CN-BIO

Organ-on-a-chip contract research services

Rapid access to organ-on-a-chip, powered by PhysioMimix® and the expertise of our team!

visit **cn-bio.com**

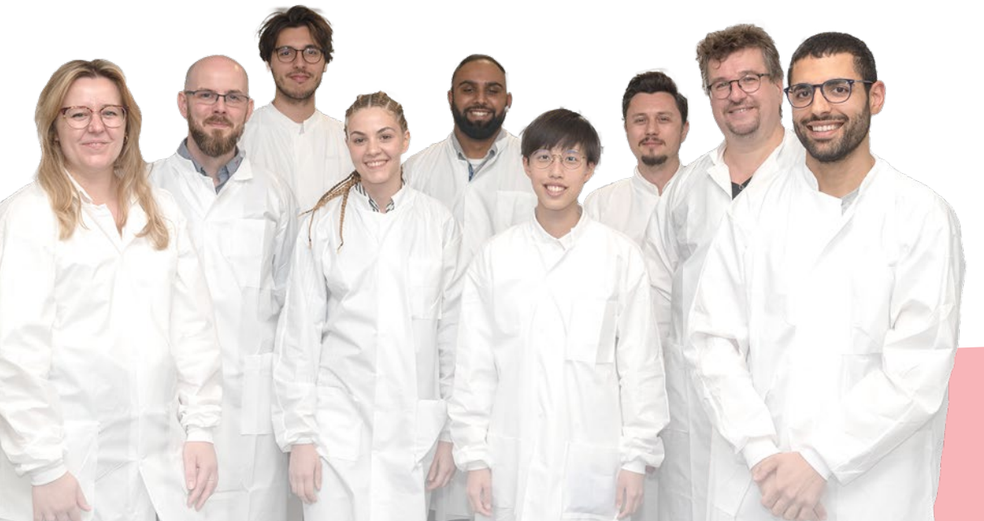
About us

We are a close-knit, passionate and creative thinking team, all working together towards our shared goal – a future where drugs are discovered more quickly, brought to patients more cost-effectively, and through the use of less animal experimentation.

CN Bio's microphysiological systems include; the PhysioMimix® Organ-on-a-chip (OOC) range for recreating human tissues and organs in the lab; and the proprietary PhysioMimix Pharmacokinetics (PK) System for anticancer drug efficacy assessment. Collectively, these systems enable researchers to perform rapid, tissue-based studies that more accurately predict human responses to drugs.

Our technology bridges the gap between traditional cell culture and human studies to help you develop safe and efficacious therapeutics, faster and more cost-effectively than ever before. Access the technology and CN Bio's expertise through our Organ-on-a-chip contract research services.

Learn more at cn-bio.com/in-vitro-services



Contents

Rapidly access human-relevant data from organ-on-a-chip models offering the highest biological relevance to de-risk decision making

Services overview

We offer advanced *in vitro* studies to screen your therapeutic candidates, investigate mechanisms of action and fast-track clinical trial design

Our services are ideal for for customers who:

1. **Wish to benefit from the insights of organ-on-a-chip (OOC) without investing in equipment or developing in-house expertise.**
2. **Require a rapid turnaround when there is a time pressure (such as with a clinical asset).**
3. **Are looking for an *in vitro* alternative to the use of xenograft models.**

We have over a decade's experience in the field to ensure you **get answers quickly** and **cost-effectively** compared to animal studies.

Our services portfolio provides you with access to meaningful, human-relevant data from *in vitro* models that offer the highest possible biological relevance.

Our objective is to rapidly answer your most urgent and unanswered questions so that you can make data-driven decisions that improve your chance of clinical success.

Our team will work collaboratively to design a bespoke study that matches your research goals. Your project lead will remain in close communication throughout the study, providing progress updates before **delivering actionable data to you within weeks**.

Studies are performed using PhysioMimix® microphysiological systems, which provide large scale tissue and media volumes to obtain high content multi-omics and microscopy data.

- Endpoint assays from our in-house menu
- Sample delivery back to you for further profiling
- Transfer of samples to specialist analytical service providers

Our technology

Studies are performed using PhysioMimix® microphysiological systems

PhysioMimix OOC

We co-culture physiologically relevant combinations of primary human cells under perfused conditions to form healthy or diseased single- and multi-organ microtissues that recapitulate the key pathophysiology, phenotypes and functions of human organs *in vitro*.

Our complex organ models accurately predict human drug responses and remain functional for up to one month enabling both acute and chronic dosing studies that improve the translatability of data between the laboratory and the clinic.

The technology underpins our *in vitro* NAFLD/NASH, DILI and ADME Services.

PhysioMimix PK

Xenograft models are commonly used to evaluate the relationship between PK/PD and efficacy for oncology treatments, however, there is now an *in vitro* alternative that improves the human relevance of drug dosing.

Using PhysioMimix PK, we apply human or animal PK drug profiles as mono- or combination therapies to tumor models to ascertain optimal dose regimens, and therapeutic schedules, thereby bridging the gap between *in vitro* studies and actual drug responses *in vivo*.

This proprietary technology underpins our Oncology Services.

Get started with a proof of concept study

Ensure our approach matches your needs before fully investing with rapid turn around proof of concept studies.

Service

Non-alcoholic steatohepatitis (NASH)

A complex *in vitro* model to accurately study a complex human disease

Access a human-relevant model that replicates key disease phenotypes and reports clinical biomarkers to allow translatability to clinical trials.

Utlizing our extensive expertise, we adapt our industry-validated NAFLD/NASH assay as necessary to explore the effects of your therapeutic(s).

- The model uses validated cells with known NASH-related genotypes
- Captures clinical markers with proven translatability
- Assesses inflammation, fibrosis, steatosis, and cell health biomarkers

> Inipharm is developing a drug that targets a genetic metabolic target which has metabolomics differences between mice and men. For this reason, we evaluated several different primary human testing systems that have features of NASH.
>
> We found CN Bio has developed a system that has steatotic, inflammatory, and fibrotic features that have been very useful in evaluating our lead compounds. The scientists at CN Bio are very knowledgeable and have worked with us on the study details to obtain the best quality of results in a timely manner.

Heather Hsu
Chief Scientific Officer, Inipharm

Key endpoints

Functionality biomarkers

Albumin production
Urea production

Clinical liver heath biomarkers

Lactose dehydrogenase (LDH) release
Aspartate transferase (AST)
Alanine amino transferase (ALT)

Disease biomarkers

Luminex®/ELISA assays

Fibrosis (e.g. TIMP-1, Pro-collagen, Fibronectin)
Inflammation (e.g. IL-6, IL-8 TNF-α)

Confocal microscopy

Smooth muscle actin (alpha-sma)
Collagen
Fat accumulation (Nile Red staining)

Service flexibility

Time course (10 day standard) and dosing frequency adjustments.

Alternative endpoint assays including RNA isolation for transcriptomic analysis.

Periodic media sampling to enable secreted biomarker assessment.

Our NASH service

Through the co-culture of primary human hepatocytes and non-parenchymal cells and the evaluation of multiple endpoints, our assay offers a complete assessment of NASH drug efficacy.

Your dedicated contact will work collaboratively with you from the start to the end of the project.

1
Design and finalize the experimental plan

2
Customer supplies the required amount of drug(s)

3
Three to four weeks to complete cell culture

4
Three to four weeks to run endpoint assays, analyze data and complete the report

5
Two to three months to complete the study from receiving an order

Service

Drug-induced liver injury (DILI)

A sensitive and specific means to predict human hepatotoxicity

Employing our Liver-on-a-chip hepatic co-culture model (evaluated by collaborators at the U.S. FDA), our DILI service can screen molecules of any type and gene editing reagents to establish human DILI risk.

Our service assesses at least six hepatic health parameters simultaneously to achieve the sensitivity and specificity required to identify hepatotoxins missed in animals, and other *in vitro* assays.

- Explore a range of conditions: healthy, inflammation, fatty
- Compare acute *vs* chronic toxicity responses
- Investigate drug-drug interaction events
- Check for CYP induction or inhibition

> I worked with CN Bio on a DILI services project to predict which formulation of the same test agent would be safe for humans. Previous *in vivo* studies demonstrated inter-species differences between the formulations in animals but thanks to the expertise of CN Bio, I was able to rapidly gain human-relevant data that helped to move my project forward.
>
> **Professor Gerry Boss M.D. UCSD**
>
> **Professor Gerry Boss M.D. UCSD Distinguished Professor of Medicine, Department of Medicine.**

Key endpoints

Functionality biomarkers

Cytochrome P450 enzyme activity
Albumin production
Urea production

Clinical liver heath biomarkers

Lactose dehydrogenase (LDH) release
Adenosine triphosphate (ATP)
Aspartate transferase (AST)
Alanine amino transferase (ALT)

Optional profiling analysis

Quantitative PCR
Transcriptomics

Service flexibility

Assess compound availability and drug metabolism by media sampling for LC-MS.

Time course adjustments to the standard four-day dosing period.

Flexibility regarding the frequency of dosing and biomarker assessment.

Alternative endpoint assays including transcriptomics to explore idiosyncratic DILI.

Bespoke multi-organ, or studies with circulating immune cells available on request

Our DILI service

Through the co-culture of primary human hepatocytes and Kupffer cells, and the evaluation of multiple endpoints, our assay offers a complete assessment of DILI risk.

Your dedicated contact will work collaboratively with you from the start to the end of the project.

1
Design and finalize experimental plan

2
Customer supplies required amount of drug(s)

3
Two weeks to complete cell culture

4
Two to three weeks to run endpoint assays, analyze data and complete the report

5
Approximately two months to complete the study

Service

ADME

More efficiently predict human tissue drug exposure

Studies investigating drug metabolism, metabolite identification, permeability, and bioavailability are conducted using our human highly functional, metabolically competent single- and multi-organ models.

We offer highly metabolically active, long-term cultures to derive unique *in vitro* data to better inform the selection of lead candidates with desirable ADME properties.

- Hepatic clearance including low clearance compounds, plus Phase I and II metabolite identification
- Gut metabolism and permeability
- Lung permeability in upper and lower airway models
- Multi-organ (Gut/Liver, Lung/Liver) models simulate route of administration to predict bioavailability
- Method developed with protein-free cell culture medium and low non-specific binding multi-chip assay plates

> Working with CN Bio has been a pleasure, the team listened to our non-trivial requirements and made useful suggestions to help meet objectives.
>
> During the course of the project, the team were responsive and helpful.
>
> The results were delivered as agreed and helped us to move towards our goals.

Dr Giuseppe Ferrandino
Senior Translational Scientist, Owlstone Medical

Key endpoints

Liver

Functionality biomarkers

Cytochrome P450 enzyme activity

Albumin production

Urea production

Lactose dehydrogenase (LDH) release

Profiling analysis

Media samples ready for LC-MS analysis

Quantitative PCR assessment of Cytochrome P450 enzyme functionality

Gut, or Lung

Functionality biomarkers

Trans epithelial electrical resistance (TEER)

Lactose dehydrogenase (LDH) release

Profiling analysis

Media samples ready for LC-MS analysis

Service flexibility

Alternative endpoints such as transcriptomics or confocal imaging to assess areas such as mucus production.

Adjustments to dosing regimens and time courses.

Our ADME service

Using single- or multi-organ models, our assays generate insights into the human body's effects on drugs previously only possible using animals.

Your dedicated contact will work collaboratively with you from the start to the end of the project.

1: Design and finalize experimental plan

2: Customer supplies required amount of drug(s)

3: Assay dependent preparation of organ models - between four and 21 days

4: Compound dosing and sample collection over one to four days

5: One to two weeks to run endpoint assays, analyze data, and complete the report

6: Approximately two months to complete the study

7: Media samples sent to the customer, or a third party for LC-MS analysis

Service

Oncology

Explore drug pharmacokinetics, scheduling, and combinations without xenografts

Explore anticancer drug efficacy using our unique Oncology service. The service combines innovative technology with deep cell culture expertise to enable a first– the exploration of pharmacokinetic/pharmacodynamic (PK/PD) and efficacy relationships *in vitro* .

Simultaneously optimize dose regimes and therapeutic schedules by applying customized pharmacokinetics to human-derived tumor models.

- Compare *in vitro* cell and tumor model responses to existing or modeled PK profiles
- Explore the effects of drug combination therapies and dosing schedules
- Evaluate *in silico* predictions and reverse translation of clinical observations

Key endpoints

Sample collection

Timepoint or endpoint sample collection

- Live and/or fixed samples

On demand biomarker detection

Demonstrate PK/PD relationships

- Protein/RNA extraction from endpoint/ timepoint samples

Endpoint assays

Biochemical/imaging

- Luminescence viability assays
- Live-dead microscopy assays
- Multiplexed viability/apoptosis assays

Service flexibility

Customized adaptors (inserts, scaffold supports, extracellular matrix encapsulation) support a variety of sample types.

Experimental duration can be customized or extended. We offer flexibility regarding the frequency of dosing and biomarker assessment.

Alternative endpoint analysis such as LC-MS and imaging can be included.

Our Oncology service

Using your sample of choice (biopsies, tissue slices, spheroids/organoids), our assay enables you to validate and explore *in vivo* or *in silico* findings and perform experiments that wouldn't be possible otherwise.

Our specialist team works with you to formulate an experimental design.

1

You submit your test agent and *in vitro* model for culture in 2D or 3D

2

We apply PK profiles (of one or two drugs in combination) that accurately recapitulate *in vivo*, or *in silico* profiles

3

PK profiles are repeated according to the experimental design, or to recreate clinically approved therapeutic schedules

4

Full report with option to receive cell and media samples for molecular mechanism investigation

Bespoke service offering

At CN Bio, we believe in partnering to find the right solution for your drug discovery and development needs

We can work with you to adapt our models to suit your research question or work together on collaborative projects.

If you would like to discuss how we can help you please get in touch to arrange an exploratory meeting.

sales@cn-bio.com

Data compliance

CN Bio attaches great importance to the privacy and protection of your data. When you deal with CN Bio. You can be assured that your data are in good hands. We have processes and procedures in place that maintain strict levels of confidentiality between our scientists and your project team at all times.

To learn more about our data protection policy please contact us

Resources hub

Dive deeper into our technology, its applications, and how its helping enhance the development of tomorrow's medicines around the world.

Webinars	App notes	Posters
Scientific papers	Brochures	SOPs

cn-bio.com/resources

visit **cn-bio.com**

CN-BIO

332 Cambridge Science Park
Milton Road, Cambridge, CB4 0WN

+44 (0) 1223 737941

sales@cn-bio.com