# 22nd LSACJ 2022

## International Conference on Interdisciplinary Life Sciences 2022

DATE: November 26 (Sat), 2022
VENUE: Online Meeting

PROGRAM COMMITTEE

**CO-CHAIRS**
**Dan Ohtan WANG**
RIKEN BDR
**Yu-Shi TIAN**
Osaka University
**Bin ZHOU**
Learning Health Society Institute

**PRESIDENT of LSACJ (2022)**
**Biao MA**
RIKEN R-CCS

**LSACJ COUNCIL**

LSACJ Address: 2-19-28-5F, Showa-cho, Abeno-ku, Osaka, Japan
E-mail: lsacj_group@lsacj.org
Homepage: http://lsacj.org

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# Greetings from the Co-Chairs of 22nd LSACJ 2022

It has been a while since we entered the data-driven era. Keywords such as informatics, artificial intelligence (AI), and machine learning have come to be heard in various fields. They also play extremely important roles in the medical and pharmaceutical fields. In the clinical field, informatics plays an extremely important role, centering on the utilization of clinical diagnostic data. In drug discovery, the analysis of molecular behavior and intermolecular interactions using quantum chemistry and the search for drug candidates using virtual screening and molecular dynamics simulation are also widely used. Advances in these core technologies have led to the development of a diverse range of drug discovery modalities for next-generation medicine and drug discovery, not only research centered on experiments. In recent days, digital medicine has begun to appear in clinical sites. We believe that such rapid technological progress will surely lead to people's health and society's prosperity. The theme of ISL2022 is "From Basic to Clinical" and it focuses on bridging basic research and clinical research. We plan to actively discuss the latest research results and academic content, regardless of the research fields.
We look forward to your participation.

データ駆動型時代に突入してから、しばらくたちました。情報学、人工知能（AI)、機械学習などのキーワードはさまざまな分野で聞くようになり、医学薬学領域においても、極めて重要な役割を果たしています。臨床領域において臨床診断データの活用を中心に、情報学は極めて重要な役割を果たしつつあります。更に創薬領域では、量子化学を用いた分子の挙動・分子間相互作用の解析、バーチャルスクリーニングや分子動力学シミュレーションを用いる薬物候補探索なども盛んに行っています。こうした次世代の医療・創薬の核心的な技術の進歩により、従来の実験のみを中心とする創薬研究から、多様な創薬モダリティーへの発展を遂げています。以前では考えられないデジタル医療も臨床現場に登場しはじめています。こういった技術的進展は、人々の健康、社会の豊さにつながると確信しております。ISL2022 は“基礎から臨床へ”をテーマとし、基礎研究と臨床研究の橋渡しに注目しています。研究者、医療従事者、製薬企業の担当者を招待し、分野を問わず、最新の研究成果や学術内容を活発に議論する予定です。
皆様のご参加を心よりお待ちしております。

我们进入数据驱动时代已经有一段时间了。信息学、人工智能（AI)、机器学习等关键词已经出现在各个领域。在临床领域，信息学被广泛应用于临床诊断发挥着极其重要的作用。在药物研发领域，使用量子化学手法来分析分子举动和分子间相互作用，使用虚拟筛选和分子动力学模拟来搜索候选药物业已成为日常。我们已经从传统的以实验为主题的药物探索转型为多种多样的药物探索的形态。近年来，以前难以想象的数码医疗也开始步入医疗现场。我们相信，如此快速的科技进步，势必为人类的健康带来更多的保证、为社会带来更大的繁荣。ISL2022 的主题是“从基础到临床”，我们关注于基础研究和临床研究的桥接。我们不限研究邻域地诚邀各位学者、医疗工作者、制药企业人员来积极地讨论最新的研究成果和学术相关内容。
我们期待非常您的参加。

**Yu-Shi Tian Ph.D.**

Graduate School of Pharmaceutical Science, Osaka University

Assis. Prof.

**Dan Ohtan WANG Ph.D.**

RIKEN Center for Biosystems Dynamics Research

Team leader

**Bin ZHOU Ph.D.**

Learning Health Society Institute

Chief Scientist

# Greetings from the President of LSACJ (2022)

The Life Science Association of Chinese in Japan (LSACJ) was established in 1995 as a multidisciplinary and comprehensive academic society focusing on life sciences by Chinese scientists and Chinese students in Japan with a history of 27 years. The association was founded in 1995 as the Kansai Region Chinese Students' Association for Molecular Biology, and later developed into the Kansai Chinese Life Sciences Association, which was renamed to the present Life Sciences Association for Chinese Residents in Japan in 2005 on the occasion of the 10th anniversary of the association. Since its foundation, the association has been committed to the spirit of openness, tolerance, friendship, unity, and endeavor to improve communication and cooperation among its members, and to pursue scientific and technological innovation. The Association is also committed to promoting exchanges and cooperation between China and Japan in the field of life sciences.

In LSACJ 2022, we will focus on the theme of "Bench to Bedside", and experts and researchers will be invited to share the latest cutting-edge research results from basic to clinical stages. We will also invite experts who are familiar with pharmaceutical policies in China and Japan to explain the regulations and application process of clinical research in China and Japan. It is hoped that this conference will promote the translation of basic research into clinical applications and provide a platform for communication and interaction between Chinese and Japanese colleagues in different research fields.

We sincerely hope that all of you will participate.

留日中国人生命科学协会（the Chinese Society of Life Sciences in Japan; LSACJ）成立于 1995 年，是一个拥有 27 年历史由在日华侨华人科学家和中国人留学人员发起成立的以生命科学为中心的多学科综合性学术团体。协会源于 1995 年创立的关西地区中国留学生分子生物学协会，随后发展成为关西中国人生命科学协会，在协会成立 10 周年之际，于 2005 年更名为现在的留日中国人生命科学协会。自协会创办以来一直秉承开放包容，友好团结，奋发图强的精神，致力于增进会员间的交流与合作，追求科技创新。协会同时也致力于促进中日两国间的生命科学领域的交流与合作。

LSACJ2022 是由我们主办的为期一天的学术交流大会。本届大会将于 2022 年 11 月 26 日（周六）通过线上会议系统举办。在这次会议上，我们专注于生命科学领域的基础研究到临床转化研究的知识分享。我们将主题定为“从基础到临床”。我们希望以易于理解的方式呈现各个研究阶段的最新科研成果和相关政策介绍。生命科学是一个广泛的研究领域，它囊括生物学、生物化学、农业、医学、齿学、药学、护理学、医工学和其他相关的跨学科领域。我们相信这次年会将是一个汇集来自中国、日本和其他国家的所有一线研究人员和学生的良好机会。我们可以在这个平台上进行公开、深入地讨论，并寻求相互协作的机遇。

我们真诚地希望大家都能够来参加本次会议。

留日中国人生命科学協会（LSACJ）は、1995 年に設立され、27 年の歴史を有する在日中国人科学者と留学生によって始められた生命科学における学際的な学術交流プラットフォームです。 1995 年に「関西地区中国分子生物学留学生協会」として発足し、その後「関西中華生命科学協会」に発展し、10 周年を迎えた 2005 年に現在の「在日中国人生命科学協会」に名称を変更しました。 当協会

は設立以来、開放と寛容、友情と連帯の精神、科学技術の革新の追求、会員間のコミュニケーションと協力の強化に取り組んでいます。 また、当協会は、ライフサイエンス分野における日中間の交流・協力の促進にも力を注いでいます。

LSACJ 2022 Annual Conference では、「基礎から臨床へ・Bench to Bedside」をテーマに、基礎から臨床までのあらゆるステージで、専門家や研究者が最新の最先端の研究成果を発表します。 また、中国と日本の薬事政策に詳しい専門家を招き、中国と日本における臨床研究の規制や申請プロセスについて実践的な知見を提供します。 中日国交正常化 50 周年を機に、この会議がライフサイエンス研究の異なる分野に携わる日中の研究者の交流の場となり、基礎研究の臨床応用を促進することが期待されています。

**Biao MA**
President of LSACJ (2022-)
Research Scientist
HPC- and AI-driven Drug Development Platform Division, RIKEN Center for Computational Science

# Guidance /参加者へのご案内/会议一般说明

## 1. Registration / 登録 / 报名

Register in advance for this meeting:

https://us06web.zoom.us/meeting/register/tZMocO-rrDwsE93K6u-WvhyOwQ4isjZDGoUm

After registering, you will receive a confirmation email containing information about joining the meeting.

このミーティングに事前登録する:

https://us06web.zoom.us/meeting/register/tZMocO-rrDwsE93K6u-WvhyOwQ4isjZDGoUm

登録後、ミーティング参加に関する情報の確認メールが届きます。

提前注册此会议：

https://us06web.zoom.us/meeting/register/tZMocO-rrDwsE93K6u-WvhyOwQ4isjZDGoUm

注册后，您将收到关于加入会议的信息的确认电子邮件。

Zoom Meeting QRcode

WeChat Group QRcode

## 2. Fees / 登録費/ 参加费

Free of charge

無料

免费

# About LSACJ

## List of the Presidents of LSACJ

| Period | Chairpersons |
|---|---|
| 2022 ~ | Biao Ma, PhD. |
| 2020 ~ 2022 | Li Sun, PhD. |
| 2018 ~ 2020 | Yu-Shi Tian, PhD. |
| 2016 ~ 2018 | Tao Yu, PhD. |
| 2008 ~ 2016 | YuQuan Lu, PhD. |
| 2008 ~ 2008 | Xin Zhao, PhD. |
| 2007 ~ 2008 | Jitian Zhang, PhD. |
| 2006 ~ 2007 | Cho Azuma, PhD. |
| 2005 ~ 2006 | Lei Shi, PhD. |
| 2004 ~ 2005 | Guolong Zhang, PhD. |
| 2002 ~ 2004 | Yi Dai, PhD. |
| 2000 ~ 2002 | Gang Huang, PhD. |
| 1999 ~ 2000 | Ping Zou, PhD. |
| 1998 ~ 1999 | Wei Shi, PhD. |
| 1997 ~ 1998 | Kai Chen, PhD. |
| 1996 ~ 1997 | Zhihua Zou, PhD. |
| 1995 ~ 1996 | Jun Sheng, PhD |

# LSACJ Committee in 2022

President: Biao MA

Vice Presid. in Charge: Dan Ohtan WANG

Vice Presidents: Xiangji JIANG, Yi ZHOU

Secretariats: Yi ZHOU, Lu CHEN

IT Director: Xiangji JIANG, Zixuan WANG

Financial Director & Cashier: Xiaochun ZHANG, Duligengaowa Wuergezhen

External Contactor: Ning LI

Public Relation: Yidan ZHU

# Program

| Opening | 10:00-10:10 |
|---|---|

## Session 1: AI for Life Science

| Moderator: Yu-shi Tian, Osaka University (25+5 min) | 10:10-12:10 |
|---|---|

**S1-1** **Imitation and Innovation:Reflections on the Development of Intelligent Technology and the Progress of Human Society（模仿与创新:智能科技发展与人类社会进步的思考）**

Zhiwei Luo, Prof., Ph.D.

Kobe University

**S1-2** **Development of drug discovery AI platform for comprehensive target predictions（开发用于全面预测目标的药物发现人工智能平台）**

Teruki Honma, Team Leader, Ph.D.

RIKEN BDR

**S1-3** **Research and development of next-generation AI medical treatment systems and devices（新一代 AI 医学诊疗系统及设备的研发）**

Xuejun Zhang, Prof., Ph.D.

Guangxi University

**S1-4** **Practical Massively Parallel Monte-Carlo Tree Search Applied to Molecular Design（应用于分子设计的实用大规模并行蒙特卡洛树搜索法）**

Xiufeng Yang, Researcher, Ph.D.

Chugai Pharmaceutical Co., Ltd.

## Photograph

| Zoom | 12:10-13:30 |
|---|---|

## Luncheon Seminar

| Zoom | 12:10-13:30 |
|---|---|

**LS-1：EPS 株式会社（EPSHD）**
**LS-2：上海人才交流协会**
**LS-3：北京深势科技/DPTechnology（AI+分子模拟新工具打造药物设计新流程）**
**LS-4：株式会社アフィニティサイエンス（Affinity Science Corporation）**

## Session 2: Research for translational breakthrough

| Moderator: Dan Ohtan Wang, RIKEN BDR (25+5 min) | 13:30-16:00 |
|---|---|

**S2-1**

**Self-scavenging and micro-nano drug delivery system for improved tumor targeting and safet（提高肿瘤靶向性和安全性的自清除和微纳米药物输送系统）**

Wenli Zhang, Associate Prof., Ph.D.

China Pharmaceutical University

**S2-2**

**Development of genome analysis technology to elucidate the function of the human genom（开发基因组分析技术以阐明人类基因组的功能）**

Yasuhiro Murakawa, Prof., Ph.D.

Kyoto University

**S2-3**

**Disease and Genetics: Disease Genetic Research in the Era of Individualized Medicine（疾病与遗传：个体化医疗时代的疾病基因研究）**

Long Guo, Deputy Team Leader, Ph.D.

RIKEN

**S2-4**

**Novel Technologies Enable and Accelerate Research and Development of New Drug（新技术赋能加速新药研发）**

Chao Liu, Director, Ph.D.

药明康德化学服务部 (Chemistry Service Unit, WuXi AppTec)

**Endothelial cell mechanoresponse to haemodynamic forces during blood vessel lumenization（血管腔化过程中内皮细胞对血流动力的机械反应）**

**S2-5** Li-Kun Phng, Team Leader, Ph.D.

Affiliation: RIKEN BDR

| **Break** | **16:00-16:10** |
|---|---|

## Session 3: Translational Medicine and Clinical Science

| **Moderator: Bin Zhou, LSHI (25+5 min)** | **16:10-17:10** |
|---|---|

**Current Status of investigator initiated trials and future prospects in China（中国医师主导试验的现状和未来前景）**

**S3-1** Peimin Yu, Associate Prof., Ph.D.

Department of Neurology, Huashan Hospital, Fudan University

**Investigator-initiated clinical trials in Japan（日本的医师主导临床试验）**

**S3-2** Tsutomu Nishimura, Prof., Ph.D.

Kyoto University

| **Break** | **17:10-17:20** |
|---|---|

## Session 4: All Other Interdisciplinary Life Science Studies

## Moderator: Shengqun Hou, RIKEN BDR (15+5 min) 17:20-18:20

**S4-1** **Direct effect of food-derived macromolecules on intestine--Apple-derived exosome-like nanoparticles mediate down-regulation of intestinal transporter expression by microRNA--（食物衍生的大分子对肠道的直接影响）**

Qiunan Zhu, Ph.D.

Kanazawa University

**S4-2** **Reactive Oxygen Species Cause Exercise-Induced Angina in a Myocardial Ischemia-Reperfusion Injury Model（活性氧在心肌缺血再灌注损伤模型中导致运动诱发的心绞痛）**

Xiaohang Wang, Ph.D.

Hyogo Medical University

**S4-3** **Structural studies on cyanobacterial trimeric Photosystem I-related protein complexes（蓝藻三聚体光系统 I 相关蛋白复合物的结构研究）**

Jiannan Li, Ph.D.

Osaka University Institute for Protein Research, Osaka University

## Closing 18:20-18:30

# Session 1
# AI for Life Science
10:10-12:10

# 模仿与创新:智能科技发展与人类社会进步的思考

Zhiwei Luo[1,*]

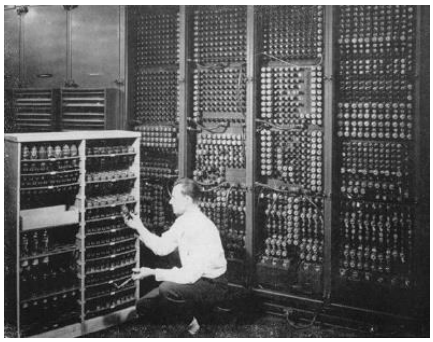
Keywords: 健康文艺复兴 模仿与创新 智能科技创

## 一、科技智能化与人类社会

伴随着计算机技术，互联网技术，无线通信技术的发展与普及，近年来万物所发出的信息的采集，传输，储存以及共享等数字化科技得以迅猛发展。对于海量数据的价值挖掘及其社会应用的需求与期待日益高涨，以人工智能为代表的智能科技的创新性研发及创新型社会运用受到人们的广泛关注。未来学家们甚至形象化地提出有关人工智能发展的所谓奇异点的论述，预测将在未来短短的 25 年内，人工系统的智能就会大大超越人类的智能并以指数增长速度拉开两者的距离。

纵观近 70 年来的智能科技发展速度，的确让我们认识到当今科技发展的总体趋势正向着数字化，智能化的方向发展；的确让我们体会到智能化科技正在从量的提升发展到质的飞跃；的确让我们觉悟到与人工系统的智能化进程相对比人类社会自身的退化危机。

如图 1 所示，从计算机的运算速度来看，1946 年曾被誉为巨型大脑（Giant Brain）的 ENIAC 的运算速度是每秒 385 次乘法，而就在今年（2020 年），经过短短的 74 年，日本公布的当今世界最快的设置在神户的超级计算机富岳的运算速度已达到惊人的每秒 10 的 18 次方乘法。



（1）ENIAC，1946 年 每秒 385 次乘法


（2）富岳，2020 年 每秒 10 的 18 次方乘法

**图 1 计算机技术的发展比较**

如图 2 所示，从运动功能来看，五十年前的机器人还仅仅只是孩子们的玩具，而在 2006 年作者所领导的团队在日本理化学研究所研发的世界首台机器人・作 I-MAN 就可以安全实现对人的护理操作。

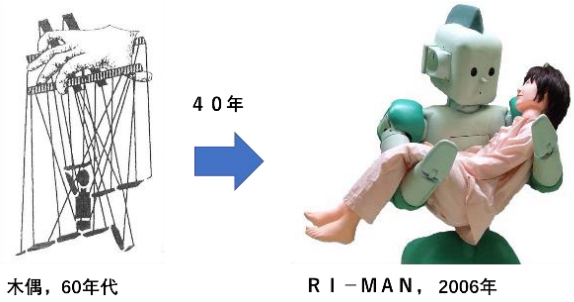



**图 2 机器人技术的发展比较**

从智能程度来看，1997 年 5 月由 IBM 公司研制的深蓝（DEEP BLUE）计算机战胜了国际象棋大师卡斯帕洛夫（KASPAROV），2016 年计算机 AlphaGo 取胜国际围棋大师。加上近年来的自动驾驶技术，无人机技术，人脸识别技术，语言处理技术以及情感识别技术，深度学习等等算法，人工系统的智能化的确发生了革命性演变。由此，人们把机械智能化誉为从十八世纪工业革命开始以来的第四次产业革命。在日本，如图 3 所示，政府正积极主导提倡所谓社会 5.0 的构想，推动虚拟空间（Cyberspace）与现实社会（Real world）的高度融

1 Graduate School of System Informatics, Kobe University

✉ Zhiwei Luo, luo@gold.kobe-u.ac.jp

合，实现智慧化社会发展。

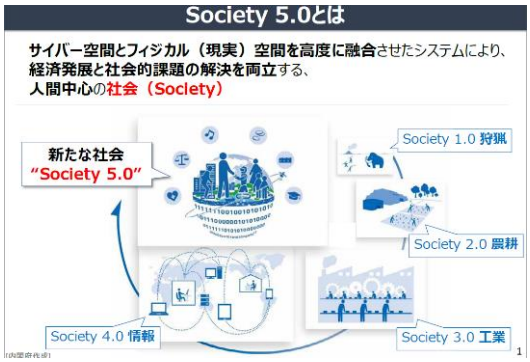



**图 3 日本内阁府的社会 5.0 构想**


**图 4 机器人取代人的各种职业**

不可否认，科技智能化的迅猛发展不仅给人们带来了对未来美好生活的憧憬与梦想，同时也带来了不安，怀疑，甚至恐惧。事实上，当我们实际面对当代人类社会时，我们不难发现，至今为止当代社会由人来担当的大量的劳动职业如图 4 所示已经开始渐渐地被机器人所代替。我们不难感叹智能科技知识的拥有度带来了人们劳动收入的极大差异。特别是，我们不难看到与人工系统的智能化相对比，我们人类当代所面临的严峻的健康难题，诸如，人口老年化，晚婚，生活周期病，疲劳，认知疾病，世界范围的传染疾病流行等等。

由此，本演讲将从模仿与创新的角度出发，以中世纪文艺复兴为参照，分析对未来科技智能化的理解，探讨其在人类健康社会治理中的合理的发展方向，积极提倡面向健康文艺复兴的科技智能化发展。

## 二、文艺复兴的启示

在当今科技智能化迅猛发展的形势下，人们的主流意识是在积极倡导科技的创新，期盼科技创新带来社会经济发展。相反，对于模仿似乎往往理解为创新的反义词，从而抱以轻视，加以批判，甚至采取予以否定的认识和态度。与此同时，人们在面对诸如人工智能对我们人所从事的现有职业的取代危机的认识似乎又是来源于模仿的思维模式。因此，在探讨科技智能化与未来社会治理的问题上有必要对模仿与创新的相互关系以及各自的价值所在从新予以深刻思考和理解。认真分析科技智能化在未来社会治理中的必然性与必要性，正确把握好科技发展与社会实际应用的大方向。与以往任何科技相对比较，当今技术的智能化极大地拉近了人与科技的距离。科技与人，以及人类社会的相互影响将发挥到极致。

不可否认，当前的人工智能发展还仅仅是从科技角度上的信息科学技术发展的必然趋势，它对于人类社会的文明进步以及社会健康发展上的必然性与必要性有待我们更为广泛地，更为深刻地予以思考，而不能以眼前利益和兴趣为驱动加以乱用。从这个角度出发，历史上发生在中世纪的文艺复兴运动也许会给我们某些有益的启示和教诲。

文艺复兴(Renaissance)发生于 14 世纪到 17 世纪被称为黑暗时代的欧洲。在社会背景上由于宗教对包括文学、艺术、哲学，科学，社会等一切的过度禁锢，加之黑死病在欧洲的蔓延为导火索，人们心中的绝望与恐慌相互交汇，对宗教神学的绝对权威产生极大的怀疑，对于模仿乃至回归到古代希腊和罗马的艺术，文化，建筑产生了极大的向往。

古希腊可谓欧洲文明之源。前希腊时期的大哲学家德谟克里特就提出了模仿论，其后的柏拉图和亚里士多德都肯定模仿是人的本能，主张文艺来源于模仿。在这些哲学思想的影响下，伴随着资本主义萌芽以及资产阶层的形成，加上有关透视学，解剖学等科技的发展，文艺复兴时期人们把模仿发展到极致并且以此为手段展现人文主义价值观。比如，著名画家达芬奇就十分强调最高的艺术来于模仿。

如果对比图 5 的两幅巨作，我们也许会领略到达芬奇的艺术模仿的境界，同时品赏到毕加索的艺术创新的挑战。

Mimesis or Innovation

**模仿　　创新**

**图 5 达芬奇与毕加索的艺术对比**

文艺复兴(Renaissance)迎合了从封建社会向资本主义社会的发展过度阶段，从艺术，文学，建筑，思想解放，人文主义，多样性等各大方面振兴了，创新了人类文明，其价值所在至今都得到人们的高度评价和认可。如今当我们漫步在意大利的大街小巷，当我们在观览在弗洛伦萨的美术博物馆，我们依然会感受到文艺复兴带来的浓浓的人文气息；我们依然会惊叹那一件件艺术作品的艳丽；我们依然会体验到那一栋栋建筑的力度与美感。文艺复兴乃是人类历史上的文明进步的模仿与创新的典范。

思考文艺复兴对当代科技智能化与我们未来社会治理中带来的启示，作者认为，我们既不要用对立的观点来看待模仿与创新，来轻视模仿，同时也不必一味以模仿的思维方式去理解人工智能在取代人上带来的恐惧感。在模仿中谋求创新，在创新中提炼模仿。模仿不同于单纯的复制，仿制和拷贝。模仿与创新既是我们的思维方式也是实际手段，其目的是要为解决社会课题对症下药，提升社会价值，谋求人类福祉，赋大众以阳光。

## 三、倡导健康文艺复兴

模仿应该包含形体性模仿，动作性，功能性模仿以及社会运用端模仿等各大层次。如果我们仅仅局限于形体性模仿，功能性模仿，我们就无法产生对于社会运用端层次的模仿的期盼和欲求。当我们还在谈论智能科技带来的第四次产业革命与创新的时候，人们已把目光姚望起什么是第五次产业革命的技术核心。

从 650 万年悠久的人类进化史来看，经历了漫长的在自然界生存的原始社会时代，人类在一万年前才进入到了农耕时代。农业技术的运用有效地保证了粮食，带来了人口增长。近代 200 年的工业革命把人们引进到工业社会时代，工业生产带来了社会经济的发展，科技的飞跃和人们的生活富裕。接下来的的后工业时代促进了社会金融，国际贸易以及服务业的蓬勃发展。所有这些社会时代的划分都来自标志性的科技创新和有效的社会运用。来自科技与产业，经济的高度融合。科技与产业发展的贡献从保障生活进一步发展为提高人们的生活质量。

然而，面对未来社会发展与人类进步，我们无法避开如何增进人类健康这一恒古以来的永恒的命题。在日本，人口老年化已成为所谓国难级的社会难题。人口老年化直接带来的是社会整体的老年化。它不仅局限在日本，未来不久的中国等世界各国都将会面对这一难题。与此同时，从今年以来在世界范围广泛流行的新冠肺炎等来看，人类健康问题已成为当今世界共同的首要社会课题。面对如此严峻的社会现实，仅靠现有以医疗为中心的社会健康体系是否足以担当？智能化科技在健康医疗领域中应该如何发展？有何真正用武之处？如何获取人们的实际信赖？这些课题强力驱动着我们要站在更高的层面上模仿文艺复兴，开创健康文艺复兴的新纪元。

中国国家主席习近平高度重视在社会治理中人民健康的重要性，高瞻远瞩地号召要把以治病为中心转变为以人民健康为中心，关注生命全周期，健康全过程。这一重要指示为我们指明了道路，对于开创广大社会范围的健康文艺复兴必将发挥领导性关键作用。

模仿文艺复兴中的诸如透视学，解剖学等科技发展，在我们大力推动健康文艺复兴的实践中，首先需要对于健康学给与充分的探讨以及体系化认知。

在健康学的体系化框架下，从以下各健康阶段，大数据与人工智能都将会贯穿其纵横，在健康学的体系中大有作为，引领健康科技的创新。

**（1）检查・诊断**：超微量检查、图像、动态影像、可视化、模型化

**（2）手术・治疗**：定位、导航、手术训练、低侵袭

**（3）康复・锻炼**：脑神经系统、上肢、步行、全身运动

**（4）日常生活辅助**：假肢、福利、养老

**（5）予知・予防**：智慧检测、ICT、健康教育

在以人民健康为中心的崇高理念的指导下，伴随着健康学的体系化确立以及智能科技的辅助，我们就有希望一改现在的以在医院为主的诊断，治疗，疗养为主要流程的被动式医疗，创新为理想的以在日常生活中的预知，预防，促进为根本的主动式健康。这样的根本性健康大变革同时也将会为健康产业的兴欣发展开拓广阔天地，带来社会经济的良性循环。人民的健康，社会的健康必将有力推动人类文明的大幅度进步。图 6 介绍作者有关健康科技的研究项目。


**图 6 健康科技研究探索**

## 四、社会治理与可持续发展

不容置疑，以大数据，人工智能为代表的智能化科技不仅对工业的结构性提升，对金融业，服务业的模式创新可以发挥巨大作用，在社会治理，特别是在健康医疗领域也开始展示其无与伦比的威力。面向长远的社会治理与人类社会的可持续发展，建议提倡以下几项方策。

**第一．人才教育为本：**

在高度智能化的互联网环境中，弄清如何教，教什么的基本问题。注重智能科技与日常生活运用的大众科普教育，发展终生教育。由此提高人们对智能科技的基本认识，技能以及正确的创新思维能力，创新实践能力。

**第二．人文探索为心：**

在探求新兴科技的同时，需要对科技发展的社会观，历史观，价值观，伦理观，服务模式得课题加以全面的人文研究。从而得以正确把控科技在社会对人类的有效运用，使得文理之间更加相互交融，更加相互促进。

**第三．研究协作为源：**

在科学研发方面，认清数据，算法，实现，平台的意义与价值，积极开展国际合作，推动资源开放与共享，挽回由于产业革命初级阶段所引发的自然环境破坏的全球性难题。推动对动物以及人脑的机能加以全面的，系统性的，定量化功能的科学发现。

**第四．社会实践为道：**

在智能科技的社会实践中，注重系统的信赖性、透明性，预判其可能发生的对人类，对社会的危害性，危险性等风险。探求以人为本的理念，摸索社会整体的智慧化，智能化功能，创新智慧化，智能化的服务模式。开创以服务促生产，以服务得人心的崭新产业模式。

古希腊的思想家，哲学家德谟克利特指出，从蜘蛛我们学会了织布和缝补，从燕子学会了造房子，从天鹅和黄莺等歌唱的鸟学会了唱歌。在当代，从在蓝天飞翔的鸟类所得到的启发我们制造出了飞机，靠着模仿人类大脑的计算和记忆功能我们开发了计算机，从人和动物，昆虫的灵巧的运动我们研发了机器人，从探求人脑的分析，识别，判断，分类，决策等功能我们迎来了人工智能。所有这些技术创新

的灵魂都来自对自然的模仿，进而用来影响自然和人类。

有关技术创新对人类社会影响的问题，公元前369 年的中国古代道家庄子已有了深刻的探讨和生动的阐述。庄子用朴素的寓言方式在诸如丈人圃畦以及混沌等故事中提示了人们对这一重大技术伦理问题的思考。在物理学，生命科学等现代科技高度发展的今天，庄子的思考依然具有重要的现实意义。我们在破除固步自封，大力提倡科技创新发展与实际社会应用的同时，也必须清醒地认识到现有科学的局限性，必须以科学的的态度对科技与人的关系，科技与社会的关系加以广泛深入的思考和讨论。只有这样才能真正地达到理解智能科技，把控智能科技，保证社会可持续化发展，促进人类文明不断进步。

人们预测第五次产业革命将是智能科技与生物科技的高度融合，它必将贯穿健康医疗，工业，能源以及农业等方方面面，真正实现根本服务人类的产业的革命。

# Author Information

Zhiwei Luo

luo@gold.kobe-u.ac.jp

## Field

Intelligent Robotics, System Control, Artificial Intelligence

## Education Experiences

1980-1984 Huazhong Univ. of Science and Technology Bachelor

1989-1991 Nagoya Univ. Master

1991-1992 Nagoya Univ. Ph.D.

## Work Experiences

1992-1994 Assistant Prof. of Toyohashi Univ. of Technology

1994-1998 Frontier Researcher of RIKE

1998-2001 Associate Prof. of Yamagata Univ.

2001-2008 Team Leader of RIKEN

2006- Professor of Kobe Univ.

## Major Publications

Refer to the information of Prof. Luo's research map

https://researchmap.jp/read0133499/

# Development of drug discovery AI platform for comprehensive target predictions

Teruki Honma[1,*]

drug discovery, artificial intelligence, structure generation model

Since the latter half of the 2010s, the development of artificial intelligence (AI) methods including deep learning, the lowering of the hurdles to obtain big data, and the development of hardware that can be used for AI such as general-purpose GPUs have led to AI has become more useful and practical. In Japan, in 2016, led by Prof. Okuno (Kyoto University), Life Intelligence Consortium (LINC) was launched to accelerate the applications of AI to the entire life science fields, including drug discovery and medical care. activity was performed. Through the 1st phase of LINC, we have developed various AI-related elemental technologies by building and verifying prototypes of AI that can be used in various fields, mainly using public data. In addition, mutual understanding and sharing of future issues among life-related companies, IT companies, and academic research institutes progressed.

In the next phase of social implementation of LINC, it is very important from the viewpoint of practicality to develop AI models by integrating not only public data but also confidential data historically collected in companies. Under such circumstances, a project of the Japan Agency for Medical Research and Development (AMED) named “DAIIA” to build a drug discovery AI platform by linking AI technologies of academia and drug discovery-related assay data of pharmaceutical companies started in August 2020.

The AMED DAIIA project has built an AI platform that comprehensively supports drug design from hits to development candidates by combining AI models that comprehensively predict compound profiles such as on/off targets and ADMET, and AI that generates new structures (generative model). The goal is to streamline drug discovery for small and middle-sized molecules. In particular, we are focusing on off-targets, building prediction models for more than several hundred targets, and measuring new data for 44 targets that are particularly important for side effects. As for learning data, in addition to public data, we are planning to receive in-house data and learning results from 18 pharmaceutical companies. In terms of key technologies, we are developing and implementing multimodal learning by GCN, semi-supervised/self-supervised learning, multi-objective optimization by reinforcement learning, and federated learning. In particular, we are promoting development with an emphasis on practicality in the field of drug discovery and are working on fine tuning of AI models using new internal data in ongoing projects, visualization of the applicability domain, and use for structure generation.

1 Center for Biosystems Dynamics Research, RIKEN
✉ Teruki Honma, honma.teruki@riken.jp

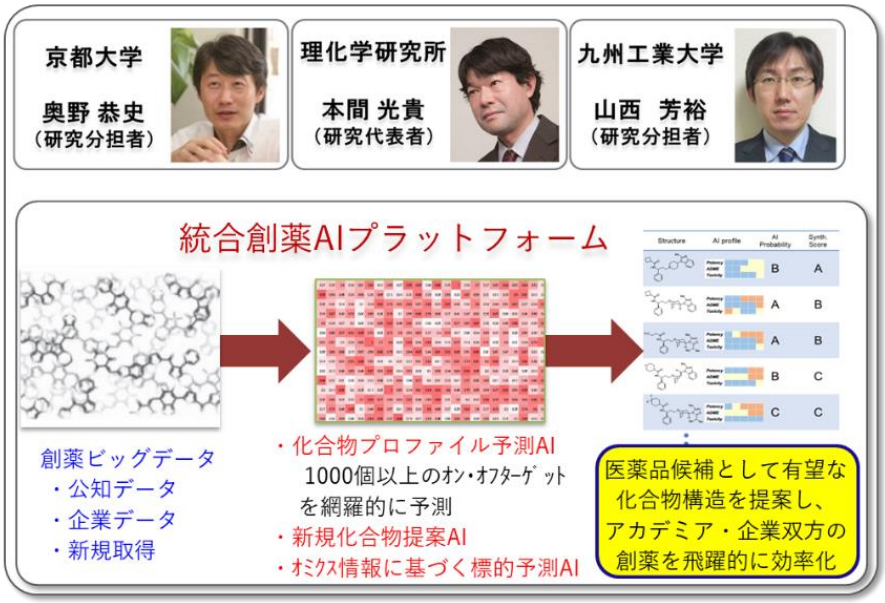



**Fig. 1 AMED DAIIA (Next generation drug discovery AI project)**

# Author Information

Teruki Honma
honma.teruki@riken.com

## Field

Drug design, artificial intelligence, molecular simulation

## Education Experiences

1987-1991 Hokkaido univ. Bachelor
1991-1993 Hokkaido univ. Master
2001 Hokkaido univ. Ph.D.

## Work Experiences

1993-2004 Banyu Pharmaceutical Co. Ltd.
2004-2007 Pfizer
2007- RIKEN (2008- Team leader)

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# 新一代AI医学诊疗系统及设备的研发

张学军[1,*]

Keywords: 人工智能，计算机辅助诊断，远程医疗，边缘云计算

目前，针对医学图像的疾病诊断主要依靠医生的视觉诊断，这就带来了两方面的问题。一方面，每位医生的临床经验和能力不同，做出诊断所消耗的时间和精力也不同，随着患者数量的激增，如何提高医生的工作效率是一个难题；另一方面，医生主要是通过肉眼对图像进行观察以发现病变区域，而医学图像中包含许多人眼无法直接观察到的与疾病相关的信息，因此如何获取并利用这些重要的“肉眼不可见”信息十分重要。随着人工智能(Artificial Intelligence, AI)技术的发展，传统机器学习方法以及深度学习方法与医学图像的处理及分析方法的联合使用，有效地解决了以上两方面的问题。在新一代信息技术变革的背景下，5G及物联网的普及和应用为AI远程医学诊疗打下了良好的基础，也为打破国内外医疗资源不均衡的现状提供了有效解决途径。然而在其实用化之前必须解决数据安全性和网络处理AI算法速度的难点。

当前我国的远程云服务器使用主要以阿里云、腾讯云、华为云等大型公有云为主，虽然公有云目前有云算量巨大、成本低等优点，但是对于医院等特殊机构具备大量隐私、敏感信息操作的用户来说，将敏感信息存储到公有云中进行计算具有较大风险；且对于医学信息处理算法具有有限性，信息在公有云中的运算必须要在公有云设计的框架中运行，这对很多复杂的算法（如深度学习图像识别算法等）提出了高难度的挑战。而目前的部分私有云服务虽然可以对上述问题作出进行一定程度的解决，但现在依旧存在以下问题：1.无法相应的对客户的终端物联网进行定制化设计。2.进行大数据信息处理（如3D建模、深度学习等）时间缓慢。因此，现阶段企业等进行信息化改进迫切需要一个具备从终端物联网到云端服务器搭建技术闭环的解决方案。

针对新一代AI医学诊疗系统及设备的研发过程中对互联网高速响应的要求，我们团队将近端的多个节点与具有相当算力的边缘服务器相连，使用XOJO构筑私有云服务架构体系，并基于边缘计算技术对大数据信息进行算法架构与FPGA硬件加速处理，突破了云端深度学习从分钟级到边缘端秒级计算响应的关键技术，最终形成了基于边缘计算的私有云服务体系，提出了“三端”架构：即智能物联网终端、边缘加速端、私有云端。先后已经在腹部器官的3D建模、肝癌的计算机辅助诊断系统、腹腔镜微创手术协作机器人系统研发上取得了先期研究成果，为传统医疗系统及设备的信息化改造升级提供了解决方案。

1 广西大学计算机与电子信息学院

✉张学军, xjzhang@gxu.edu.cn.

# Author Information

张学军
xjzhang@gxu.edu.cn

r

## Field

计算机辅助诊断系统(computer aided diagnosis, CAD)的开发，涉及医学图像处理，模式识别，机器人视觉，触觉，计算机图形学等领域的研究；物联网云平台的图像处理加速技术

## Education Experiences

1987.9-1991.7 广西大学物理系无线电技术专业 学士
1999.4-2001.3 日本岐阜大学工学部电子信息系 硕士
2001.4-2004.9 日本岐阜大学工学部电子信息系 博士

## Work Experiences

1991.7-1994.5 广西省计划委员会信息技术中心 助理工程师
1994.5-1998.6 南宁市岸丰电子实业有限公司 工程师
2004.10-2007.3 日本岐阜大学医学研究科 博士后
2006.10 德国不来梅大学Mevis研究所 访问教授
2010.4-2011.3 日本岐阜大学医学研究科 访问教授
2014.8-2015.9 美国南加州大学生物医学工程学院 访问学者
2007.9—至今 广西大学计算机与电子信息学院 教授/博导

## Major Publications

1. Huan Lao and **Xuejun Zhang***, "Regression and Classification of Alzheimer's Disease Diagnosis Using NMF-TDNet Features From 3D Brain MR Image," ***IEEE Journal of Biomedical and Health Informatics***, Vol. 26, No. 3, pp.1103-1115, 2022.

2. **Xuejun Zhang***, Yanjiao Ban, Huan Lao, "Diagnosis of Alzheimer's Disease Using Structure Highlighting Key Slice Stacking and Transfer Learning", ***Medical Physics***, 2022;49:5855–5869,

3. Chan Liang, Huan Lao, Tao Wei, Xuejun Zhang*, "Alzheimer's Disease Classification from Hippocampal Atrophy based on PCANet-BLS", ***Multimedia Tools and Applications***, 81(8), 11187–11203, 2022.

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# Practical Massively Parallel Monte-Carlo Tree Search Applied to Molecular Design

Xiufeng Yang[1], Tanuj Kr Aasawat[1], Kazuki Yoshizoe[1]

Keywords: Distributed parallel, Molecular design, Search

1 This work was done when all the authors affiliated with RIKEN, AIP

It is common practice to use large computational resources to train neural networks, as is known from many examples, such as reinforcement learning applications. However, while massively parallel computing is often used for training models, it is rarely used for searching solutions for combinatorial optimization problems. In this paper, we propose a novel massively parallel Monte-Carlo Tree Search (MP-MCTS) algorithm that works efficiently for 1,000 worker scale, and apply it to molecular design. This is the first work that applies distributed MCTS to a real-world and non-game problem. Existing work on large-scale parallel MCTS show efficient scalability in terms of the number of rollouts up to 100 workers, but suffer from the degradation in the quality of the solutions. MP-MCTS maintains the search quality at larger scale, and by running MP-MCTS on 256 CPU cores for only 10 minutes, we obtained candidate molecules having similar score to non-parallel MCTS running for 42 hours. Moreover, our results based on parallel MCTS (combined with a simple RNN model) significantly outperforms existing state-of-the-art work. Our method is generic and is expected to speed up other applications of MCTS.

Recently, the combination of (non-parallel) MCTS and DNN has been applied to molecular design problems, which aims to find new chemical compounds with desired properties[1-2], utilizing the ability of MCTS to solve single-agent problems. In general, designing novel molecules can be formulated as a combinatorial optimization or planning problem to find the optimal solutions in vast chemical space and can be tackled with the combinations of deep generative models and search[3-6]. However, there are no previous studies about massively parallel MCTS for molecular design.

In this research, we propose a novel distributed parallel MCTS and apply it to the molecule design problem. This is the first work to explore viability of distributed parallel MCTS in molecular design. Our experimental results show that a simple RNN model combined with massively parallel MCTS outperforms existing work using more complex models combined with Bayesian Optimization or Reinforcement Learning (other than UCT).

To evaluate the quality of the solutions and to compare against state-of-the-art methods, we use the octanol-water partition coefficient (logP) penalized by the synthetic accessibility (SA) and large Ring Penalty score, a popular benchmarking physicochemical property used in molecular design[7-8].

Table 1: Penalized logP score (higher the better) of TDS-UCT, TDS-df-UCT and MP-MCTS, with 10 minutes time limit, averaged over 10 runs.

| Methods \ cores | 4 | 16 | 64 | 256 | 1024 |
|---|---|---|---|---|---|
| TDS-UCT | 5.83±0.31 | 6.24±0.59 | 7.47±0.72 | 7.39±0.92 | 6.22±0.27 |
| TDS-df-UCT | 7.26±0.49 | 8.14±0.34 | 8.59±0.49 | 8.22±0.41 | 8.34±0.46 |
| **MP-MCTS** | 6.82±0.76 | 8.01±0.61 | 9.03±0.85 | **11.46±1.52** | **11.94±2.03** |
| ⋆non-parallel-MCTS (#cores × 10 minutes) | 6.97 ± 0.49 | 8.54 ± 0.34 | 9.23 ± 0.53 | 11.17 ± 0.88 | – |

To evaluate the distributed MCTS approaches, we study the quality of the solutions obtained, analyze the performance of different parallel MCTS algorithms, and compare the performance of MP-MCTS with state-of-the-art work in molecular design.

**Maximizing penalized logP score.** Table 1 presents the penalized logP score of distributed MCTS approaches for varying number of CPU cores. With increasing number of cores available, more number of simulations can be performed in parallel, which improves the quality of the score. TDS-UCT suffers from communication contention, with increasing number of cores the load imbalance becomes more significant, hence yields lower score. TDS-df-UCT[9] achieves more uniform load balancing but only slightly improves the score (discussed later in this section). Our MP-MCTS, which mitigates the issues of other approaches, shows strict improvement in score with increase in number of cores leveraged.

**Quality of parallel solution over non-parallel solution.** As mentioned earlier, any parallel MCTS must speculatively start to search before knowing the latest search results, and it may return different outcomes from those of the non-parallel version. Also, it is significant to compare the quality of distributed MCTS solution with non-parallel MCTS. The bottom row of Table 1 presents the penalized logP score for non-parallel MCTS. Note that non-parallel MCTS was run for equivalent core-hours (for example, 256 cores

for non-parallel MCTS indicates it was run for 256×10 minutes on a single core; while distributed MCTS is run on 256 cores for 10 minutes). While taking much less time, the distributed-MCTS is on-par and yields higher score than non-parallel when large computing resources (i.e. with 256 and 1024 cores) are leveraged.

| Methods | 1st | 2rd | 3rd | |
|---|---|---|---|---|
| JT-VAE (Jin et al., 2018) | 5.30 | 4.93 | 4.49 | reported results |
| GCPN (You et al., 2018a) | 7.98 | 7.85 | 7.80 | reported results |
| MolecularRNN (Popova et al., 2019) | 10.34 | 10.19 | 10.14 | reported results |
| MolDQN (Zhou et al., 2019) | 9.01 | 9.01 | 8.99 | reported results[a] |
| Mol-CycleGAN (Maziarka et al., 2020) | 9.76 | 7.29 | 7.27 | reported results |
| GRU-based (Yang et al., 2017) | 6.47 | 5.65 | 5.01 | 8 hours x 10 runs |
| **MP-MCTS** using GRU | **15.13** | **14.77** | **14.48** | 10 min. x 10 runs |

Table 2 : Comparison of the best three penalized logP scores

**Comparison against related work in molecular design.** Table 2 presents the top 3 penalized logP scores obtained by the existing state-of-the-art work (description in section 6). The scores of MP-MCTS are the best among 10 runs (10 minutes each), which outperforms the existing work significantly in maximizing the penalized logP score. It is also notable that MP-MCTS significantly improved the score of the GRU-based model. The bottom two lines compare the results obtained from 10 minutes random sampling from the GRU-based model[1] with score obtained by MP-MCTS which uses the same model (as mentioned in Section 4). This result suggests the possibility of improving existing work by combining their models with parallel MCTS.

**Conclusion.** Applying MCTS to molecular design is relatively less explored. Ours is the first work to explore distributed parallel MCTS for molecular design. The extensive experiments have shown that an efficient distributed MCTS significantly outperforms other approaches that use more complex DNN models combined with optimizations such as Bayesian Optimization or Reinforcement Learning (other than UCT). Further, it does not trade off search ability (w.r.t non-parallel MCTS) for a real world problem. It would be an interesting future work to further enhance the performance of molecular design by using more complex and improved models with parallel MCTS. Also, MP-MCTS could be applied to other MCTS applications, including retrosynthetic analysis to which an AlphaGo-like approach is applied (Segler et al., 2018b). Furthermore, although we analyzed the performance for molecular design, the parallelization technique is independent of the chemistry specific components and could be applied to other game and non-game applications. Our experiments strongly suggest that MCTS can be a better alternative for real-world optimization problems.

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# Author Information

**Xiufeng Yang**
yangxiufengsia@yahoo.com
yang.xiufeng38@chugai-pharm.co.jp

## Field

Computational chemistry, Bioinformatics

## Education Experiences

2007-2011 Qingdao university of science and technology. Bachelor
2011-2014 University of Chinese academy of sciences. Master
2015-2018 University of Tokyo. Ph.D.

## Work Experiences

2018-2019 Chief data scientist.MI-6, Ltd.
2019-2020 Postdoc.RIKEN-AIP.
2020- Researcher. Chugai Pharm.

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4. Xiufeng Yang; Tanuj Aasawat; kazuki yoshizoe ; Practical Massively Parallel Monte-Carlo T ree Search Applied to Molecular Design, International Conference on Learning Representations 202

# Session 2
# Research for translational breakthrough
13:30-16:00

# Self-scavenging and micro-nano drug delivery system for improved tumor targeting and safety

Wenli Zhang *, Jianping Liu

Keywords: Size/ligand-adapting, micro size effect, biosafe distribution

Despite the tremendous theranostics potentials, the safety and tumor-targeting efficiency of nano-scale drug delivery systems (NDDS) are compromised by their poor tumor tissue penetration and undesirable accumulation in normal tissues with widespread vascular endothelial gaps[1]. In this report, two drug delivery systems using self-scavenging and micro-nano strategies were introduced.

Firstly, a stimuli responsive size-adaptable and ligand (biotin)-sheddable drug delivery system (DDS) combined with two-step strategy of biotin-avidin system was designed to seek a balance between tumor targeting and penetration as well as to self-scavenge the nonresponsive nanocarriers in normal tissues[2] (Fig 1). This DDS was composed of 'multi-seed' polymeric liposomes (ASL-BIO-MPL) with asulacrine-loaded micelles as seeds in their aqueous cavities. The shell of such liposomes was modified with MMP-9 cleavable polymer-polypeptide functionalized with the tumor targeting ligand biotin. ASL-BIO-MPL could disintegrate into mixture of irregularly-shaped liposomes (~200 nm) and scattered tiny micelles (~40 nm) after incubation with MMP-9. The fluorescence-labeled BIO-MPL could travel to the center of the 4T1 breast tumor spheroids under the action of MMP-9, possibly benefited from the relay of released tiny micelles. Conversely, neither the biotin-modified micelles nor non-MMP-9-responsive multi-seed liposomes could penetrate into the spheroids possibly due to the potent binding-site barrier[3] of biotin and

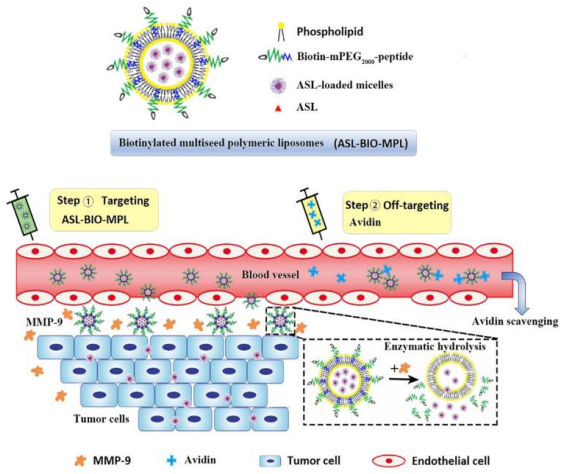


**Fig 1. Schematic design of Biotinylated multiseed polymeric liposomes (BIO-MPL) structure and principle of stimuli-responsive size/ligand adapting strategy with two-step method of biotin-avidin system.**

large size, respectively. In tumor-bearing mice, ASL-BIO-MPL exhibited the strongest drug penetrability and thus the optimal inhibition of tumor growth compared to other formulations. Following administration of avidin with a rational dosage regimen, the number of apoptotic cells in normal tissues induced by ASL-BIO-MPL reduced without affecting their targeting effect, suggesting the followed administration of adivin could scavenge the DDS in non-target site. Overall, the size/ligand adapting MPL system combined with two-step strategy of biotin-avidin may provide potential avenues for nanocarriers to enhance deep tumor tissue targeting and protect normal tissues.

Department of Pharmacy, China Pharmaceutical University

✉ Wenli Zhang, zwllz@163.com

Although self-scavenging strategy could remove the nanocarriers in non-target site. Most of the NDDS were wasted and accumulation in normal tissue still occurred. Therefore, we explored a micro-nano biomimetic cascade delivery system[4] to address the above drawbacks (Fig 2). By forming a hierarchical biosafe system, micro-sized platelet "ghost" (PGs, 1.32 μm) was employed as tumor-targeted delivery carrier to transport hollow gold nanoparticles (HGNs, 58.7 nm). It was demonstrated that this micro-size system could maintain platelet membrane structure thus prolong in vivo circulation, while avoiding extravasation into normal tissues. PG@HGNs could sensitively respond to the acidic microenvironment near tumor vessel via down-regulation of glycoprotein Ib and rapidly release "nano-bullets"-HGNs to further penetrate into the tumor tissues through EPR effect, thus enhancing photothermal efficacy generated by HGNs under NIR irradiation. Collectively, the micro-scaled PGs could be biosafe vehicles for improved tumor-targeted delivery.

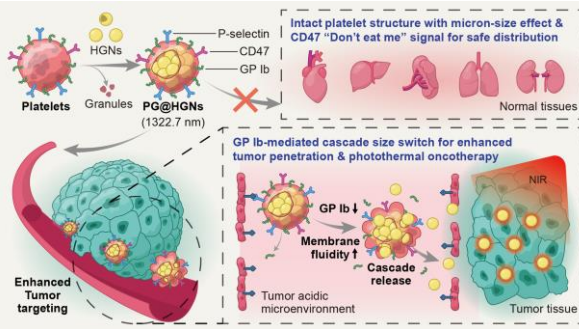


**Fig. 2 Schematic illustration of PG@HGNs mechanism for biosafe distribution and enhanced tumor targeting treatment.**

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# Author Information

Wenli Zhang
zwllz@163.com

## Field

Pharmaceutics, Cosmetics

## Education Experiences

2001-2005 Zhengzhou University, Bachelor
2005-2008 China Pharmaceutical University, Master
2008-2011 China Pharmaceutical University, Ph.D,

## Work Experiences

2011-2016 Lecturer, China Pharmaceutical University
2012-2014 Postdoc, The University of Auckland, Auckland
2016- Associate Prof. China Pharmaceutical University

## Major Publications

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# Development of genome analysis technology for elucidating the functions of the human genome

Yasuhiro Murakawa [1,*]

Keywords: human genome, RNA molecules transcription, new genome analysis technology

Although it has been almost 20 years since the first draft of the human genome was published, there are still large numbers of regions of the human genome with unknown function. Understanding the human genome has required the continuous development of new methodologies. To understand the function of the human genome, it is useful to analyze RNA molecules transcribed from the genome in a reticular manner. This presentation will introduce recent efforts to understand the structure of the human genome and its medical applications through the development of new genome analysis technologies.

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1 Kyoto University Institute for Advanced Study (KUIAS).

✉ Yasuhiro Murakawa, yasuhiro.murakawa@riken.jp.

# Author Information

Yasuhiro Murakawa
yasuhiro.murakawa@riken.jp

## Field

biochemistry, molecular biology, systems biology, informatics, primatology and medicine

## Education Experiences

2004-2008 Kyoto University School of Medicine, Bachelor
2010-2014 Max Delbrück Center for Molecular Medicine in Berlin, Germany, Kyoto University Hospital

## Work Experiences

2008-2010 Kyoto University Hospital
2016-2018 Unit Leader. RIKEN Innovation Center
2018- Team Leader. RIKEN Center for Integrative Medical Sciences since 2018, Group leader.
2020- Professor. Kyoto University Institute for Advanced Study (KUIAS)

## Major Publications

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# 疾病与遗传：个体化医疗时代的疾病基因研究

郭 龙[1,*]

关键词：遗传学，基因，个体化医疗

疾病的发生是遗传因素和环境因素单独或共同作用的结果。环境因素包括内环境和外环境两个方面。内环境因素包括年龄，性别，免疫力等；外环境因素包括生活习惯（吸烟，饮酒，饮食，运动等），微生物感染（新冠病毒，支原体，幽门螺杆菌，弓形虫等），药物使用，精神压力等。狭义的遗传因素指的是生殖细胞基因组层面的改变，能够遗传给后代，对疾病的发生发展产生促进或保护作用。广义的遗传因素还涉及体细胞突变以及表观遗传学层面的改变，可以在亲子代细胞之间进行传递，但不会遗传给后代。

由遗传因素引起的疾病统称为遗传性疾病，分为单基因遗传病和多因子遗传病（表1）。单基因遗传病，也就是狭义的遗传病，遵守已知的遗传学规律，由单个基因的改变引起。该基因称为致病基因。一般为罕见病。多因子遗传病，一般为常见病，由多个基因的改变引起，这些基因称为易感基因。每个易感基因的效应一般很小，多个易感基因的联合效应加之环境因素最终导致疾病。

遗传学研究的历史从孟德尔揭示遗传学基本规律开始，逐步进入了以表现型与基因型的关系为研究中心的实验研究阶段。进入新世纪的二十年间，高通量测序技术(Next Generation Sequencing, NGS)突飞猛进的发展极大推动了人类遗传学研究的进步。从人类基因组测序草图的完成（2001年）到1千美元基因组时代的来临（2014年）仅用了13年时间。测序通量的持续提高以及测序价格的持续降低使得以往需要庞大家系进行联锁分析才能定位致病基因的时代一去不复返。取而代之的是，父母和患者构成的小家系的外显子或基因组测序足以认定多数单基因遗传病的致病基因。多因子遗传病方面，单核苷酸多态性(single nucleotide polymorphism，SNP)的芯片检测技术的发展（同时检测超过500万个SNP），实现了全基因组范围的相关性解析（genome-wide association study，GWAS），认定了大量与疾病相关的易感位点，使得常见病遗传学病因的研究成为了可能。在患者个人基因组数据分析的基础上，结合临床表现和环境因素评估个体的风险并制定疾病的预防和管理策略，是当前个体化医疗的发展特征。

从遗传性疾病的研究来看，发现致病基因或易感位点只是第一步。后续需要通过构建疾病模型和功能学实验来研究发病机制和寻找治疗靶点。基因编辑技术和诱导性多能干细胞（induced pluripotent stem cell, iPSC）技术的发明和应用，成为遗传学研究向病理学和药理学研究过渡的催化剂。

笔者临床医生出身，2010年开始从事遗传性骨骼疾病的研究，见证并参与了本领域的飞速发展。在单基因遗传病研究方面，利用NGS发现了3个新的致病基因（*TMEM53, CSF1R, SLC4A2*），并通过基因编辑在小鼠和iPSC构建疾病模型；在多因子遗传病研究方面，通过GWAS发现2个疾病易感基因（*GPR126*和*LBX1*），并利用斑马鱼构建病态模型，阐明分子病理机制（图1）。笔者借本次ILS会议的机会，与来自生命科学不同专业的同道分享本专业的一些心得和体会，希望能够通过跨学科交流，碰撞出新的思想火花。

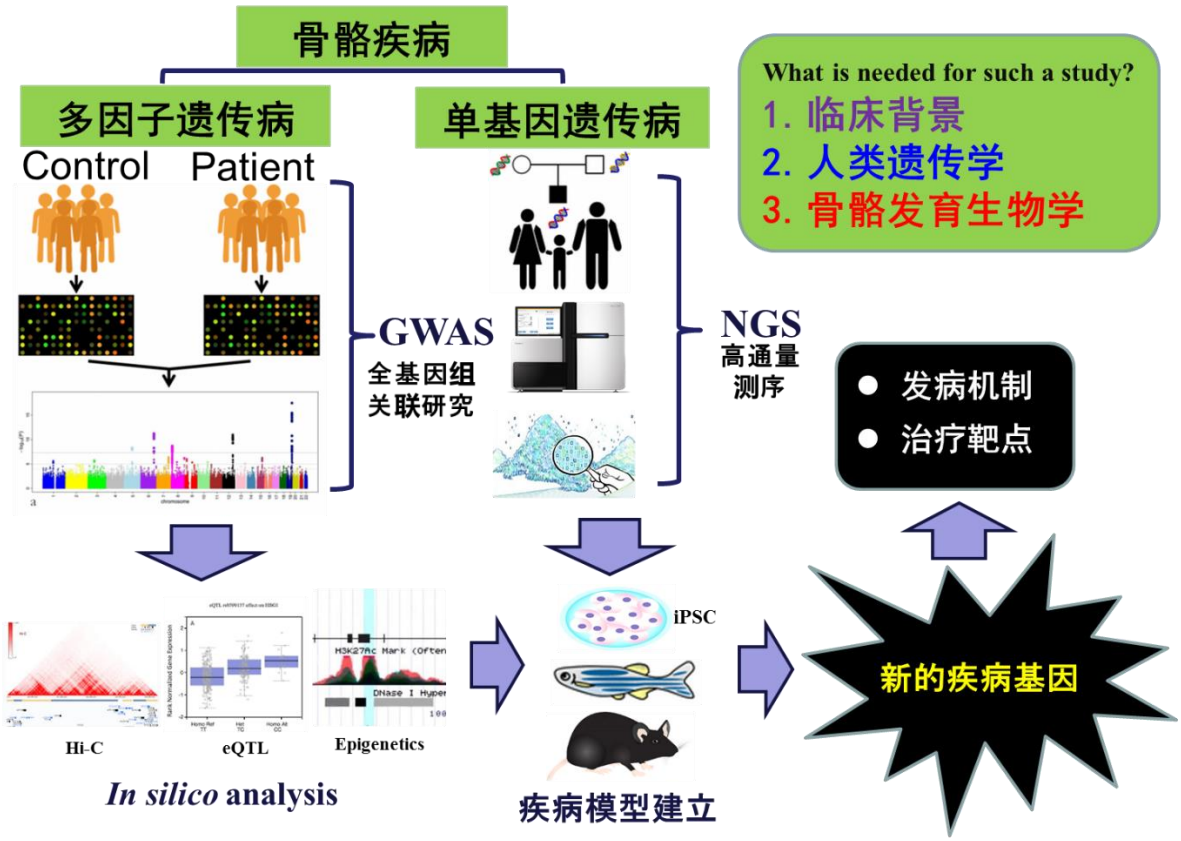
[1] 理化学研究所生命医科学研究中心

✉ longguo601@gmail.com.

表 1. 遗传性疾病的分类和特征

| | 单基因遗传病 | 多因子遗传病 |
|---|---|---|
| 疾病 | 狭义的“遗传病”<br>心脏离子通道病，成骨不全 | 常见病，生活习惯病<br>冠心病，骨质疏松 |
| 发病率 | 一般小于万分之一 | 百分之几到百分之几十 |
| 遗传形式 | 孟德尔式 | ? |
| 基因 | 致病基因 | 易感基因 |
| 基因的影响力 | 决定因子 | 危险因子 |
| 研究方法 | NGS（如外显子测序） | 相关性解析（如 GWAS） |

图1 遗传性骨骼疾病的研究策略



# Author Information

Long Guo
longguo601@gmail.com

## Field

Human genetics, Developmental biology, Clinical medicine

## Education Experiences

2002-2007 Xi'an Jiaotong Univ. Bachelor, Clinical medicine
2007-2009 Xi'an Jiaotong Univ. Master, Surgery
2010-2016 Kyoto Univ. Ph.D.

## Work Experiences

2016-2018 Post Doc., RIKEN.
2019-2021 Research Scientist, RIKEN.
2021-2021 Senior Scientist, RIKEN.
2021-present Deputy Team Leader, RIKEN.

## Major Publications

1. Xue JY, Grigelioniene G, Wang Z, Nishimura G, Iida A, Matsumoto N, Tham E, Miyake N, Ikegawa S, **Guo L**. SLC4A2 Deficiency Causes a New Type of Osteopetrosis. Journal of Bone and Mineral Research. 2022.
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# Novel Technologies Enable and Accelerate Research and Development of New Drug.

# 新技术赋能加速新药研发

**Dr. Chao Liu, CSU, WuXi AppTec.**

**About WuXi AppTec**

As a global company with operations across Asia, Europe, and North America, WuXi AppTec provides a broad portfolio of R&D and manufacturing services that enable the pharmaceutical and healthcare industry around the world to advance discoveries and deliver groundbreaking treatments to patients. Through its unique business models, WuXi AppTec's integrated, end-to-end services include chemistry drug CRDMO (Contract Research, Development and Manufacturing Organization), biology discovery, preclinical testing and clinical research services, and cell and gene therapies CTDMO (Contract Testing, Development and Manufacturing Organization), helping customers improve the productivity of advancing healthcare products through cost-effective and efficient solutions. WuXi AppTec received AA ESG rating from MSCI in 2022 and its open-access platform is enabling more than 5,900 customers from over 30 countries to improve the health of those in need – and to realize the vision that "every drug can be made and every disease can be treated."

**About WuXi AppTec Chemistry Service Unit**

Accelerating chemistry projects with efficient, flexible, and high-quality research and manufacturing services to enable our business partners globally.

# Author Information

Dr. Chao Liu
liu_chao0606@wuxiappte.com

## Field

Flow chemistry, photochemistry, electrochemistry, process chemistry, API synthesis

## Education Experiences

2003-2007 College of Chemistry and Chemical Engineering, Northwest University, China. Bachelor
2007-2012 Institute of Chemistry, Chinese Academy of Sciences, Beijing, China. Ph.D. course
2009-2012 College of Chemistry and Molecular Engineering, Peking University, China. Ph.D.

## Work Experiences

2012-2014 Postdoc, Department of Chemistry, The University of Tokyo, Japan
2014-2020 Scientist, Scientist, API Process Research Department, Towa Pharmaceutical, Japan
2020-2022 Senior Scientist, Tokyo Research Center, HighChem Co., Japan
2020-present Director, CSU, WuXi Apptec, China.

## Major Publications

1. Sekine R.; Ravat P.; Yanagisawa H.; Liu C.; Kikkawa M.; Harano K.; Nakamura E.* Nano- and Microspheres Containing Inorganic and Biological Nanoparticles: Self-Assembly and Electron Tomographic Analysis. *J. Am. Chem. Soc.* **2021**, *143*, 2822–2828
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# Endothelial cell mechanoresponse to haemodynamic forces during blood vessel lumenization

Li-Kun Phng[1,*]

Keywords: Endothelial cell, Mechanobiology, Blood vessel morphogenesis

Blood vessels carry pressurized and pulsatile blood from the heart to all tissues across the body. Consequently, endothelial cells, which form the inner lining of the vessels, are exposed to the mechanical forces of blood flow such as shear stress and blood pressure. During blood vessel development in the zebrafish, blood pressure deforms apical membranes of endothelial cells to form inverse blebs as vessels undergo transcellular lumenization. In turn, endothelial cells respond by generating an actomyosin-dependent repair mechanism to normalise membrane shape. More recently, we discovered that endothelial cells adapt to elevating haemodynamic forces by fortifying the cell cortex with increased assembly of actomyosin cytoskeleton and a balance network of linear and branched actin bundles. The failure of endothelial cells to resist the deforming forces of blood flow results in ectopic membrane blebbing, cell shape changes and vessel malformation (Fig.1) .

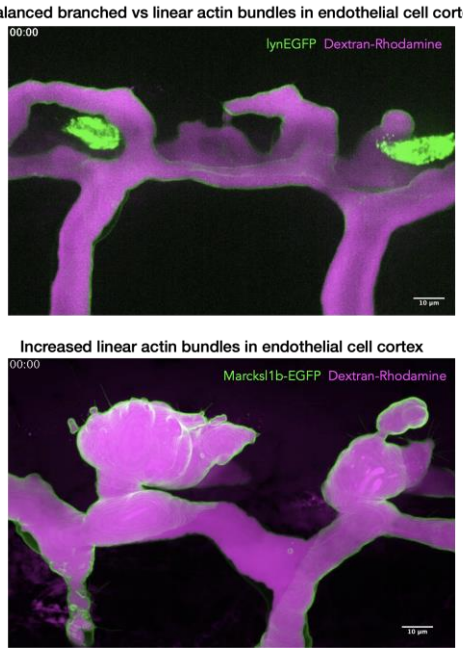


**Fig. 1 Actin organization in endothelial cell cortex plays a role in regulating blood vessel morphology and diameter.**

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1 Laboratory for Vascular Morphogenesis, RIKEN BDR, Kobe

✉ likun.phng@riken.jp

# Author Information

Li-Kun Phng
likun.phng@riken.jp

## Field

Vascular biology, Mechanobiology, Zebrafish

## Education Experiences

1998 – 2002 University of Bristol, UK. BSc
2003 – 2004 University of Edinburgh, UK. MSc
2004 – 2009 University College London, UK. PhD

## Work Experiences

2009 - 2011 Postdoctoral Research Fellow, EMBL, Heidelberg, Germany.
2011 - 2014 Postdoctoral Research Fellow, KU Leuven/VIB, Belgium.
2014 – 2016 Postdoctoral Research Fellow, NCVC, Japan.
2016 – present Team Leader, RIKEN CDB/BDR, Japan.
2020 – present Guest Associate Professor, Osaka University, Japan.

## Major Publications

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# Session 3
# Translational Medicine and Clinical Science
16:10-17:10

# Current Status of investigator initiated trials and future prospects in China

Peimin Yu[1,*],

Keywords: Investigator initiated research, Investigator-initiated trials, Keyword3

Investigator initiated research （IIR） is a form of research widely existing in the medical field worldwide. In China, IIR is now not for profit or drug registration, but to expand and optimize existing therapies, such as the discovery of new indications for marketed drugs or the comparison of the advantages and disadvantages of multiple clinical treatment methods, as well as the treatment of rare diseases, etc., which complement each other with the enterprises initiated clinical trials, and promote the depth and breadth of drug research, obtain more research data, and provide a basis for evidence-based medicine.

There are no specific IIR regulations in China, but the basic management model is similar to that in the United States. For new drug registration trials, studies of post-market expansion of indications and other studies that may increase the risk of participants, regardless of whether the initiator is a pharmaceutical company, a researcher or an academic institution, a new drug trial application should be submitted to the CFDA, and after approval, it will be implemented under the supervision of the CFDA and relevant research materials should be submitted regularly

In China, IIR that does not increase the risk of treatment of subjects, or of which medication risk has been clarified by literature or clinical practice, can be reviewed and approved by the academic professional committee and ethics committee of the investigator's institution, and under the supervision of the above institutions. The Institute is conducted under the supervision of the Center and does not require separate notice to the CFDA. Some institutes have detailed regulations on the IIR application process and regulation.

Registered studies initiated by investigators, which can also be called investigator-initiated trials, are almost not conducted in China. The purpose of basic medical research is to translate it into clinical applications, benefit patients, and ultimately solve clinical problems. Researchers find problems from clinical practice, and the needs are very clear. Encouraging investigator-initiated trials will encourage researchers to conduct various basic research in the early stage and carry out the research to the end. As the main implementer of clinical trials, the clinical trial protocol initiated and designed by the investigator will be more reasonable and operable. The role of doctors in clinical trials is not only passive participation, but the main force and active participation.

However, research funding, personnel matching, implementation, data acquisition, storage, analysis, output, etc. are all problems faced by researchers in

1 Department of Neurology, Huashan Hospital, Fudan University

✉tracypmyu@163.com.

initiating clinical trials. If these problems are solved, it will greatly promote the development of clinical trials initiated by researchers in China, so that valuable research results can be truly translated into clinical application in the hands of researchers throughout the whole process.

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# Author Information

Peimin Yu

tracypmyu@163.com

## Field (14.5pt, remove : mark)

Neurology, Epileptology, Sleep medicine, Clinical trials

## Education Experiences

1998-2003 Fudan University. Bachelor

2003-2005 Fudan University. Master

2009-2015 Fudan University. Ph.D.

## Work Experiences

2003-2008 Resident, Department of Neurology, Huashan Hospital, Fudan University,

2008-2017 Attending Doctor, Department of Neurology, Huashan Hospital, Fudan, University,

2017- Associate Professor, Department of Neurology, Huashan Hospital, Fudan, University,

## Training

Sep. 2012 – Mar. 2013: Fellow, Epilepsy Institute in the Netherlands Foundation, Heemstede, The Netherlands. Involved in clinical research and participation in the development of a method to assess cortical excitability using various stimulation, provocation and modulation techniques in combination with quantitative methods to measure the effects.

## Experience in Clinical Trials

Participate in several global trials with the indication of epilepsy, secondary stroke prevention, Alzheimer's disease, neurological pain and take the role of sub-investigator or study coordinator.

An open-label, multicenter, extension study to evaluate the long-term safety, tolerability, and efficacy of Padsevonil when used as adjunctive therapy for partial-onset seizures in adult subjects with highly drug-resistant focal epilepsy (Indication: Epilepsy; Role: Principle investigator)

- A multicenter, double-blind, randomized, placebo-controlled, parallel-group study to evaluate the efficacy and safety of lacosmide as adjunctive therapy in Japanese and Chinese adults with uncontrolled partial-onset seizures with or without secondary generalization. (Indication: Epilepsy; Role: sub-investigator and stud coordinator)
- A Double-Blind, Placebo-Controlled, Dose-Escalation, Parallel-Group Study to Evaluate the Efficacy and Safety of E2007 (perampanel) Given as Adjunctive Therapy in Subjects with Refractory Partial Seizures (Indication: Epilepsy; Role: sub-investigator and stud coordinator)
- A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Multicenter Study to Evaluate the Efficacy, Safety, and Tolerability of RWJ-333369 as Adjunctive Therapy in Subjects with Partial Onset Seizures Followed by an Open-Label Extension Study (Indication: Epilepsy, Role: sub-investigator and stud coordinator)
- PRoFESS - Prevention Regimen For Effectively Avoiding Second Strokes: A Double-blind, Active and Placebo Controlled Study of Aggrenox Versus (vs.) Clopidogrel, With and Without

Micardis (Indication: Ischemic Stroke, Role: sub-investigator and stud coordinator)

- A 13-week, randomized, multi-center, double-blind, placebo-controlled, parallel-group study to evaluate the efficacy, safety and tolerability of pregabalin (150-600 mg/d) using a flexible dosing schedule in the treatment of subjects with central post-stoke pain (Indication: Neurological Pain, Role: sub-investigator and stud coordinator)
- A 24-week, double-blind, double-dummy, randomized, parallel-group study to investigate the effects of rosiglitazone (extended release tablets), donepezil, and placebo as monotherapy on cognition and overall clinical response in APOE ε4-stratified subjects with mild to moderate Alzheimer's disease (Indication: Alzheimer's Disease, Role: sub-investigator and stud coordinator)

## Major Publications

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# Investigator-initiated clinical trials in Japan

Tsutomu Nishimura[1,]

Keywords: IIT, registration trial,

医師主導治験とは、2003年に薬事法が改正され、製薬企業等と同様に医師自ら治験を企画・立案し、治験計画届を提出して治験を実施できるようになりました。この治験の準備から管理を医師自ら行うことを医師主導治験といいます。医師主導治験では医師自らが、治験実施計画書等の作成から始まり、治験計画届の提出、治験の実施、モニタリングや監査の管理、試験結果を取りまとめた総括報告書の作成など、実施医療機関と協力しながら治験のすべての業務の実施並びに統括しなければなりません。

# Author Information

Tsutomu Nishimura
tnishimu@kuhp.kyoto-u.ac.jp

## Field

Clinical trial management, epidemiology

## Education Experiences

2002-2004 Kyoto univ. Associate degree
2004-2006 Kyoto univ. Master
2006-2010 Kyoto univ. Ph.D.

## Work Experiences

2011-2018 Translational Research Center for Medical Innovation
2018- Associate Prof. Kyoto Univ.

## Major Publications

1. Nishimura T, Tsai IJ, Yamauchi H, Nakatani E, Fukushima M, Hsu CY. Association of Geomagnetic Disturbances and Suicide Attempts in Taiwan, 1997-2013: A Cross-Sectional Study. Int J Environ Res Public Health. 2020 Feb 12;17(4):1154.
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6. Nishimura T, et al. Lizards Respond to an Extremely Low-Frequency Electromagnetic Field. Journal of Experimental Biology 2010; 213: 1985-1990.
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# Session 4
# Other Interdisciplinary Life Science Studies
17:20-18:20

# Direct effect of food-derived macromolecules on intestine --Apple-derived exosome-like nanoparticles mediate down-regulation of intestinal transporter expression by microRNA--

Qiunan Zhu[1,*], Shinya Usui[1], Hisakazu Komori[1], Yoshiyuki Shirasaka[1], Ikumi Tamai[1]

Keywords: Apple-derived nanoparticles, microRNA, Intestinal transporters

Food sometimes affects expression and activity of intestinal transporters and enzymes. Mechanisms of such effect have been considered due to small molecules in foods. However, since there are a number of macromolecules in foods, it is reported that exosome-like nanoparticles containing macromolecules may mediate inter-species communication. Thus, we hypothesized that exosome-like nanoparticles contribute to food effect on intestinal transporters *via* "cargo" inside of the particles.

In the present study, we chose apple as model food and examined effect of nanoparticles in apple on intestinal transporters OATP2B1/*SLCO2B1* and ASBT/*SLC10A2*, which typically transport exogenous drugs and endogenous bile acids, respectively, in Caco-2 cells. Freshly prepared apple juice decreased the mRNA expression of OATP2B1 and ASBT, and nanoparticles, which were prepared by ultracentrifugation of freshly prepared juice, caused reduction of their expressions more potently[8]. Size distribution and shape were then detected by qNano and electron microscopy respectively, indicating that it matches to "nanoparticles". Additionally, nanoparticles appeared to be internalized through clathrin-dependent endocytosis in Caco-2 cells[9]. Furthermore, apple micro RNAs, miR-160a-e, miR-7121a-c and miR-7121d-h, included in the nanoparticles as cargo, diminished OATP2B1 expression by interacting with 3'UTR of OATP2B1 gene, *SLCO2B1*[9]. In the case of ASBT, micro RNAs seem to downregulate RARα, a positive regulator of ASBT expression, through 5'UTR of ASBT gene, *SLC10A2*. In addition to mRNA expression level, OATP2B1 protein expression level and transport activity were reduced by nanoparticles significantly in Caco-2 cells.

These results demonstrated a novel mechanism of food effect on intestine that macromolecules in food directly affect intestinal functions through exosome-like nanoparticles. This also provides the possibility for oral administration of protein or nucleic-acid drugs instead of injection, which can improve QOL of patients significantly.

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1 Department of Pharmaceutical Science, Institute of Medical, Pharmaceutical and Health Sciences, Kanazawa University

✉ Qiunan Zhu, zhuqiunan@stu.kanazawa-u.ac.jp

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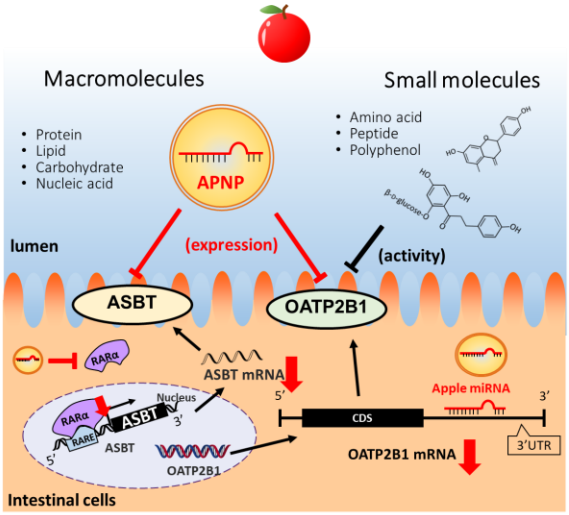


**Fig. 1 Mechanisms of food-derived macromolecules on intestinal functions.**

Food sometimes affects expression and activity of intestinal transporters and enzymes, although in ordinary it is considered as the effect of small molecules, such as polyphenols. Our study shows the other possibility: macromolecules (microRNA, for an example) could regulate the expression of intestinal transporters as a cargo in apple-derived exosome-like nanoparticles (APNPs). The regulation happens in multiple pathways. We have confirmed 2 pathways of them: binding to the 3'UTR to suppress its transcription directly or modifying the transcriptional factors to regulate the transcription indirectly.

# Author Information

Zhu Qiunan / 朱 秋楠
zhuqiunan@stu.kanazawa-u.ac.jp; zhu_qiunan@outlook.com

## Field

Biopharmaceutics, Membrane Transport

## Education Experiences

2013-2018 Shenyang Pharmaceutical Univ. Bachelor
2019-2021 Kanazawa Univ. Master
2021- Kanazawa Univ. Ph.D.

## Work Experiences

No work experiences

## Major Publications

1. Zhu, Q., Komori, H., Imamura, R., Tamai, I. A Novel Fluorescence-Based Method to Evaluate Ileal Apical Sodium-Dependent Bile Acid Transporter ASBT. Journal of pharmaceutical sciences, 110(3): 1392–1400, 2021.
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# Reactive Oxygen Species Cause Exercise-Induced Angina in a Myocardial Ischemia-Reperfusion Injury Model

Xiaohang Wang [1 2], Hirosato Kanda [2 3], Takeshi Tsujino [2], Yoko Kogure [2], Feng Zhu [2], Satoshi Yamamoto [2], Taichi Sakaguchi [1], Koichi Noguchi [3], Yi Dai [3 *]

Keywords: effort angina; p-ERK; hydrogen peroxide; TRPA1; myocardial I/R injury

Effort angina refers to the classic type of chest pain related to myocardial ischemia. A typical presentation of stable angina is that of chest discomfort and associated symptoms precipitated by some activity such as running, walking, etc. The mechanisms underlying effort angina and its revascularization therapy are still poorly understood; hence, the treatment or guideline for effort angina remains unclear. Thus, this study aimed to investigate the mechanisms underlying effort angina in animals following myocardial ischemia-reperfusion (I/R) injury. Phosphorylated extracellular signal-regulated kinase (p-ERK), a marker for painful stimulation-induced neuronal activation, was used for the investigation. After a forced treadmill exercise (FTE), the number of p-ERK-expressing neurons increased in the superficial dorsal horn of the I/R model animals. Moreover, FTE evoked hydrogen peroxide (H2O2) production in the I/R-injured heart, inducing angina through TRPA1 activation on cardiac sensory fibers. Notably, the treatment of a TEMPOL, a reactive oxygen species scavenger, or TRPA1$^{-/-}$ mice successfully alleviated the FTE-induced p-ERK expression in the dorsal horn. The production of $H_2O_2$, a reactive oxygen species, through physical exercise contributes to angina development following I/R. Hence, our findings may be useful for understanding and treating angina following revascularization therapy.

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1 Department of Cardiovascular Surgery, Hyogo Medical University, Nishinomiya 663-8501, Hyogo, Japan

2 Department of Pharmacy, School of Pharmacy, Hyogo College of Medicine, Kobe 650-8530, Hyogo, Japan

3 Department of Anatomy and Neuroscience, Hyogo College of Medicine, Nishinomiya 663-8501, Hyogo, Japan

✉ ydai@hyo-med.ac.jp

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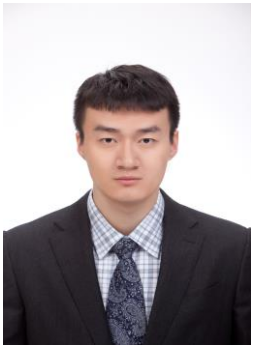

Xiaohang Wang
ds1913@hyo-med.ac.jp

## Field

The Department of Cardiovascular surgery, neuro-cardiology

## Education Experiences

2013-2018 Chongqing Medical University. Bachelor
2019-2023 Hyogo Medical University. Ph.D.

## Major Publications

1. Wang, X.; Kanda, H.; Tsujino, T.; Kogure, Y.; Zhu, F.; Yamamoto, S.; Sakaguchi, T.; Noguchi, K.; Dai, Y. Reactive Oxygen Species Cause Exercise-Induced Angina in a Myocardial Ischemia-Reperfusion Injury Model. Int. J. Mol. Sci., 2022, 23 (5), 10.3390/ijms23052820

# Structural studies on cyanobacterial trimeric Photosystem I-related protein complexes

Jiannan Li[1], Noriyuki Hamaoka[1], Fumiaki Makino[2], Akihiro Kawamoto[1], Yuxi Lin[3], Matthias Rögner[4], Marc M. Nowaczyk[4], Young-Ho Lee[3], Keiichi Namba[2], Christoph Gerle[5*] & Genji Kurisu[1*]

Keywords: Cryo-EM, Photosynthesis, Electron transfer

Oxygenic photosynthesis consists of light and dark reactions, the former of which starts from photon absorption and drives the photosynthetic electron transport chain originating from water up to the final electron carrier protein, ferredoxin[1] (Fd). Four large membrane protein complexes, Photosystem II[2], Cytochrome (Cyt) $b_6f$[3], Photosystem I[4] (PSI), and NADH-like complex I[5] (NDH-1) operate in the electron transport chain within the thylakoid membrane. Plastoquinone, plastocyanin (Pc), Cyt $c_6$, and ferredoxin act as mobile electron carriers to shuttle electrons between these membrane complexes. These electron carriers form transient complexes with their redox partners. The electron transfer events should be sequential, occur with a high degree of specificity and in a kinetically efficient manner. In short, the rate of electron transfer is key to maximum performance of the complete electrochemical reaction. Intermolecular interaction of lipophilic organic molecules, plastoquinone or quinone analogs, between Photosystem II and Cyt $b_6f$ have been well characterized by kinetics and X-ray crystallography[6]. However, the protein-protein interactions of water-soluble electron carriers Pc and Fd with Cyt $b_6f$, PSI, and NDH-1 are difficult to study due to the large molecular size of the redox-dependent structures.

PSI executes a light-driven fast charge separation for the transfer of electrons across the thylakoid membrane. With a quantum efficiency of close to 100%, PSI is the most efficient energy converter found in nature[7]. Using excitation energy funneled to it by the surrounding antenna pigments in the PSI reaction center, charge separation takes place at a pair of chlorophyll a/chlorophyll a′ molecules referred to as P700. The activated electron is then transferred through the electron transfer chain (ETC), and relayed via the [4Fe-4S] clusters $F_A$ and $F_B$ to the downstream water-soluble electron acceptor Fd at the stromal side. The strong reductant Fd provides electrons to a variety of downstream reactions such as production of NADPH, nitrogen and sulfur assimilation, or fatty acid desaturation. Oxidized P700 is subsequently reduced by

1 Institute for Protein Research, Osaka University, Japan

2 Graduate School of Frontier Biosciences, Osaka University, Japan

3 Research Center for Bioconvergence Analysis, Korea Basic Science Institute, South Korea

4 Faculty of Biology and Biotechnology, Ruhr University Bochum, Germany

5 RIKEN SPring-8 Center, Japan

✉ christoph.gerle@riken.jp

✉ gkurisu@protein.osaka-u.ac.jp

a luminal electron donor protein, Cyt $c_6$ or Pc, launching the next round of electron transfer. Cyanobacterial PSI is primarily a homotrimer, although monomeric or tetrameric forms are present. Each PSI protomer comprises up to 12 subunits that host more than 100 prosthetic groups, which make up a third of the total mass of the complex[8]. The X-ray structure of trimeric cyanobacterial PSI from *Thermosynechococcus elongatus* (formerly *Synechococcus elongatus*) was determined in 2001 at 2.5 Å resolution (PDB ID: 1JB0), and in 2018 that from *Synechocystis* sp. PCC 6803 also at 2.5 Å resolution (PDB ID: 5OY0). Later, several other PSI structures, including green plant-type PSI complexed with light-harvesting chlorophyll proteins I (LHCI), were revealed at a higher resolution by X-ray crystallography and also by cryogenic electron microscopy (cryo-EM); namely, PSI-LHCI from pea at 2.4 Å (PDB ID: 7DKZ), PSI-LHCI-LHCII (PDB ID: 7D0J) from green algae, and two PSI-LHCI complexes from a diatom at 2.38 and 2.4 Å resolution (PDB IDs: 6LY5, 6L4U). After the resolution revolution[9] in cryo-EM, two more cryo-EM structures of cyanobacterial PSI at slightly higher resolution were published; namely trimeric PSI from *Halomicronema hongdechloris* C2206 at 2.35 Å (PDB ID: 6KMW), and tetrameric PSI from a heterocyst-forming *Anabaena* sp. PCC7120 at 2.37 Å (PDB ID: 6K61).

To better understand the PSI-related transmembrane electron transfer mechanism, various methods such as co-crystallization or chemical cross-linking were applied to PSI with its electron transfer partner(s). Fd:PSI was crystallized in 2002, despite being a non-covalent electron transfer complex. In 2018 our group reported the first X-ray structure of an Fd:PSI complex at 4.2 Å resolution. The structure confirmed Fd-binding sites on the stromal side of PSI, which were previously suggested by site-directed mutagenesis and kinetic analysis. In this Fd:PSI X-ray structure, gallium-substituted ferredoxin (Ga-Fd), whose protein structure is identical to that of native Fd, was used to fix the redox state of bound Fd to the oxidized form even when illuminated by light. Recently, several non-covalent electron transfer complex structures of PSI determined by cryo-EM have been reported, such as PSI:Fd (PDB ID: 7S3D), PSI-IsiA complex with bound flavodoxin (PDB ID: 6KIF), and the triple complex of Pc:PSI-LHCI:Fd (PDB ID: 6YEZ). However, low local resolution of bound mobile carrier proteins prevented a detailed analysis at the residue level except for the Pc:PSI-LHCI supercomplex at 2.74 Å (PDB ID: 6ZOO) for the binding mode of the luminal electron donor Pc. Despite extensive efforts[10] to visualize the electron transfer complex of PSI: Cyt $c_6$, thus far neither X-ray nor cryo-EM structure of the PSI:Cyt $c_6$ complex has been reported.

Higher resolution structures of PSI together with its electron donors and acceptors under a controlled redox state are required to better understand the protein－protein interactions involved in the electron relay system. Here, together with thermodynamic measurements on Fd binding to PSI, we describe the structure of cyanobacterial PSI from *Thermosynechococcus elongatus* BP-1 bound with its electron transfer partners Fd and Cyt $c_6$ as analyzed by single-particle cryo-EM at overall resolution of 1.97 Å.

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# Author Information

Jiannan Li
jiannanli@protein.osaka-u.ac.jp

## Field

Structural biology, Microbiology

## Education Experiences

2010-2014 Shandong Normal Univ. School of Life Science. Bachelor
2014-2017 Shandong Univ. State Key Laboratory of Microbial Technology. Master
2017-2022 Osaka Univ. Institute for Protein Research. Ph.D.

## Work Experiences

2020-now Specially Appointed Researcher/Fellow. Osaka Univ.

## Major Publications

1. Li, J., Hamaoka, N., Makino, F. *et al.* Structure of cyanobacterial photosystem I complexed with ferredoxin at 1.97 Å resolution. *Commun Biol* 5, 951 (2022)

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**Business Contact:**

**North America:** Declan Ryan, declan.ryan@wuxiapptec.com

**Europe and Israel:** Dave Madge, dave_madge@wuxiapptec.com

**China:** Muhong Shang, shang_muhong@wuxiapptec.com

Marcher Xu, xu_longji@wuxiapptec.com

**Japan and Korea:** Suk Young Cho, sycho@wuxiapptec.com

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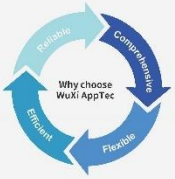


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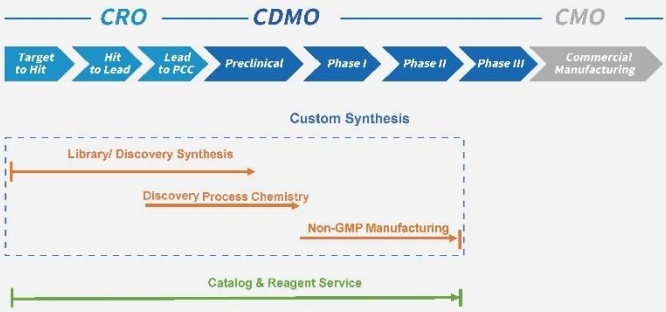


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# 湘栄ジャパンのミッション

1996年1月の設立以来、医療と研究分野においては常に最新かつ最高の技術とサービスを提供する事を使命とし、輸出と輸入メーカーとしてその技術サービスを提供して参りました。

2021年8月に世界最細でヨーロッパ販売量No.1を誇る、ディスポーザブル尿管腎盂鏡を日本に導入し、尿道狭窄のある患者さんに最も安全な選択肢を提供することができました。同時に、高速遠心瓶、抗原、抗体、IVD業界の磁気ビーズ、科学研究用超音波診断装置、分光光度計、振とう培養機などを再生医療や科学研究の分野に提供しております。


## 取扱商品

### 再生医療・科学研究分野

**分子生物学用機器及び消耗品**

- 抗原、抗体、磁気ビーズ
- 分光光度計、ルミノメーター、振とう培養機

**超音波画像診断装置**

- 超音波画像診断装置

### 医療分野

**泌尿器科機器**

- ディスポーザブルデジタル尿管腎盂鏡

**消化器科機材**

- 生検鉗子 Sシリーズ
- ポリープトラップ、マウスピース

# 深圳市駐日経済貿易代表事務所

Shenzhen Economic And Trade Representative Office In Japan

当代表事務所は、深圳市と日本との経済交流を促進するため、深圳市政府によって 2005 年 1 月 25 日に設立された。深圳市の窓口として、日本ー深圳間の投資、貿易に関わるあらゆるビジネスサポートを無償でご提供します。どうぞお気軽にご質問・ご相談をお寄せください。

## 主な業務内容

1. 日本における広報活動
   - 深圳市の社会制度、経済環境、金融事情、文化生活などの情報発信
   - セミナーの開催や各種展示会の出展によるプロモーション活動の展開

2. 経済交流の促進
   - 日本の政府機関・経済団体、企業との交流により、相互の連携の促進 、ネットワークの強化
   - 日本・深圳間の経済交流促進活動の展開
   - 深圳現地での視察訪問・ビジネス・マッチング・各種展示会出展へのサポート

3. 日本企業の深圳市への誘致促進
   - ビジネスに役立つ各種情報の提供
   - 個別企業へのアドバイスや各種相談、進出支援

4. 深圳市内企業への日本ビジネス展開の支援
   - 日本の経済産業、社会制度、マーケットなどの情報収集と提供
   - 関連団体・企業の紹介
   - 展示会・商談会への出展支援

〒105-0013 東京都港区浜松町 1-30-5
浜松町スクエアステューディオ 1908 号室
TEL: **03-5733-2244** FAX: **03-3432-5333**
E-mail: info@shenzhenoffice.jp
URL: www.shenzhenoffice.jp

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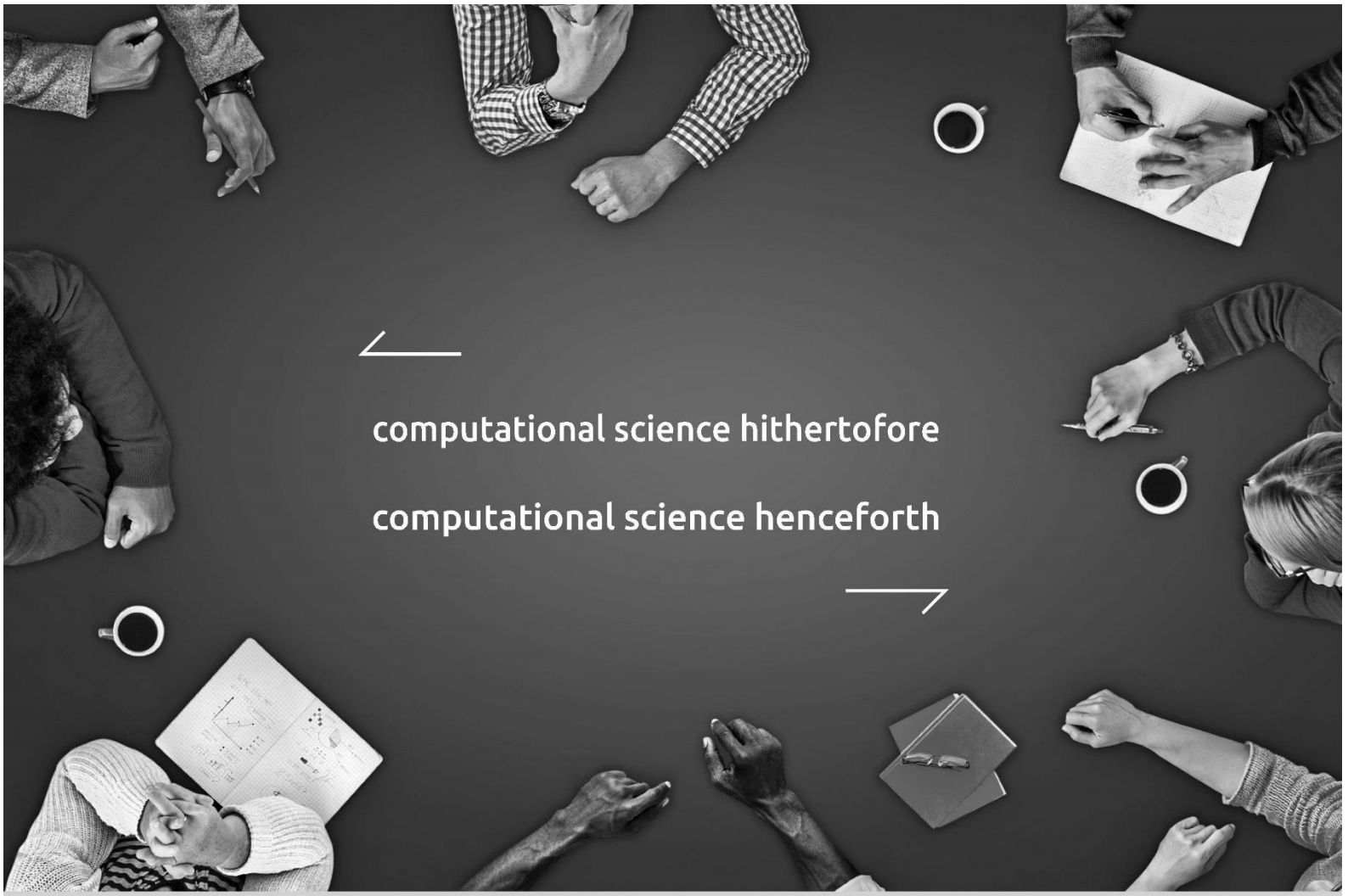


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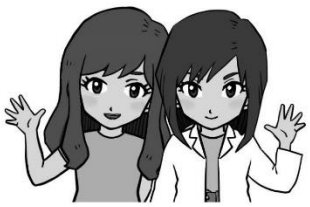

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**Affinity Science Corporation**
Aios Gotanda Ekimae, 1-11-1 Nishi-gotanda, Shinagawa-ku,
Tokyo 141-0031 JAPAN
Email. info@affinity-science.com

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