筑波大学
University of Tsukuba

筑波大学生命環境系
Faculty of Life and Environmental Sciences
University of Tsukuba

MPS World Summit 2023 報告

筑波大学 生命環境系
AMED-MPS2事業　集中研究拠点
安東　治

概要

筑波大学生命環境系
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MPS World Summit 2023
June 26 – June 30, 2023
JW Marriott Hotel Berlin, Berlin, Germany

Hosts:
Uwe Marx (TissUse GmbH & Technische Universitaet Berlin)
Marcel Leist (CAAT-EU, Univ Konstanz)
Peter Loskill (Eberhard Karls U Tübingen; EUROoCS)

Keynote Speakers:
Mattias Lutofl (Roche)
Roser Vento-Tormo (Wellcome Sanger Inst)
Donna Mendrick (FDA)
Gordana Vunjak-Novakovic (Columbia Univ)
Thomas Hartung (Center for Alternatives to Animal Testing)
Uwe Marx (TissUse, TUB)

概要

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	Monday June 26, 2023	Tuesday June 27, 2023	Wednesday June 28, 2023	Thursday June 29, 2023	Friday June 30, 2023
8:00am	EXHIBITION HOURS Monday: 7pm-9pm Tuesday-Thursday: 8am-6pm				8:30am-10:30am Symposia
9:00am		9:00am-10:00am Keynote R. Ventor-Tormo (Wellcome Sanger Institute) Hall Berlin A-E	9:00am-10:00am Keynote G. Vunjak-Novakovic (Columbia University) Hall Berlin A-E	9:00am-10:00am Keynote T. Hartung (Johns Hopkins University) Hall Berlin A-E	1.7 Salon 16 & 17 / 2.7 Hall Berlin D-E / 3.7 Hall Berlin A / 4.7 Salon 21
10:00am	REGISTRATION HOURS Monday: 9am-4:30pm Tuesday, Wednesday: 8am-6pm Thursday: 8am-12pm	10:00am-11:30am Poster Session Drinks/Snacks	10:00am-11:30am Poster Session Drinks/Snacks	10:00am-11:30am Poster Session Drinks/Snacks	10:30am-11:00am Coffee Break
11:00am		11:30am-1:30pm Symposia			11:00am-1:00pm Symposia
12:00pm	MATCHMAKING HOURS Tuesday-Thursday: 10am-6pm	1.1 Hall Berlin D-E / 2.1 Salon 16 & 17 / 3.1 Salon 21 / 4.1 Hall Berlin A	1.3 Hall Berlin D-E / 2.3 Salon 16 & 17 / 3.3 Salon 21 / 4.5 Hall Berlin A	1.5 Hall Berlin A / 2.2 Hall Berlin D-E / 3.5 Salon 16 & 17 / 4.3 Salon 21	1.8 Hall Berlin A / 2.8 Hall Berlin D-E / 3.8 Salon 21 / 4.8 Salon 16 & 17
1:00pm					1:00pm-1:30pm Coffee Break
2:00pm		1:30pm-2:30pm Lunch Provided			1:30pm-3:30pm Keynote U. Marx (TissUse, TU Berlin) Closing Ceremony Hall Berlin A-E
3:00pm		2:30pm-4:30pm Symposia			
4:00pm		1.2 Hall Berlin A / 2.5 Salon 16 & 17 / 3.2 Salon 21 / 4.2 Hall Berlin D-E	1.4 Salon 21 / 2.4 Hall Berlin D-E / 3.4 Hall Berlin A / 4.6 Salon 16 & 17	1.6 Hall Berlin D-E / Salon 16 & 17 / 3.6 Hall Berlin A / 4.4 Salon 21	Track 1: MPS development: bioengineering models and readouts
5:00pm	4:30pm-6:30pm Opening Ceremony Keynote M. Lutolf (Roche) Hall Berlin A-E	4:30pm-6:00pm Poster Session Drinks/Snacks	4:30pm-6:00pm Poster Session Drinks/Snacks	Salon 16 & 17	Track 2: MPS for industrial and regulatory application: Standardization, QA, parallelisation and automation
6:00pm		6:00pm-7:00pm Keynote D. Mendrick (FDA) Hall Berlin A-E	5:50pm-6:50pm Round Table Hall Berlin A-E	6:00pm-7:00pm Round Table Hall Berlin A-E	
7:00pm	7:00pm-9:00pm Welcome Reception Exhibition Hall				Track 3: MPS for disease modelling, safety testing and basic research
8:00pm			8:00pm-11:00pm Macro Party		
9:00pm					Track 4: MPS highlights across disciplines
10:00pm					

計720演題

発表研究の内訳（全演題）

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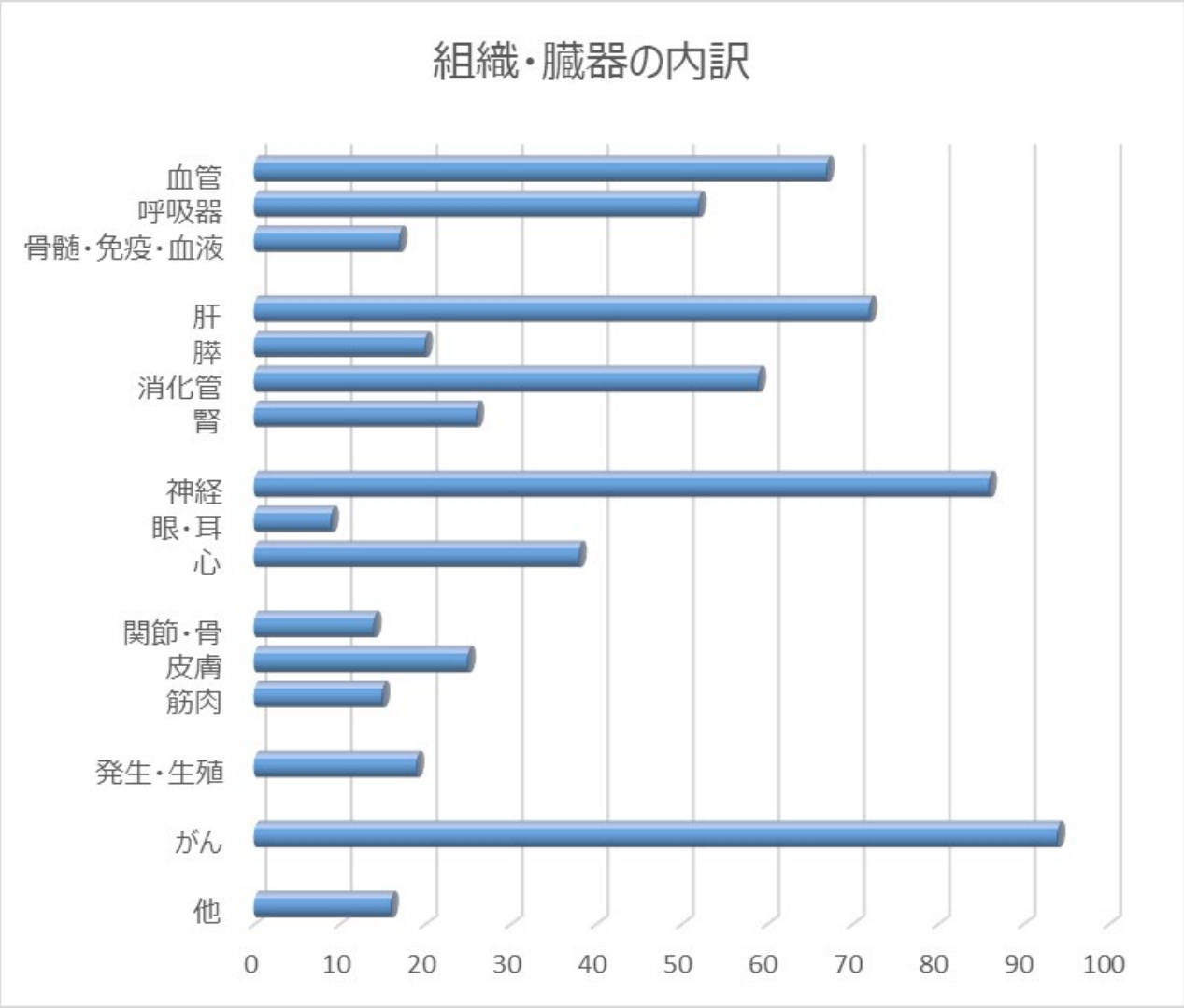

発表者

- **アカデミア**
- **MPS Provider**
- 規制側
- ユーザ企業
  60-70報程度

発表研究の内訳（ユーザ企業）

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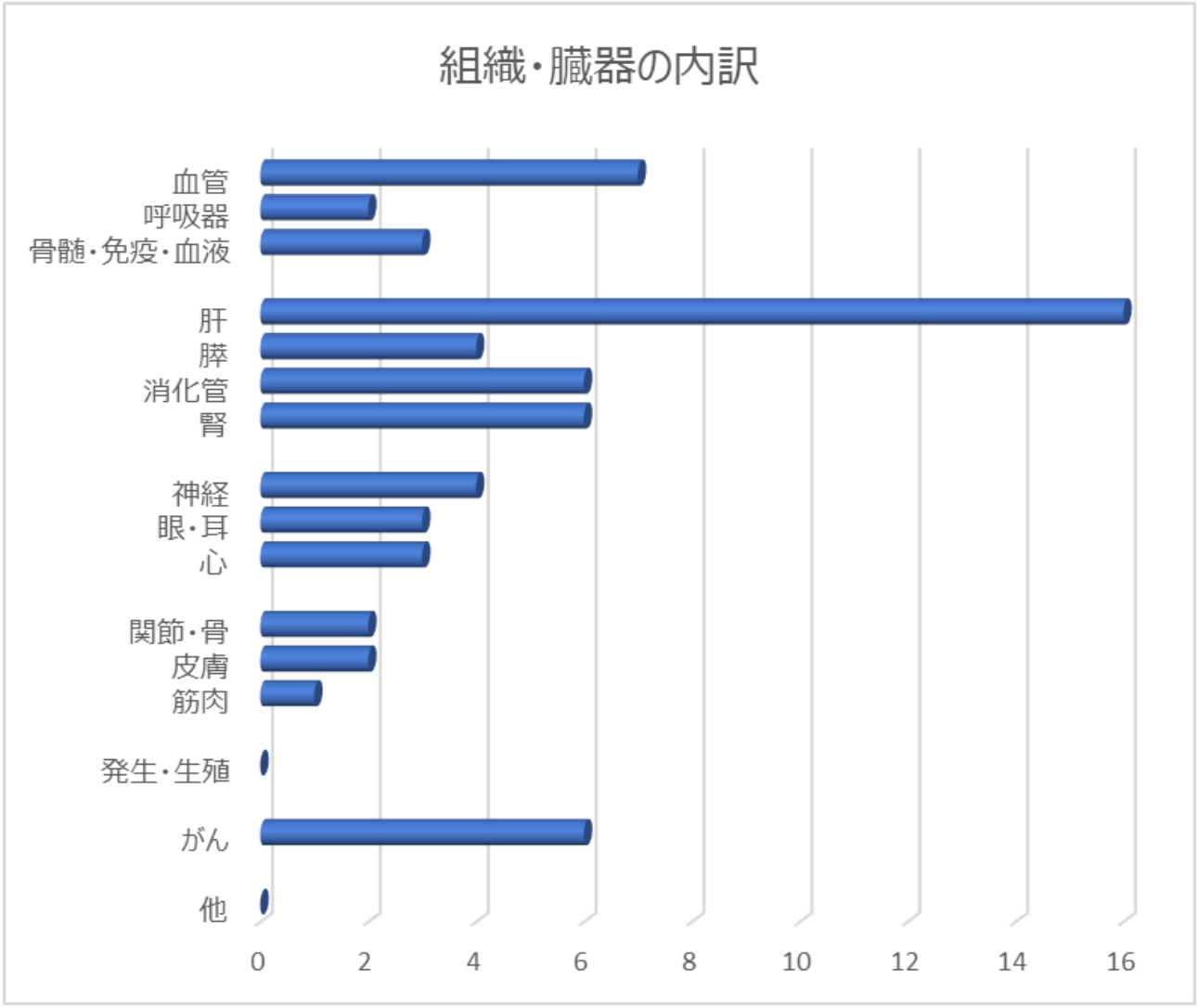

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Genentech

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- Complex model adoption at Genentech (237)
- Comparative analysis of vascular transcriptomics in 2D, transwells, and organ-on-a-chip models (504)
- Application of renal proximal tubule-on-a-chip: Challenge and benefit for supporting drug development in a pharmaceutical industry (713)

MPS use
regulatory filings→ **まだごく一部**
internal decision-making
→ **多くのプロジェクトに実装（主にnew modality）**

GI tract cancer organoid → Biobank
preclinical "efficacy, ADME safety with the same pts"

Technology platform
Analysis: comprehensive omics data
Organoid & other models
MPS: Nortis chip

Intestine
transcriptome
MoA analysis

BBB
brain shuttle, RMT
TEER

Kidney, RPTEC – nephrotox
rat-human
BM verification
reference: PMB

AstraZeneca

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発表10報以上

MPSに求めるもの

- **drug modality agnostic**
- high throughput
- automation
- real time non-destructive monitoring
- **high content**
- **immune competent**
- disease relevance
- safety and efficacy at a time

AstraZeneca – 数理モデル

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データをどう利用するか？

→ In silico modeling

- Predicting **renal drug clearance** using mechanistic modeling based on drug secretion in a kidney microphysiological model (410)
- **Pancreas-liver** in vitro and in silico hybrid model for human diabetic glucose dysregulation (138)
- Investigation of the impact of gap scheduling on the toxicity of PARP1-selective AZD5305 combined with carboplatin using the **bone marrow** microphysiological system (BM MPS) and mathematical modelling (489)
- Complementing MPS with mechanistic computer models helps overcome limitations: Translating the drug **exenatide** from MPS to humans (497)
- Mathematical modelling combined with microphysiological systems (MPSs) enables the quantitative assessment of clinical **safety** in early stages of drug development (574)

MPSデータ→ Modeling による臨床(ADMET, efficacy)予測

MPS data → 数理モデル

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- A quantitative modeling workflow for the design, analysis, and interpretation of experimental studies in **gut-liver** organ-on-a-chip systems (154)
- Complementing MPS with mechanistic computer models helps overcome limitations: Translating the drug exenatide from MPS to humans
- DigiLoCS – A digital **liver**-on-chip simulator for predicting human metabolism of drugs (301)
- Pharmacokinetic modeling of **oral and intravenous** modes of drug delivery in a pumpless microphysiological dual barrier model towards in vivo/in vitro translations (455)
- The **ADME**-chip: Studying different application routes on a PB/PK compliant preclinical tool (648)
- In silico replication of hypoxia dynamics and readouts of an **ischemia/reperfusion** MPS for system identification and pharmacological investigations (417)

AI, ML, DL etc.

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- Machine learning analysis of oxygen amplifies the physiological relevance and translational capacity of vascularized microphysiological systems (670)
- AngioMT: An *in silico* platform for digital sensing of oxygen transport through vascularized organ-chips and organoids (671)
- Leveraging population of model *in silico* approach for robust islet tissue development in microphysiological systems (708)
- On the way to a digital twin in preclinical studies – how automation and continuous data acquisition enable AI-based *in silico* models (332)
- A deep-learning-assisted image analysis and a multiparametric biochemical quantification in human 3D model of non-alcoholic steatohepatitis for high-throughput drug discovery (594)
- "The Sound of Safety" – combining MPS with Bio-AI and *in-silico* to capture the signature of the ordinary (non-toxic) behavior of MPS and the deviations under increasing concentrations of drugs (761)

新規モダリティ評価への利用

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- Assay development of novel high-throughput in vitro assay system using microvascularon-a-chip for the evaluation of **oligonucleotide-**induced platelet aggregation potential (36): *Takeda*
- Efficacy evaluation of **AAV** delivered liver specific promoters in the emulate liver chip (157): *Bayer*
- Evaluation of two complex 3D in vitro human alveolar co-cultures for prediction of lung inflammation and toxicity (355): (**Inhalation**) *AstraZeneca*
- Towards a proximal tubule microphysiological system for antisense **oligonucleotide** safety testing (578): *AstraZeneca*
- Developing novel tools for diabetes research: **AAV** serotype tropism screen in standardized human islet microtissues (163): *Boehringer Ingelheim*
- Development of a lymphoid organ-chip to evaluate COVID **vaccine** boosting strategies (645): *Roche*
- Development of a novel human microphysiological system-based SELEX method for robust identification of brain-targeting **aptamers** for CNS drug delivery (658)
- Organ-on-a-chip approach for accurate phage display screening of organ-targeting shuttle **peptide** (660)

新規モダリティ評価: CAR-T

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- Identifying a common endothelial medium to connect organson-chips for **CAR-T** safety testing (83)
- An MPS **CAR-T** cell therapy model of the immunosuppressive solid tumor microenvironment (89)
- Testing short-chain fatty acid effects on the efficacy of **CAR T** cells in a gut-on-chip system (243)
- Multi-niche human bone marrow on-a-chip for studying interactions of cell therapies with multiple myeloma (475)
- Breast tumor-on-chip applicable for efficacy and safety assessment of **CAR-T** cell therapy (483)
- Increasing predictability of antibody-triggered receptor mediated transcytosis and neurotoxicity of **CAR-T** based therapy with a novel blood brain barrier-on-chip model (508)
- The vascularized micro-tumor (VMT): A fully human microphysiological system platform for testing multiple immuno-oncology therapies (554)
- Tumor-on-chip to evaluate **CAR-T**-cell based cancer immunotherapy efficacy in vitro (636)
- Evaluation of chimeric antigen receptor **(CAR)-T** cell recruitment and efficacy on an organ-chip model system (659)
- Facilitating combination therapy studies in patient-derived 3D tumour models (697)

新規モダリティ＋当局対応非臨床試験

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◆ **Efficacy assessment of novel anti-OA therapeutic drug candidates within an advanced mechanically active osteoarthritis-on-chip model: The SYN321 case study (325): Synartro/BiomimX**

BiomimX

BiomimXは伸縮性が高いデバイスに機械刺激を与えるuBeat beating OoCを提供している。Synartroが開発中のOA薬SYN321の臨床移行に際し、スウェーデン当局から薬効メカニズム（サイトカイン抑制作用）のデータ追加を求められた。SYN321はヒアルロン酸（hyaluronan）にジクロフェナクを結合した局所徐放製剤。BiomimXデバイスの関節モデル(“uKnee model”; collagen gel中chondrocyte培養)で検討したところ、static modelと比較してジクロフェナクの放出が加速していることが明らかとなった。これは予測されていなかった発見だが、放出メカから説明はできる。目的通りにサイトカイン遺伝子発現などの分子レベルの解析ができ、IND申請資料に利用、今年初めに治験入りが承認された。

Immuno-competent models

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多数（~50演題）で免疫細胞を搭載したMPSの報告

- 薬物誘導性障害
- 病態モデル
- 薬効モデル

- 組織内在性免疫細胞
- 浸潤性免疫細胞
- Circulation → interaction → infiltration

- 自然免疫細胞
- 獲得免疫細胞
- 免疫・炎症惹起、抑制

MPS World Summit 2024

June 10-14, 2024

Seattle, Washington, USA