



Corporate HP
www.kotal-bio.com



KOTAI Bio Analytical Service
www.kotal-bio.com/service/

KOTAI supports R&D (drug/vaccine/diagnostic) by visualizing immune responses

KOTAIは免疫応答の可視化により、医薬品の研究開発をサポートします

KAZUO System

Immune repertoire analysis system, a combination of unique clustering technologies and machine learning

A powerful tool for observing patient's immune responses with small number of clinical samples

KAZUO System 2

Feature selection system using machine learning

A system that appropriately selects features without overfitting

KOTAI provides solutions at every stage

KOTAIはあらゆるステージでソリューションを提供します

Non-clinical

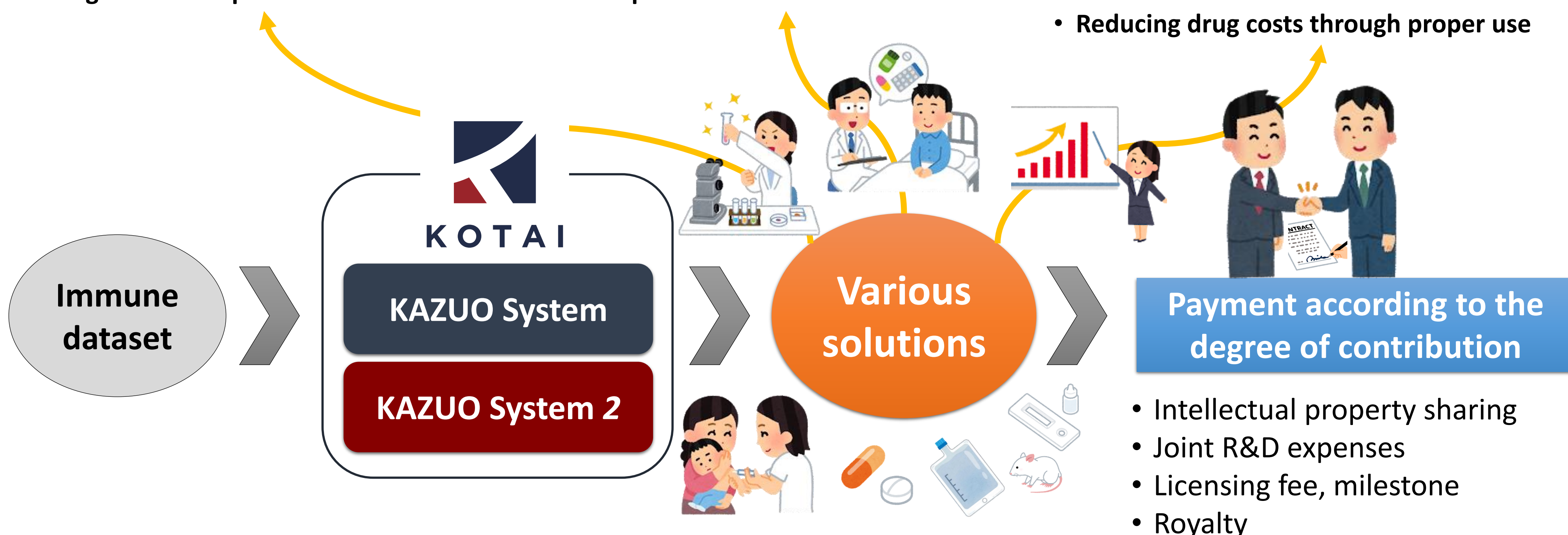
- Finding novel drug discovery targets
- Disease-specific biomarkers
- Design the more preventive vaccine

Clinical

- Successful clinical trials with low cost
- Clinical development for diseases with fewer patients

Sales · Post Marketing

- Expansion of market share by product differentiation
- Prediction of side effects
- Reducing drug costs through proper use



KAZUO System

1. Application in auto immune diseases (TCRβ repertoire analysis of peripheral lymphocytes)

Diagnostic usefulness of selected clusters

Disease (No. of samples)	AUC** of ROC curves
Behçet's disease (10)	0.922
Polymyositis (8)	0.994
Psoriasis (12)	0.948
Ulcerative colitis (10)	0.997

KAZUO System drastically reduces the number of patients required for prediction

>8~12 **VS** **>100**

KAZUO System **VS** **Conventional Approach**

Auto immune diseases: Total 50
Ankylosing spondylitis*, Behçet's disease, Crohn's disease, Polymyositis, Psoriasis*, Rheumatoid arthritis, Still's disease, Ulcerative colitis
*:One patient has psoriasis and spondylitis

Healthy: Total 493 from the public database

Flowchart: Patient lymphocyte → TCR Clusters (patients) / TCR Clusters (healthy) → Disease-related clusters selected by KAZUO System to diagnose → Selected Clusters

ROC Curve for Psoriasis: True Positive Rate vs False Positive Rate. ROC curve (area = 0.9479).

****AUC of ROC curves**

- Used to verify the cutoff value setting for diagnostic agents
- Usually takes a value between 0.5 and 1.0
- AUC = 1: 100% for both positive and negative predictive values (perfect test)
- AUC = 0.5: Random and invalid model (no value to perform)

2. Prediction of side effect of Immune check point inhibitor

❑ Nivolumab for NSCLC (2nd-line therapy)

Statistically significant specific clusters

Flowchart: Dosage of drugs → Blood sampling → Comparison of the clusters (TCR Ir AE* / TCR Healthy donors**) → TCR clusters

Statistical significance -log(P-val) vs TCR clusters

Collaboration with Osaka U Medical School (Unpublished)

Datasets: CD8+ T-cell β-chain from PBMC
*Ir AE: Immune-related Adverse Events
**Public database

KAZUO System 2

3. Application in immune check point inhibitors

❑ Efficacy/Safety prediction of nivolumab for NSCLC

Flowchart: Blood test before dosage of drugs (Total 763 features) → No feature selections → Responder*/non-responder (0.72) / Adverse event (0.63) → KAZUO System 2 Selection of features (to 5-12 features) → Responder*/non-responder (0.92) / Adverse event (0.97)

Feature Selection: Evaluated randomly generated 300 samples, (training : test) = 4:1.

AUC of ROC curves *

Responder*/non-responder	0.72
Adverse event	0.63
Responder*/non-responder	0.92
Adverse event	0.97

Flow Cytometry: Ratio of different cell types

Gene expression: 190 genes

HLA: Class I (A,B,C)

*** RECIST (1.1)** Responder(CR, PR, SD), Non-responder (PD)


**** AUC of ROC curves:** described above

Collaboration with Osaka U Medical School (Unpublished)

Highly accurate prediction of drug efficacy and safety!

◆ How KAZUO System works 4

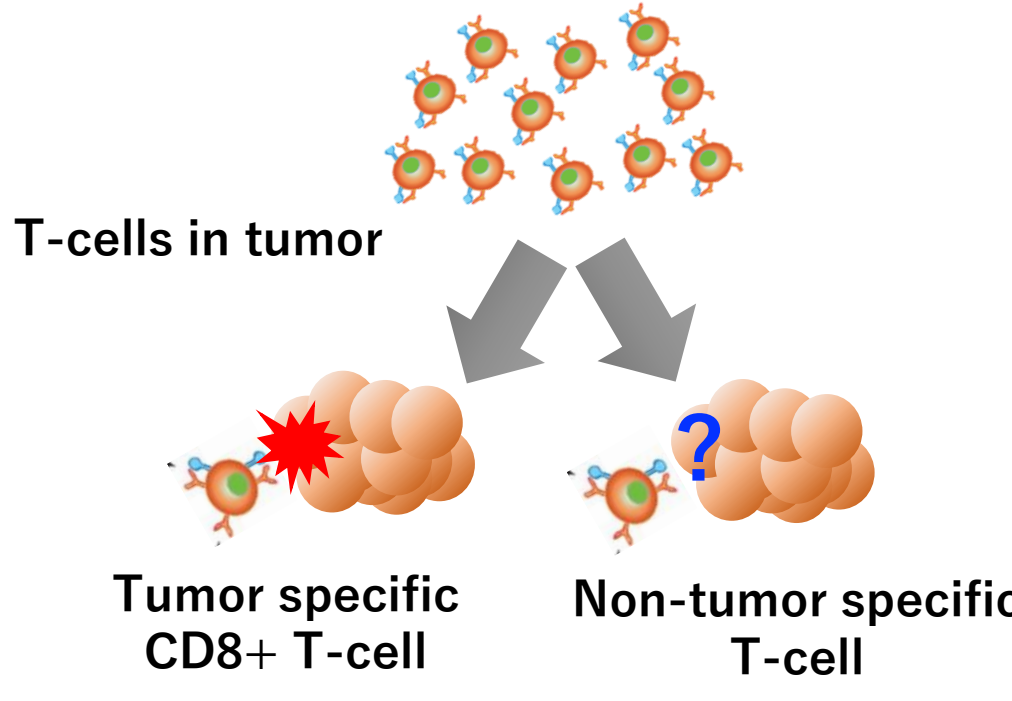
The results using KAZUO System has created the NEXT opportunity!



国立研究開発法人
国立がん研究センター
National Cancer Center Japan

Joint Research with NCC*

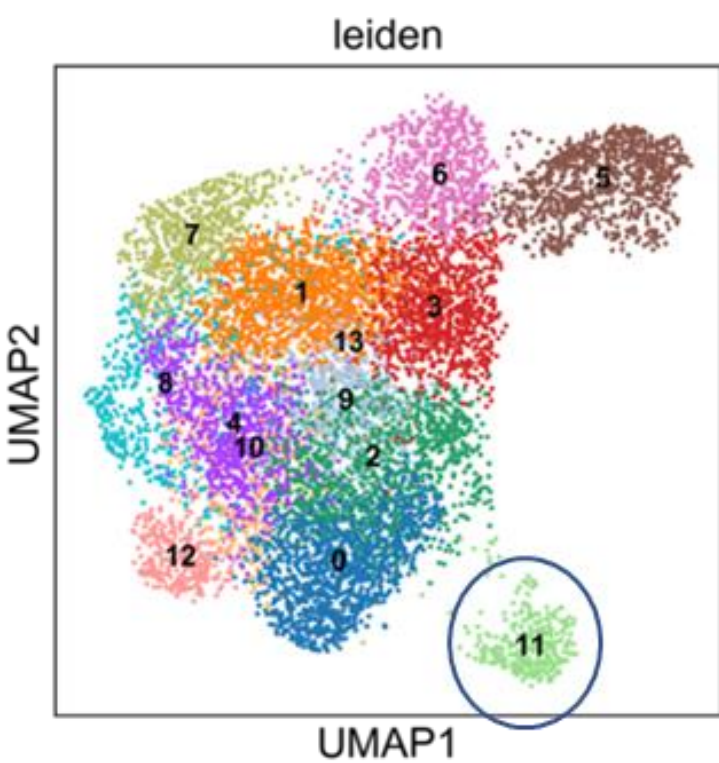
Single-cell Analysis of TIL[†]



T-cells in tumor

Tumor specific CD8+ T-cell

Non-tumor specific T-cell



leiden

UMAP2

UMAP1

➤ Confirmation of anti-cancer cytotoxic T cells by single-cell analysis of TIL from cancer tissue


➤ Discovery of surface antigens frequently expressed on the surface of anti-cancer cytotoxic T cells (patent granted)

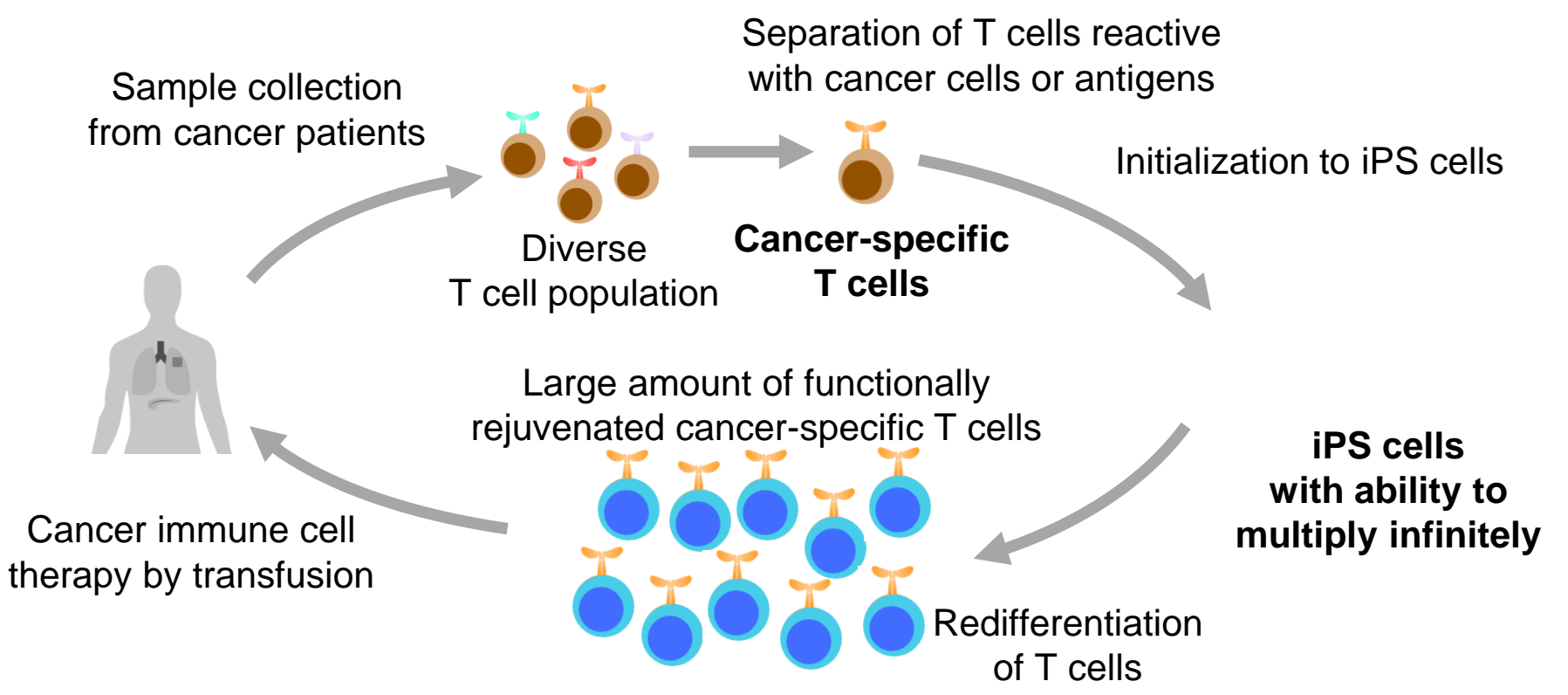
TIL[†] : Tumor Infiltrating Lymphocytes

KOTAI

Joint Research with CiRA**

Therapeutic regenerative T cells using iPS cells





Sample collection from cancer patients

Diverse T cell population

Cancer-specific T cells

Separation of T cells reactive with cancer cells or antigens

Initialization to iPS cells

iPS cells with ability to multiply infinitely

Redifferentiation of T cells

Large amount of functionally rejuvenated cancer-specific T cells

Cancer immune cell therapy by transfusion

➤ Isolates T cells from cancer tissue to conduct iPS cell induction followed by T cell redifferentiation.

➤ T cell isolation with the surface antigen discovered by the Joint Research with NCC described on the left

◆ KOTAIバイオ受託サービス

■10x Genomics社の日本における最初の認定サービスプロバイダー

10x認定アプリケーション

・3’シングルセルRNA seq解析

認定取得予定

・シングルセル免疫プロファイリング解析

・空間的遺伝子発現解析（Visium）

問合せ先: <https://www.kotai-bio.com/service/>




KOTAIバイオ受託サービス
by KOTAI Biotechnologies, Inc.

ホーム サービス サービスの流れ お問い合わせ

日本で初めての
10x Genomics認定プロバイダー

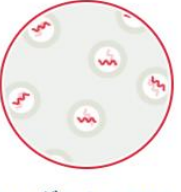
KOTAIバイオテクノロジーが日本で初めて
10x Genomics認定プロバイダーに認定されました！



Visium 空間的遺伝子
発現解析 NEW

1スポット当たり直径55 μmの
解像度で、細胞の位置情報を保
持したままmRNAの解析を行い
ます。


詳細はこちら



シングルセルRNA-
seq解析

細胞にそれぞれ異なるバーコー
ドを付与することで、細胞個々
のmRNA遺伝子発現を調べること
ができます。


詳細はこちら



シングルセルレパトア
解析

1細胞単位のTCR / BCR 発現を
調べることができ、TCR α鎖 / β
鎖あるいはBCR H鎖 / L鎖のベ
アを抽出することができます。

詳細はこちら



バイオインフォマティ
クス情報解析

情報科学や統計学等のアルゴリ
ズムを用いて、Fastqデータを
分析します。細胞集団ごと、対
象群vs比較群等で比較します。

詳細はこちら

◆ Recent News

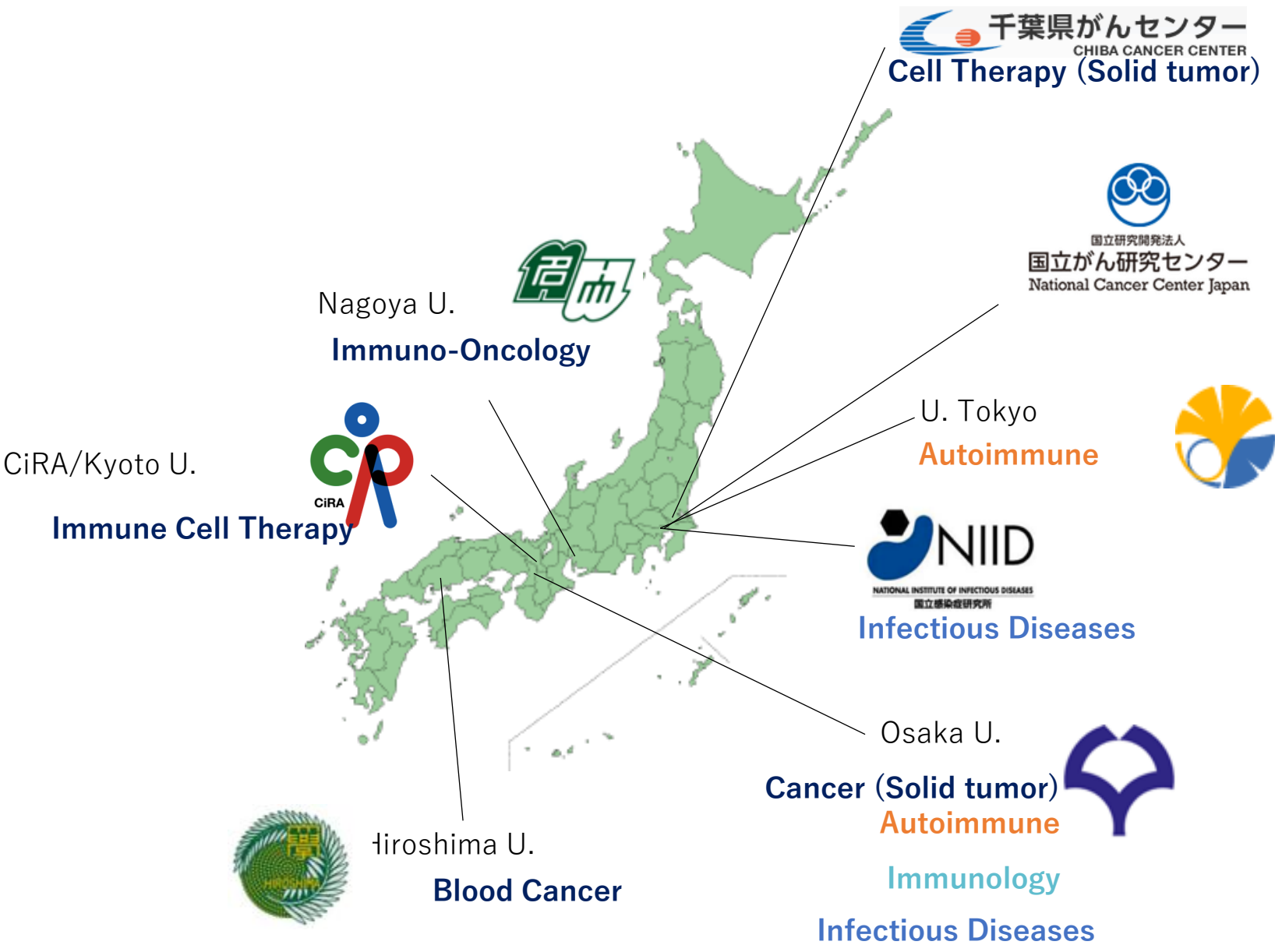
Date		Title	Partner(s)
2019	Jul 1	Utilization of “Rare Disease Research and Development Program based on patient-centered principle” and call for patient participation in “Study of Specific Immune Conditions of Autoimmune Diseases” https://www.kotai-bio.com/news/post-503/	3H Holdings
	Aug 20	Completion of the first study of the “Rare Disease Research and Development Program based on patient-centered principle” https://www.kotai-bio.com/news/post-500/	3H Holdings
2020	Jan 6	KOTAI Biotechnologies, Inc was granted as Japan’s first 10x Certified Service Provider. https://www.kotai-bio.com/news/post-1016/	10x Genomics
	Mar 24	Participation in the Clinical Research on the Coronavirus Disease (COVID-19) https://www.kotai-bio.com/news/post-1132/	NIID*
	Aug 5	Joint Research on the analysis of immune profile of COVID-19 patients https://www.kotai-bio.com/news/post-1150/	NIID, Shionogi, Osaka Univ
	Oct 1	Joint research on personalized cancer immunotherapy using regenerated T cells derived from iPS cells https://www.kotai-bio.com/news/post-1160/	CiRA**

*NIID: National Institute of Infectious Diseases

**CiRA: The Center for iPS Cell Research and Application, Kyoto University

◆ 会社概要

■ Academic collaborations
R&D network with top research institutions



■ Industry collaborations

Research: (Ongoing) two pharmaceutical companies.
Development: (under consideration) one pharmaceutical company.

◆ 科学アドバイザー

名前	役割
審良 静男 大阪大学免疫学フロンティア研究センター特任教授	免疫学の権威。研究者時代からの共同研究者。免疫学的な見地から研究結果、進め方、疾患選択についてのアドバイス、共同研究者の紹介。
坂口 志文 大阪大学免疫学フロンティア研究センター特任教授	制御性T細胞の発見者。研究者時代からの共同研究者。がん免疫学の研究にあたり、国立がん研究センターの共同研究者の紹介、シングルセル解析についてのアドバイスを提供。
黒崎 知博 大阪大学免疫学フロンティア研究センター特任教授 理化学研究所 グループリーダー	B細胞研究の第一人者。自己免疫疾患の共同研究、POCのためのデータの提供など。現在もCOVID-19の共同研究を行っている。
高木 淳一 大阪大学蛋白質研究所教授	構造生物学・生化学の専門家。研究者時代からの共同研究者。分子構造研究に対するアドバイスや、当社のがん免疫共同研究における実験手法選択についてのアドバイス等。
Mark Evans Associate Director, Exact Sciences	バイオインフォマティクスの専門家。米国のバイオベンチャーでの経歴が長く、米国市場や研究開発の状況情報提供、顧客候補等の紹介など。

◆ 連絡先



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Osaka, 565-0871, Japan

■ Company overview

Establishment : May 2016
CEO : Kazuo Yamashita (山下和男)
Capital : 100,000,000 JPY (Series A-C : 9/2016, 6/2017, 12/2018)
Employees : 13 (As of Oct. 2020. incl. 8 R&D staffs.)
Investors : Osaka University Venture Capital, Nissay Capital, Shinkin Capital, Minato Capital, Ikeda-Senshu Capital



CEO Biography :
Kazuo Yamashita, the representative director and CEO of KOTAI. Yamashita was an assistant professor and a Post Doc at Immunology Frontier Research Center (IFReC), Osaka University, in which he has published more than fifteen scientific papers in top journals. He got a Ph. D. degree in Physics from Osaka University in 2012.

■ Contract service in Japan

- Single-cell RNA sequence Analysis
- Single-cell Repertoire Analysis
- Bio-informatics Information Analysis
- Visium Spatial Gene Expression Analysis

