

Pharmacology

Comprehensive Solutions for All Your Drug Discovery Challenges!

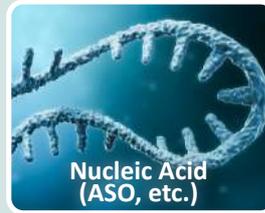
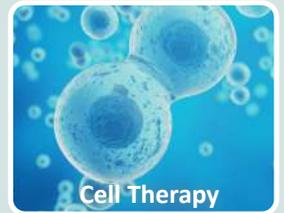
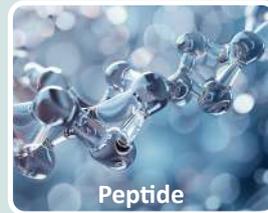
**POC Study
MOA Study**

In Vivo Assay

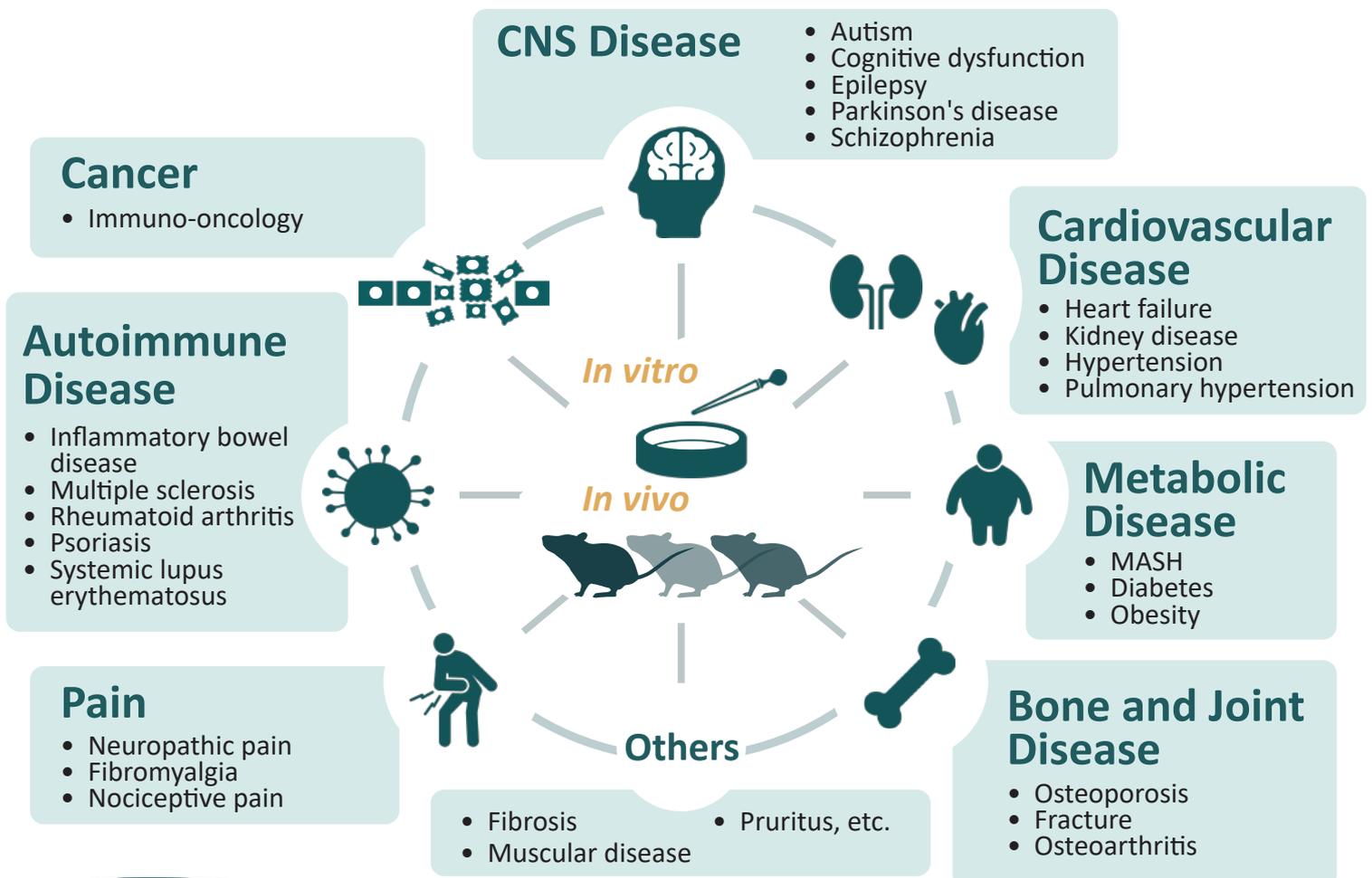
In Vitro Assay

**Translational
Research**

Supports various modalities!



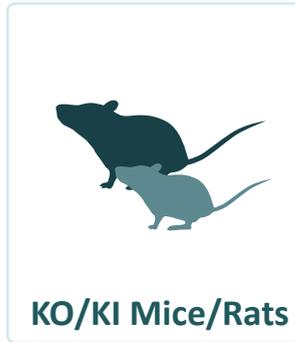
Various Disease Areas



Proof of Concept (POC) and Mechanism of Action (MOA) Study

Creation of Genetically Modified Mouse/Rat

- High-speed and high-efficiency KO mouse/rat creation
- Long chain (about 20kbp) KI mouse/rat creation
- CRISPR/Cas9 basic patent license



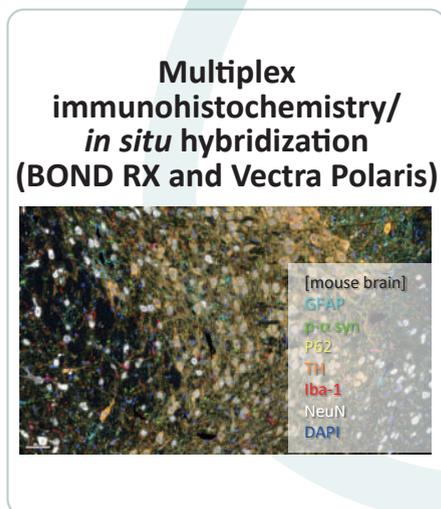
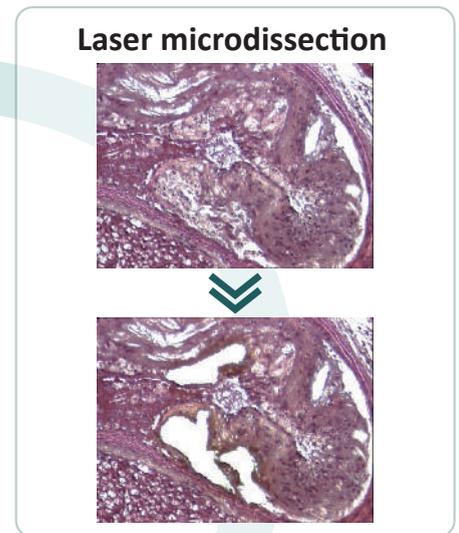
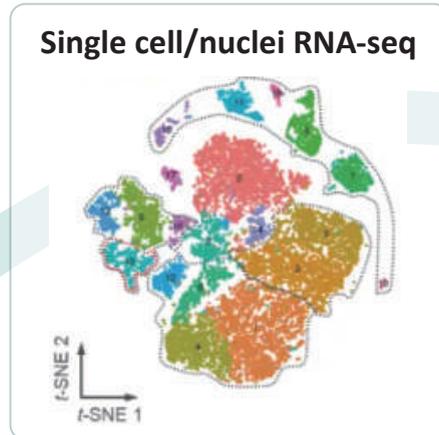
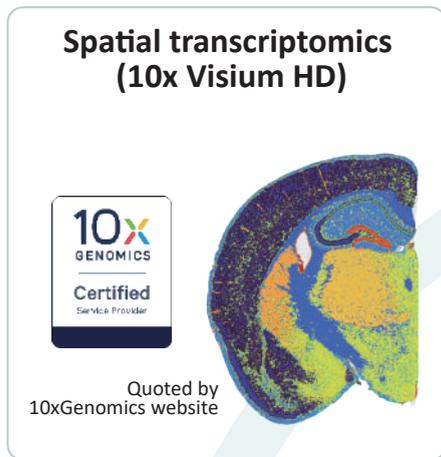
Fastest supply: dozens of F0 KO mice in 4 months

Track record of KI/KO animals (FY2017-2024)

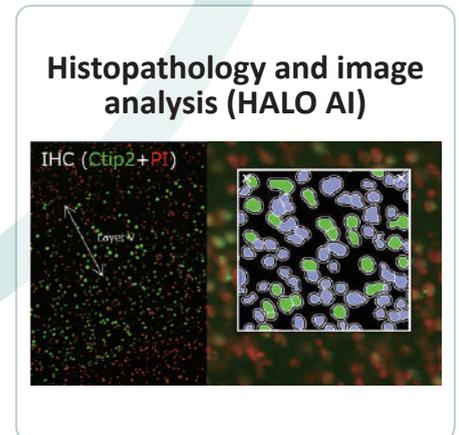
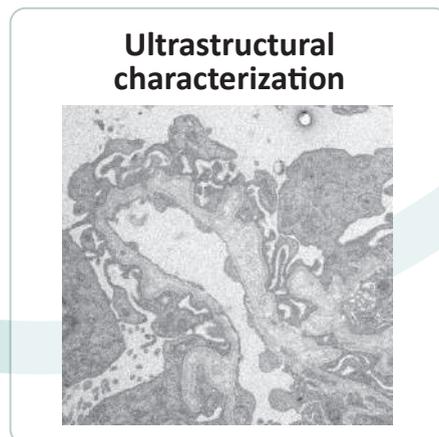
KI mice	KI rats	KO mice	KO rats
86	6	64	11

Visualization using Various Methods

Strong support for POC study, MOA analysis, Biomarker research, etc., using innovative methods integrally



Fresh frozen or FFPE tissue sample



In Vitro Assay

Cell-based Assay

Cells

- iPS-derived cells
- Human cell line
- Primary cells from mouse/rat
- Fresh human blood-derived cells
- Fresh human tissue-derived primary cells

Gene Editing

- KO/KI
 - CRISPR-Cas9
- KD/OE
 - siRNA/shRNA
 - Tet-on/off system
- TF methods
 - Electroporation
 - Transfection reagents
 - Virus (Retrovirus, Lentivirus)

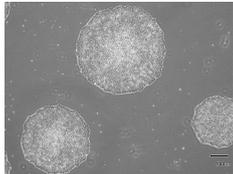
Functional Assay

- Cancer (ADCC/CDC assay, Killing assay, Combination assay, etc.)
- Immunology (Cytokine production, etc.)
- Metabolic (Glucose or lipid metabolism, Fibrosis, etc.)
- Cardiovascular (Hypertrophy, etc.)
- CNS (Phagocytosis, etc.)
- New assay setting

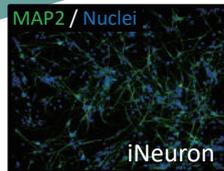
iPS Cell Platform

Gene Editing & Characterization

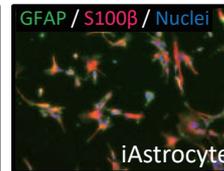
Undifferentiated iPSC



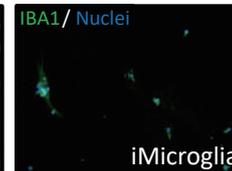
Differentiation



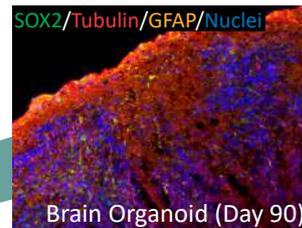
iNeuron



iAstrocyte



iMicroglia



Brain Organoid (Day 90)

Assay

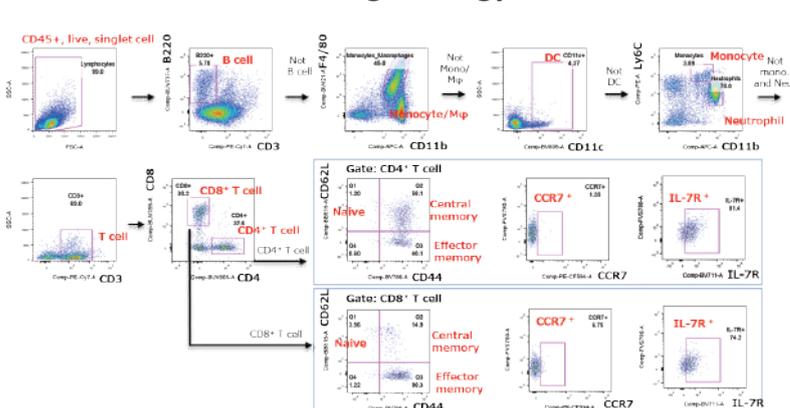
- Target validation
- Drug efficacy assay
- MOA analysis, etc.

Human iPS cell line (201B-Ff (HPS4290)) was provided by the RIKEN BRC through the National BioResource Project of the MEXT, Japan.

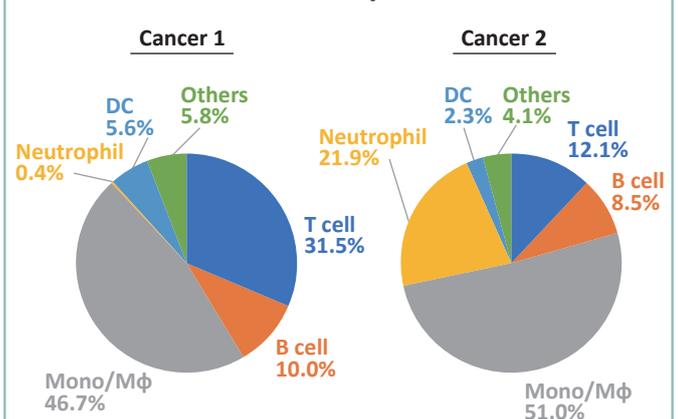
Immunophenotyping

- High-end flow apparatuses for cell analyzing and sorting
- A wide-range of immune cells from various species and clinical samples

Gating Strategy



Differential Cell Population of TIL



In Vivo Assay



- Fully certified animal facility by AAALAC International
- A wide variety of disease models and evaluation systems
- Establishment of assay platform to meet the customer's needs

Metabolic Disease

MASH

- MC4R KO mouse fed western diet model
- Choline-deficient high fat diet fed mouse/rat model
- CCl4-induced fibrosis mouse/rat model

Alcoholic hepatitis

- Chronic-plus-binge ethanol feeding mouse model

Acute liver injury

- CCl4-induced acute liver injury model

Type 1 diabetes

- STZ induced diabetes mouse/rat/pig model
- db/db mouse

Type 2 diabetes

- Zucker fatty rat
- KKAY mouse
- ob/ob mouse

Obesity

- Diet-induced obesity mouse/rat model
- MC4R KO mouse

Cardiovascular Disease

Chronic kidney disease (CKD)

- Axcelead DDP-generated Col4a5 R471X-Chronic kidney disease model mouse
- Spontaneously hypercholesterolaemic (SHC) rat (Imai rat)
- 5/6 nephrectomized (NX) rat model
- Glomerulonephritis rat model
- Unilateral ureteral obstruction (UUO) mouse model

Diabetic kidney disease (DKD)

- Unilateral nephrectomized db/db mouse

Acute kidney injury (AKI)

- Ischemia-reperfusion injury mouse model
- Cisplatin-induced mouse model

Heart failure with reduced ejection fraction : HFReF

- Myocardial infarction (MI) mouse/rat/pig model
- Ischemia/Reperfusion (I/R) rat/monkey model

Heart failure with preserved ejection fraction : HFpEF

- L-NAME/high fat diet mouse model

Hypertrophy

- Transaortic constriction (TAC) mouse model

Hypertension

- Spontaneously hypertensive rat

Pulmonary hypertension

- Monocrotaline-induced pulmonary hypertension rat model

Cancer

Xenograft/Syngeneic/PDX mouse model

(Subcutaneous or Orthotopic transplantation)

Bone and Joint Disease

Osteoporosis

- Ovariectomized (OVX) mouse/rat model
- orchidectomy (ORX) mouse/rat model
- Vertebral defect rat model

Fracture

- Closed femur fracture rat

CNS Disease

Schizophrenia

- MK-801-induced hyperlocomotion model
- Methamphetamine-induced hyperlocomotion model
- Poly (I:C) model (Sociability deficit)
- Sub-chronic phencyclidine model (cognition)

Cognitive dysfunction

- Scopolamine-induced cognitive deficit model

Autism

- Valproic acid-induced autism spectrum disorder model (Sociability deficit)

Parkinson's disease

- 6-hydroxydopamine (OHDA) -induced Parkinson model

Epilepsy

- 6Hz psychomotor seizure
- Kainic acid induced seizure
- Maximum electroshock seizure
- PTZ induced seizure

Autoimmune Disease

Inflammatory bowel disease

- Naive T cell-transferred mouse colitis model
- Activated T cell-transferred mouse colitis model
- DSS-induced mouse colitis model

Multiple sclerosis

- Mouse experimental autoimmune encephalomyelitis (EAE) model

Rheumatoid arthritis

- Mouse/rat CIA (collagen induced arthritis) model
- Mouse CAIA (collagen antibody induced arthritis) model

Psoriasis

- Mouse/rat IL-23-induced psoriasis-like skin disease model
- Mouse Imiquimod (IMQ)-induced psoriasis-like skin disease model

Systemic lupus erythematosus

- MRL/lpr mouse model

Sjögren's syndrome

- NOD/Shi Ltj mouse model

Graft-Versus-Host Disease (GVHD)

- Mouse allo-GVHD model
- Mouse xeno-GVHD model

Pain

Neuropathic pain

- Partial sciatic nerve ligation mouse model
- STZ-induced peripheral neuropathy rat model
- Paclitaxel-induced peripheral neuropathy mouse model

Fibromyalgia

- Repeated cold stress rat model

Nociceptive pain

- MIA induced knee osteoarthritis rat model

Others

Fibrosis

- Bleomycin-induced lung fibrosis mouse model
- Crystalline silica-induced lung fibrosis mouse model
- Bleomycin-induced systemic sclerosis (SSc) mouse model

Muscular disease

- B10-mdx mouse
- Tail suspension mouse/rat model

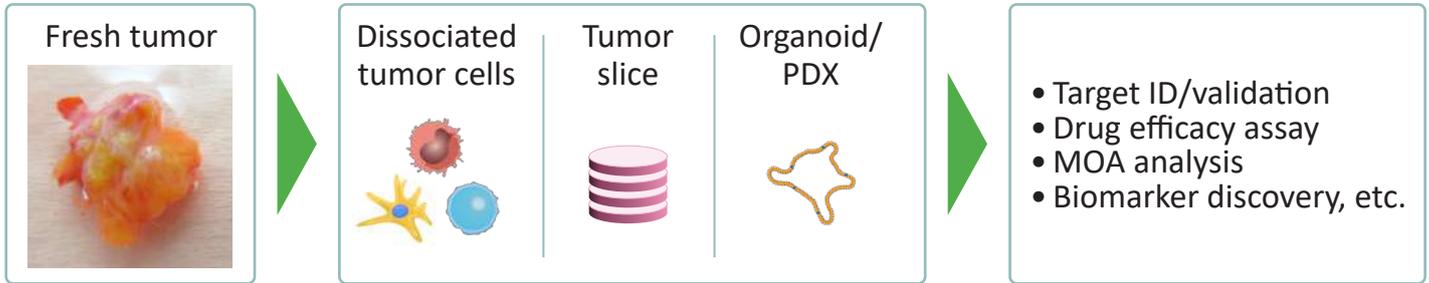
Lymphedema

- Tail Lymphedema mouse model

Translational Research

Fresh Human Samples

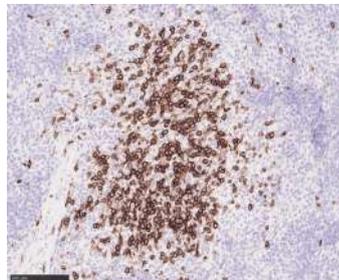
Tailored *in vitro* and *ex vivo* models from fresh human samples (blood, urine, tissue, tumor) with patient information and genetic mutation



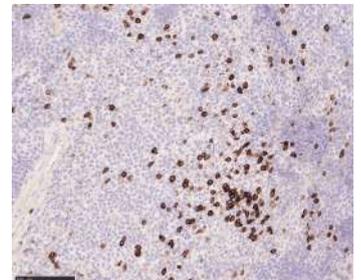
Humanized Mouse

Translational evaluation of diverse human immune cells using various NOG mouse models and Axcelead's original mouse model with co-existing T and NK cell

Localization of immune cells



T cells

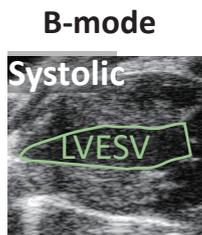


NK cells

Same Evaluation as Clinical Settings

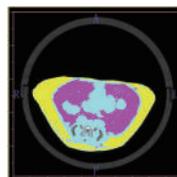
Ultrasound device (Echo)

- Cardiac function
- Tumor size
- Respiratory function
- Fibrosis of the liver

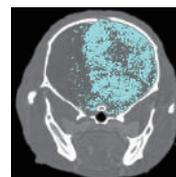


X-ray CT

Fat mass

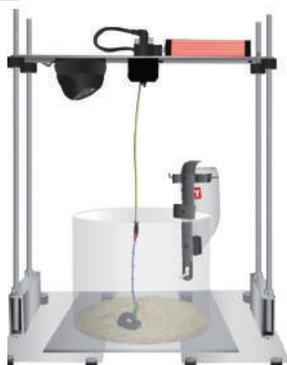


Tumor size



Electroencephalogram (EEG)

- Sleep EEG
- Epileptiform activity



Clinical blood/urine test

- Hematology
- Coagulation tests
- Blood chemistry
- Isozyme tests
- Platelet aggregation
- Complement tests



Integrated Drug Discovery Solution

Axcelead also offers fully integrated drug discovery services, from target discovery to IND-enabling translational research. Our experience and collaborative team facilitate each stage of your drug discovery project.



Axcelead Booster

What is it?

- Axcelead can leverage data of approximately 1,000 projects from Takeda/Teijin across multiple therapeutic areas.
- These exciting projects are available for co-creation of drug candidates with our customers.
- The newly generated Intellectual property in the co-creation projects is owned by our customers.



Save Time & Resources

- ◆ Ready-to-use hit/lead compounds and assay systems
- ◆ Skip the initial phases of drug discovery



Expand Your Pipeline

- ◆ Explore opportunities from our curated portfolio of 1,000 projects
- ◆ Tailor projects to meet your specific needs



Go Beyond Provision via Partnership

- ◆ Benefit from pharma-grade drug discovery services, including proprietary AI tools
- ◆ All co-created intellectual property is fully owned by the client

