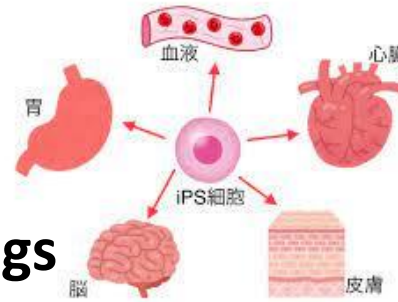


by a scanning electron microscope



Future new initiatives of NIHS

- Advanced formulations (DDS, nanomedicine, etc.)
- Advanced biopharmaceutical evaluation: middle molecule drugs
- Personalized medicine, molecular diagnostics, radioactive diagnostics
- Nucleic acid medicine
- Gene therapy products
- Regenerative/cell therapy products
- Advanced medical materials
- Drug discovery application of iPS cells etc.





Thank you for your attention !!

