In-Vivo Science Symposium

Strategic Drug Discovery Support through Integrated Utilization of Preclinical Models to Enhance Human Clinical Translatability

ヒト臨床外挿性を高める前臨床モデルの統合活用による創薬支援戦略

2025/09/24

Axcelead Drug Discovery Partners, Inc.

Pharmacology Business Unit

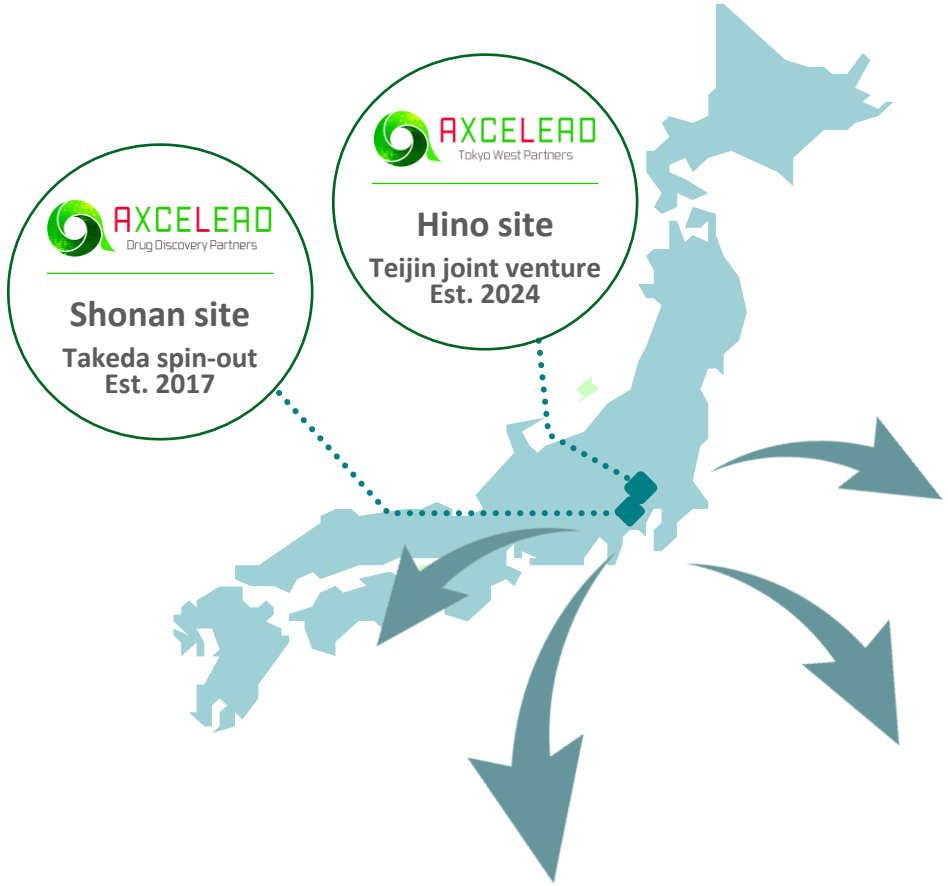
Hiroshi Tanaka

Presentation Agenda

- **Company Introduction**
- **Capabilities Aligned with Clinical Application**
  - Current Issues in Oncology Drug Discovery
  - Axcelead's Approaches

Company overview
Axcelead delivers pharma-standard drug discovery platform

Axcelead is a Japanese integrated drug discovery solution provider, founded as a spin-off from Takeda pharma and Teijin pharma



Inherited assets from pharmaceutical companies makes us unique as a drug discovery CRO

>300	>1.2 M	>1000 projects
Pharma-experienced scientist	Available compound library	Drug discovery data access

Recent business track records

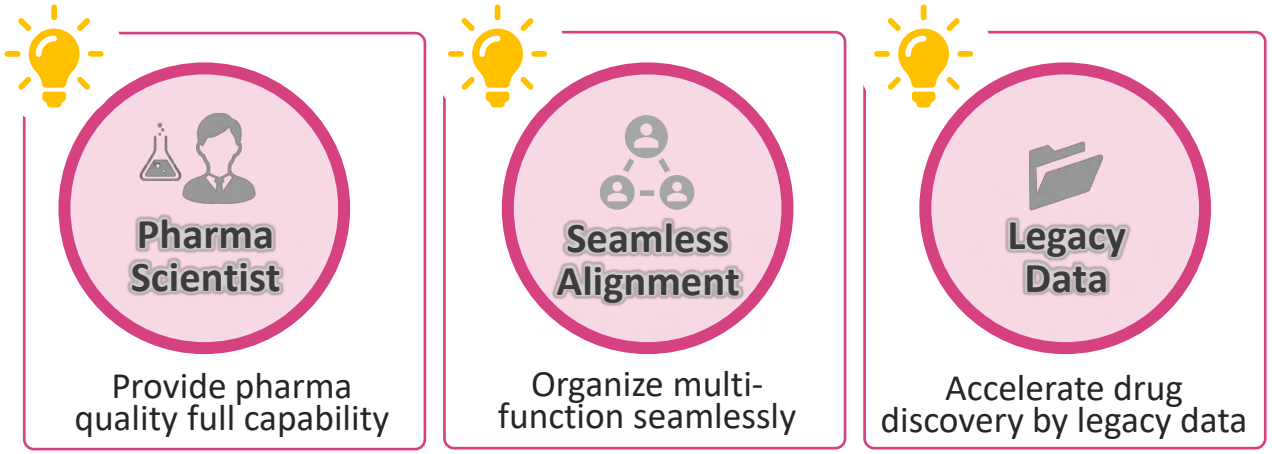
- >290 clients with approx. 90% of repeat rate
- Research collaboration with Lilly and Acadia
- 84% success rate for Lead Generation, Optimization project

Contributing to Clients' Drug Discovery Challenges Through Axcelead's Pharma-Grade Drug Discovery Platform

Axcelead meets clients' outsourcing needs while continuously enhancing its drug discovery platform with talent, technology, data, and partnerships

Comprehensive Integrated Drug Discovery

All inclusive drug discovery capability



Enables Axcelead to create new IP

Boost the Innovation

Legacy Data x AI

Increase success rate of drug discovery with proprietary generative AI

Modality Expansion

From next-generation small molecule to antibody, peptide, and oligonucleotide

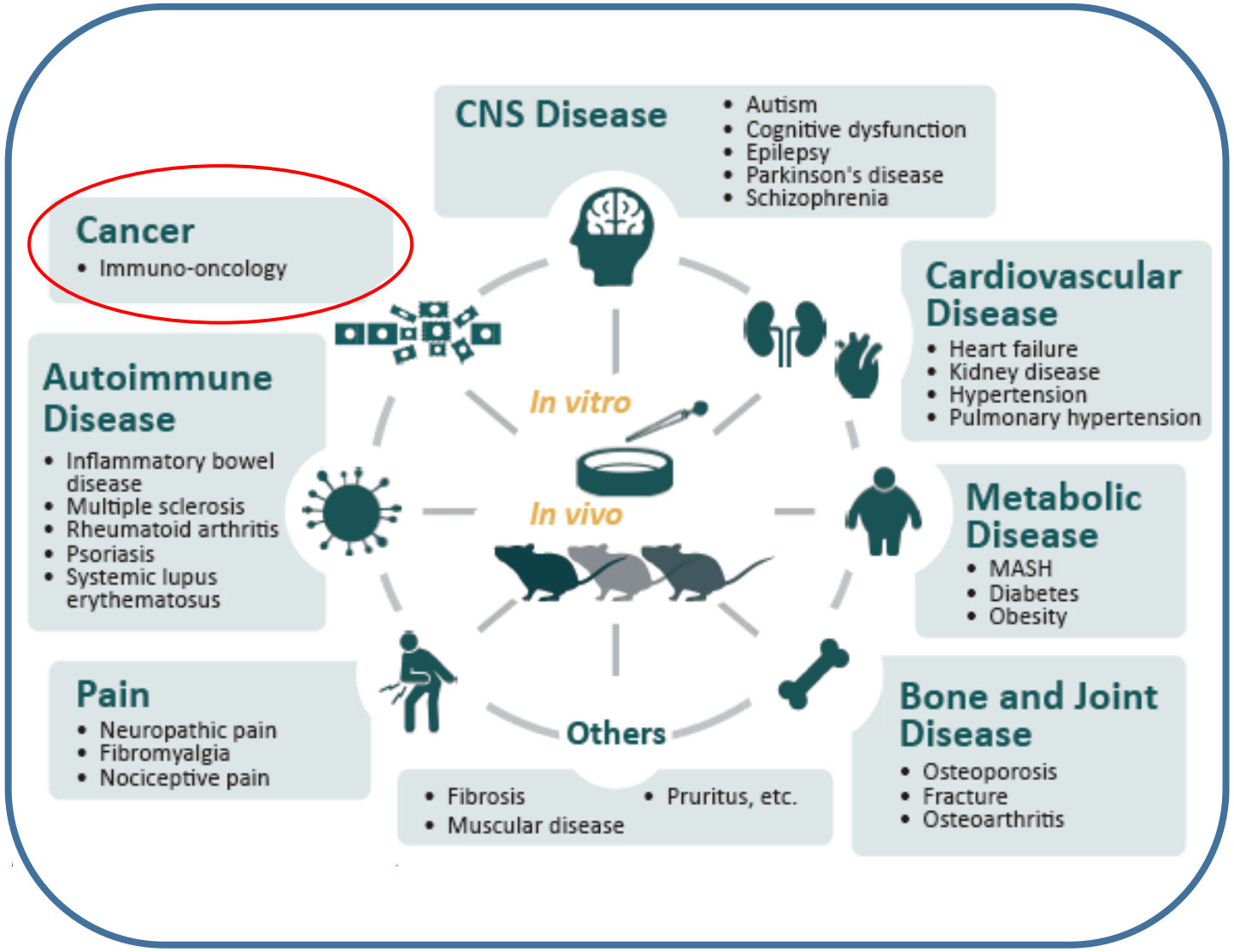
Network Capability Enhancement

Strengthen network capability through strategic partnerships

Offer high value for client's drug discovery

Characteristics of Pharmacological Capability

- 7+α disease areas
- Various modality evaluation
- Available to obtain and handle human samples
- Fully certified animal facility by AAALAC International
- A wide variety of disease models and evaluation systems
- Development of novel disease models and evaluation systems



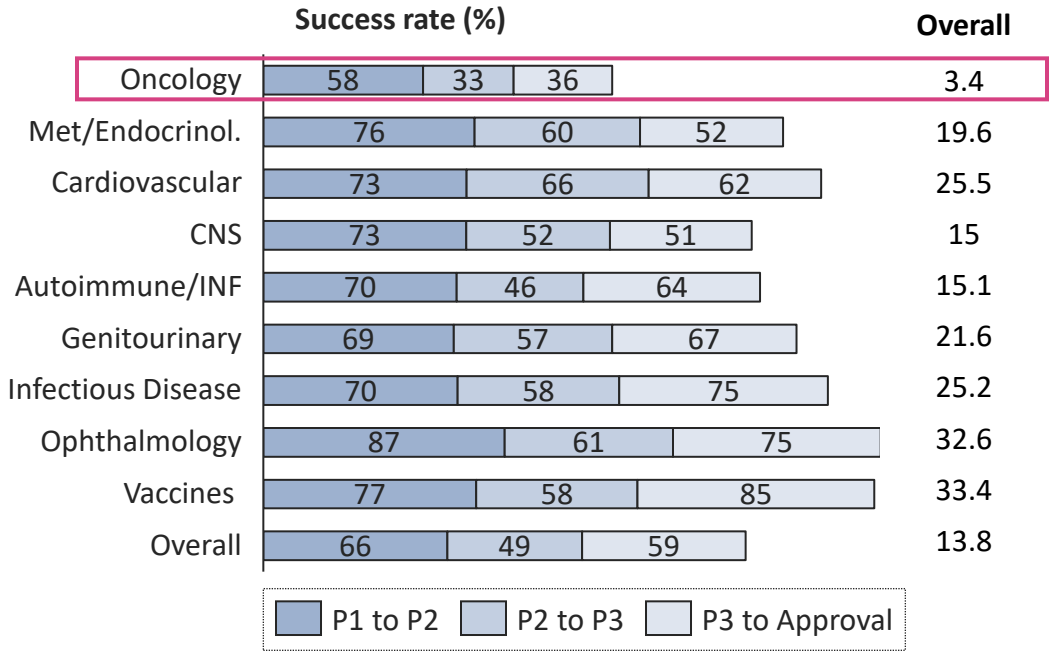
Presentation Agenda

- Company Introduction

- **Capabilities Aligned with Clinical Application**
  - Current Issues in Oncology Drug Discovery
  - Axcelead's Approaches

Current Issues in Oncology Drug Discovery
- Low clinical trial success rates

Anti-cancer drugs show the lowest clinical success rates across all therapeutic areas



Challenges in cancer drug discovery

01. TECHNICAL CHALLENGES

- Limitations of extrapolating preclinical models to humans
- Insufficient preclinical evaluation systems for diverse modalities of anti-cancer drugs

02. SCIENTIFIC CHALLENGES

- High heterogeneity and complexity of cancer
- Significant proportion of non-responders in clinical trials

03. COMMERCIAL CHALLENGES

- Fierce competition in cancer drug development

Axcelead provides an integrated approach to address technical and scientific challenges to achieve 'effective in humans'.

The success rate was referred from Biostatistics, 20, 2019

Axcelead's Approaches

➢ Fresh human tissue/Organoid

hospital

- Carefully processed at Japanese hospitals
- Precise collection for targeted tumor region

Establishment of various assay systems using high-quality samples

➢ Humanized mouse model

IVS In-Vivo Science Inc.

- A wide range of NOG mouse-based platforms
- Access to extensive basic data on various NOG mice
- No restrictions on the type of transferred cells to NOG mice
- Hydrodynamic gene delivery (HGD) method

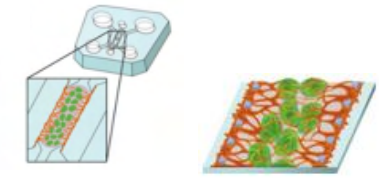
Uniquely developed humanized mouse models offering high quality and flexibility

➢ PDX mouse

- Mince surgically dissected tumor tissues into mice by trochal transplantation
- 30+ PDX development from patient tumors

Develop new models from fresh tumors in collaboration with clients

➢ MPS



- Development of tumor microenvironment
- Development of EMT model

Customizable platforms for complex tumor microenvironment studies

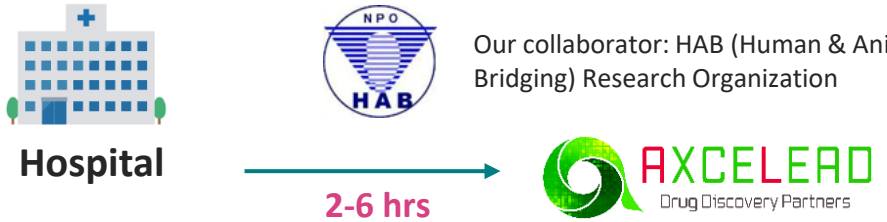
Biomicrofluidics. 12, 2018

Axcelead's Capabilities for Fresh Clinical Samples

Assays using fresh clinical tumor samples are available in Axcelead

- Multiple routes for obtaining clinical samples
  (We have plans to add more partner hospitals in the future)
- Patient information can also be provided
  (Age, gender, drug history, genetic mutation etc.)
- Ethical and Operation Excellence
  - Established ethical review process
  - End-to-end project management
- Diverse assays for immune-oncology research are available
  - Immune-profiling of TILs
  - Tumoroid culture and drug efficacy tests
  - T cell activation assays
- Cutting-edge research platforms are under construction
  - Immune cells co-culture assays
  - Tumor slice culture
  - Multiple omics analysis
    - Spatial transcriptomics
    - Single cell RNA-seq

High-quality, freshly isolated human samples



Our collaborator: HAB (Human & Animal Bridging) Research Organization

List of partner hospitals

Partner Hospital	Number of surgeries per year Colon / Lung / Ovary / Kidney / Breast / Melanoma
A hospital	55/31/10/30/101/20
B hospital	327/361/105/101/604/23
C hospital	66/288/100/32/191/21

Overview of ADDP's Assay System Using Human Fresh Tumor Tissues

Surgery

Dissociation

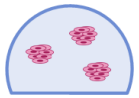
Tumoroid (3D)
(Cancer, CAF, immune, epithelial cells etc.)

Overnight culture

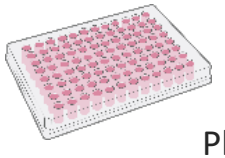
Plating

Cell viability

Cancer Organoid (3D)
(Cancer cells)



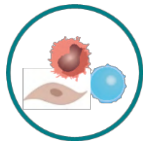
Expanded in Matrigel for over one month



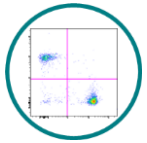
Plating

Cell viability

Tumor-dissociated cells (2D)
(Cancer, CAF, immune cells etc.)



Single cell



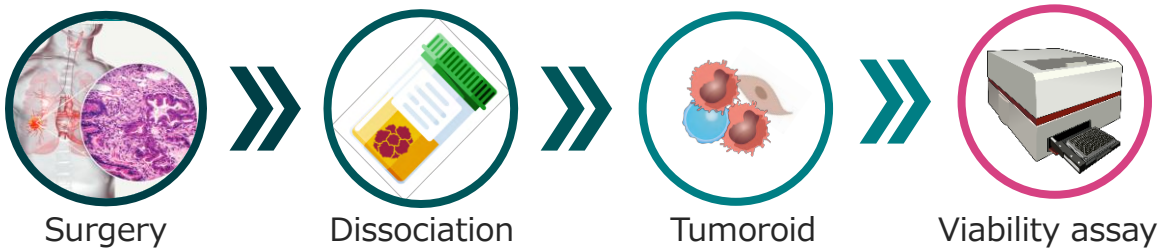
FCM

Immunophenotyping

Plating

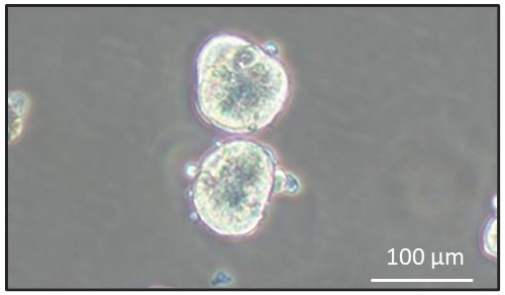
IFNγ production

Tumoroid Cell Viability Assays

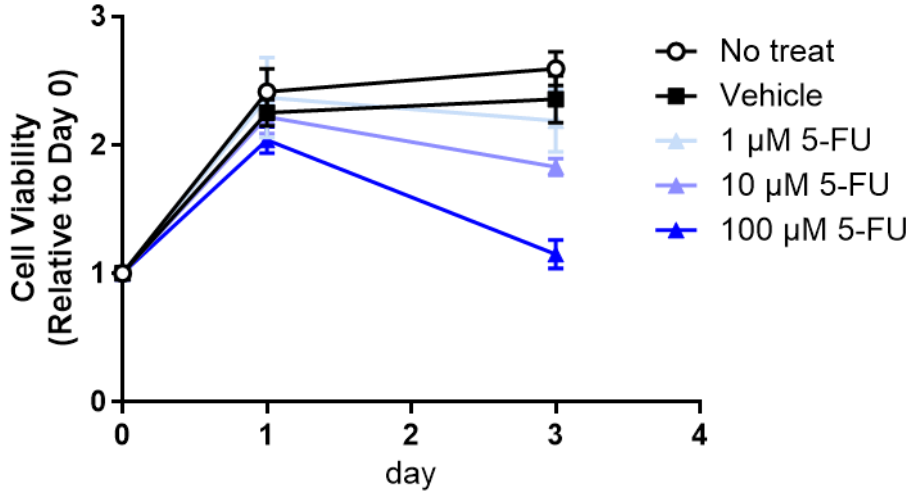


Poster #3155

Tumoroid (Colorectal cancer)



Tumoroid cell viability assay (Colorectal cancer)



n=3, mean ±SD

Tumoroid cell proportion (Colorectal cancer)

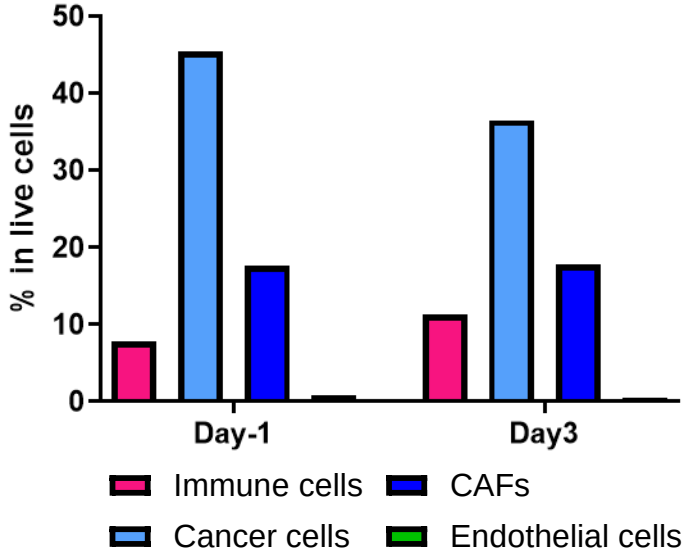
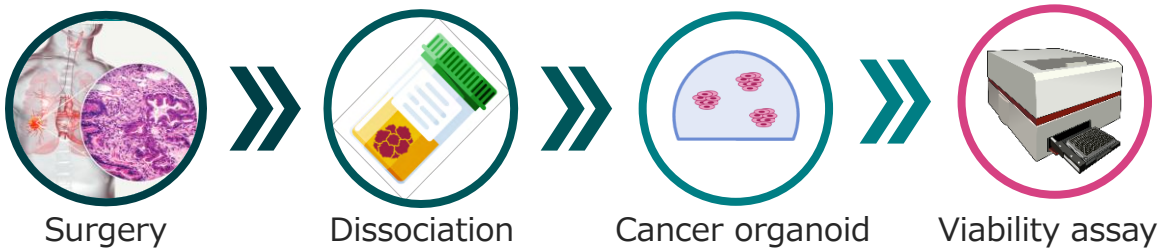


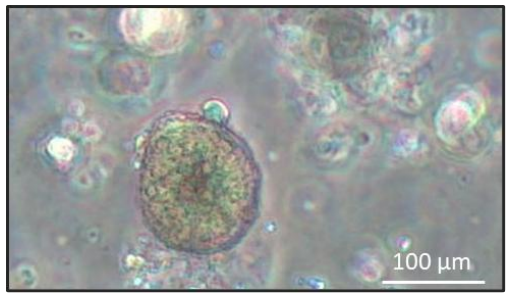
Image source: NIH BIOART Source. "Illustration from NIH BIOART Source" (https://bioart.niaid.nih.gov/bioart/161).

Cancer Organoid Cell Viability assays

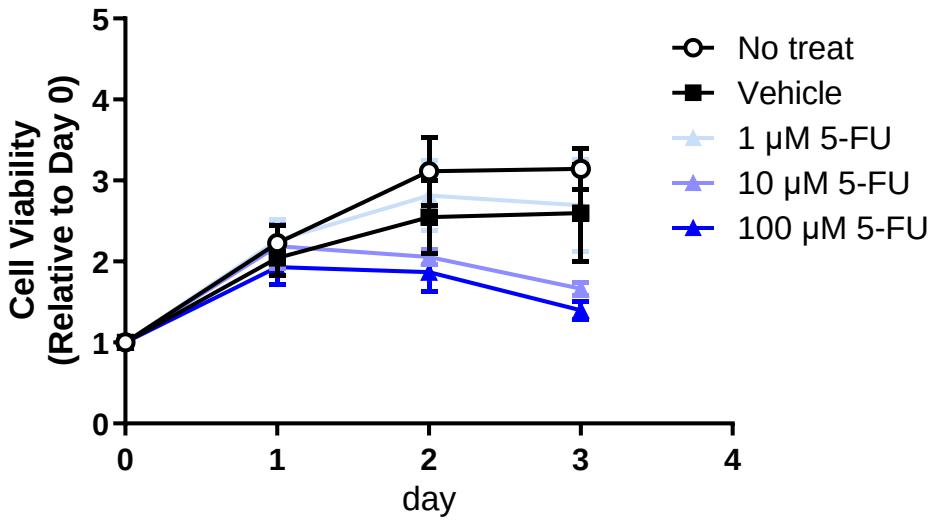


Poster #3155

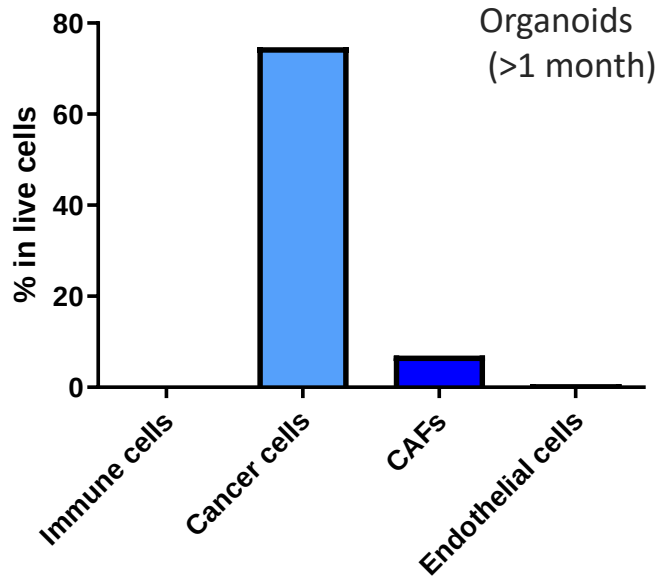
Cancer Organoid (Colorectal cancer)



Cancer organoid cell viability assay (Colorectal cancer)



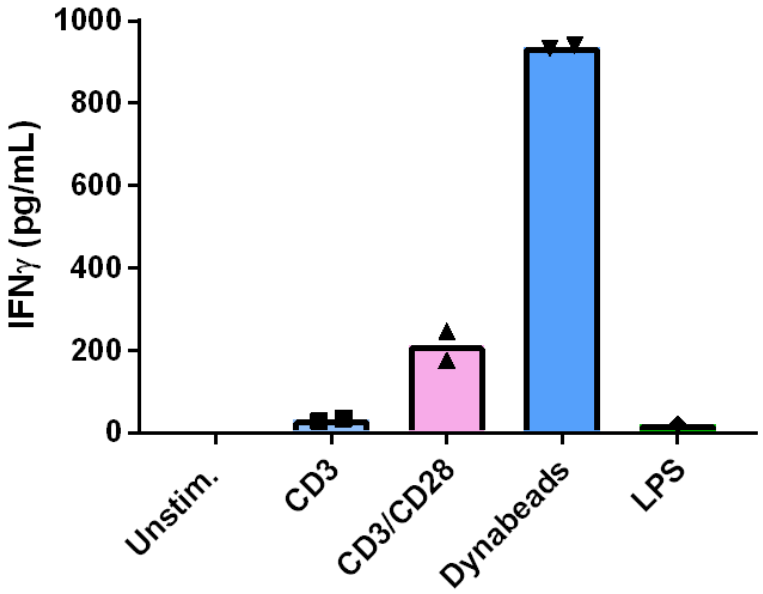
Cancer organoid cell proportion (Colorectal cancer)



T cell Activation Assay Using Tumor-Dissociated Cells

Poster #3156

IFNγ production (Colorectal cancer)



Effect of anti-PD-1 Ab on IFNγ production (Kidney cancer)

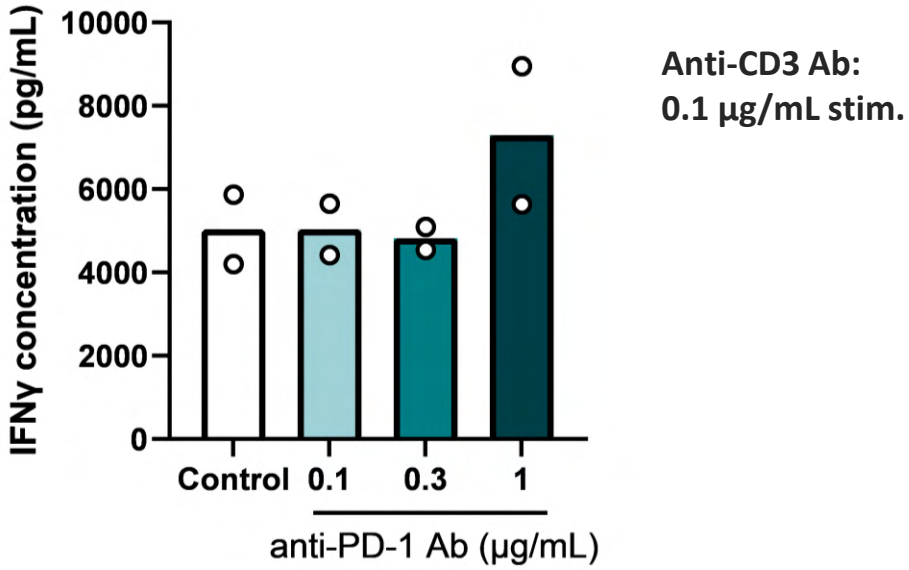


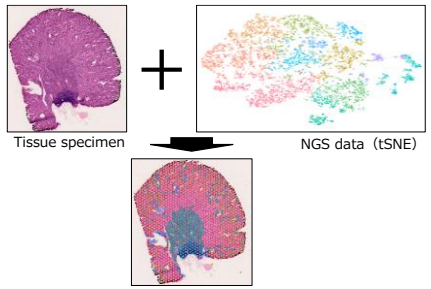
Image source: NIH BIOART Source. "Illustration from NIH BIOART Source" (https://bioart.niaid.nih.gov/bioart/161).

Comprehensive Analysis Platform using Fresh Tumor Sample

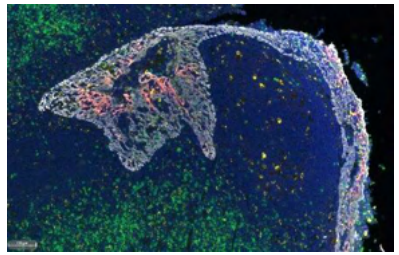
Integrated Analytical Approaches for Etiology, Target Identification and Validation, and Biomarker Discover

- Pathological evaluation using spatial transcriptomics and multiplex IHC/IF
- Single-cell/nuclear RNA-seq for cell-type-specific profiling and immune landscape analysis
- Multiple-omics analysis including transcriptome, proteome, lipidome, metabolome

Spatial Transcriptomics

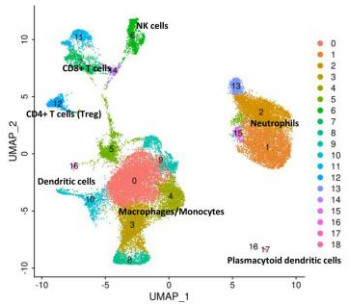


Multiplex-IHC

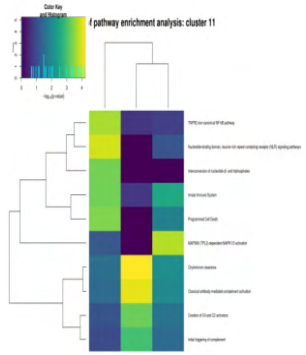


Single Cell/Nuclear RNA-seq

Cell type classification



Enrichment analysis



Transcriptome	Proteome	Phospho-proteome	Lipidome	Metabolome
NGS	High resolution MS	High resolution MS	GC/MS/MS	LC/MS/MS
Ion Torrent S5	Orbitrap Fusion	Q Exactive HF-X	GCQQQ	QTRAP5500

Future Plan

Fresh Tumor Sample

- Expansion of Cancer Types
  - Breast and blader cancer in addition to colon, kidney and lung cancer

Culture and Assay System

- Tumoroid
  - Immune cell responsiveness and drug effect evaluation (e.g., PD-1 blockade)
- Slice culture
  - Advanced tumor microenvironment study

Summary and Collaboration Opportunity

- Axcelead has established an in vitro evaluation system using fresh human tumor tissues, offering high clinical relevance.
- By integrating fresh clinical samples with advanced analytical platforms, Axcelead enables comprehensive studies such as disease mechanism analysis, target discovery and more.
- Axcelead offers a highly flexible and customizable approach tailored to diverse research needs.

“Please feel free to contact us if you are interested in specific cancer types or assays—we would be happy to support your research.”

THANK YOU!

AXCELEAD
Drug Discovery Partners

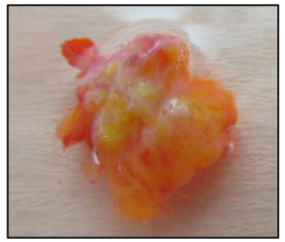
https://www.axcelead.com

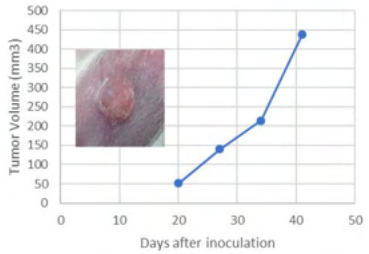
Establishment of PDX Model

30+ PDx development from patient tumors

- **We have developed new models (over 30 models) from fresh tumors in collaboration with clients as well as conducted in vivo efficacy studies with established models**

Development of PDX model





- Surgically dissected ovarian cancer
- Mince and transplant a tumor tissue into mice by trochal transplantation
- Observe tumor engraftment and growth
- Expand tumor and conduct in vivo study

Case 1. Colorectal cancer PDX model

This model was established by needle biopsy samples for the evaluation of mutation status of patients

Evaluation of tumor growth and PDx tumor profiling for MoA analysis