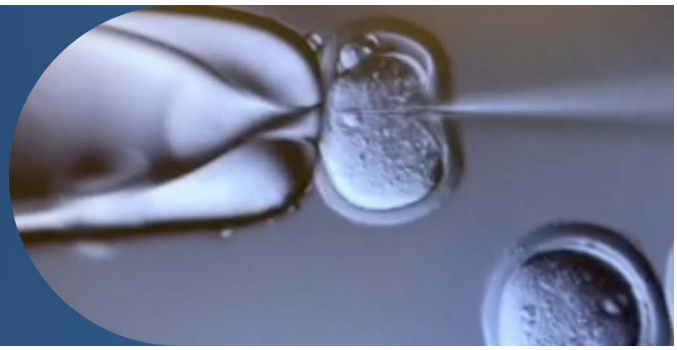
Fred Hutch Cancer Center

Preclinical Modeling

Research Administration
Seattle, WA • 501(c)(3) Nonprofit



Fred Hutch's Shared Resources are catalysts for lifesaving discoveries. This uniquely centralized program of 15 specialized core facilities and scientific services drives advances by integrating dedicated experts and cutting-edge technologies across the entire research pipeline, from basic science to clinical trial.

PDX and CDX Models: Frequently Asked Questions

Contact: Elizabeth Cromwell

Contact phone: 206.667.4176

Contact email: ecromwel@fredhutch.org

Implanting human tumor tissue into immunocompromised mice allows researchers to observe tumor behavior in an in vivo environment. Patient-derived xenograft (PDX) or cell line-derived xenograft (CDX) models offer an exemplary translational research model in which to study cancer.

Our experienced PDX team offers guidance and technical services from start to finish. We have successfully developed more than 84 PDX models, including 41 we created in-house using donated patient tumor samples and 43 sourced from pre-existing PDX models developed elsewhere. Our skilled technicians will help you devise and execute the best PDX model-based plan based on your research goals.

Here we answer common questions about PDX and CDX models and the services our team offers.

What are the different options for xenograft source material?

- **Patient-derived xenograft (PDX):** PDX models use tumor tissue surgically removed from a cancer patient.
- **Cell line-derived xenograft (CDX):** Commercially available cancer cell lines, PDX-derived cell lines or any other immortalized cell line can also be implanted into immunodeficient mice to support any tumor study.
- **Mouse autograft models:** Mouse tumor tissues or immortalized mouse cancer cell lines can be implanted into mice of same inbred genetic background (identical MHC) to develop an autograft or homograft mouse model (also known as a syngeneic model).

Where does the tumor tissue come from?

PDX models start with consented human tumor specimens acquired through collaboration with clinicians and researchers. These patient donations come from primary and/or metastatic sites and are collected under IRB consent. We can also procure, or assist in procuring, established PDX models from third parties such as The Jackson Laboratory, other academic institutions, and the National Cancer Institute Patient-Derived Models Repository. Additionally, we have more than 84 PDX models, many available for academic research, cryopreserved in our tumor bank.

Our team has developed PDX models from patient-donated samples of colorectal, lung, liver and pancreatic cancers as well as melanoma, Merkel cell carcinoma and sarcoma. Already established PDX models sourced from third parties include bladder, lung, pancreatic and triple-negative breast cancer models.

LEARN MORE

Preclinical Modeling
Priti Singh, Ph.D.
Director
206.667.6745
psingh@fredhutch.org

Where does the tumor tissue get implanted?

There are two types of PDX or CDX model, depending on where the sample is implanted:

- **Heterotopic tumor models:** Our PDX team can surgically engraft human tumor tissue or cells heterotopically in an area of the mouse unrelated to the original tumor site, usually below the skin. Subcutaneous implants are inexpensive compared to areas that require more complicated surgery and allow for easy monitoring of tumor growth. Implantation into the peritoneal cavity is popular for studying metastasis. The subrenal capsule is a highly vascularized site that is recommended for hard-to-grow cancer types. This surgery is more complex, but may have a higher engraftment rate and support faster tumor growth.
- **Orthotopic tumor model:** Our PDX team can surgically engraft human tumor tissue or cells orthotopically into the equivalent mouse organ. These models mimic the human tumor microenvironment and have high rates of metastasis, allowing researchers to more accurately predict drug response, drug resistance and metastatic proliferation. Orthotopic implantation may be required for certain cancer types (such as breast cancer) or may be more appropriate for certain research goals or treatment studies.

  The core has successfully collaborated on several studies using the following orthotopic sites:
  - Mammary fat pad
  - Kidney capsule (subrenal)
  - Liver
  - Peritoneal cavity (cells only)

  We can help you develop engraftment strategies tailored to your research needs.

How does implantation work?

Tumor tissue is implanted into immunocompromised NSG mice. Donated patient tissue should be fresh, but PDX model tissue may be fresh or cryopreserved. Tissue is usually implanted as whole solid tumor fragments (between 2mm3 and 7mm3) that retain the unique tumor microenvironment. When a tumor sample must be dissociated, or if the implant route necessitates it, we will implant a cell suspension.

Subcutaneous implantation is the standard engraftment route for initial patient samples and for reviving cryopreserved samples or models, but additional heterotopic and orthotopic implantation routes are available.

For a graphical breakdown of the PDX workflow, please see the Example Projects section of our How We Work page.

How can I use the tumor tissue from my PDX model?

After tumors are collected, the excised tissues can be used for a variety of purposes, including but not limited to:

- Serial repassaging in mice
- Implantation into experiment-ready cohorts
- Downstream characterization of cancer tissue (protein assays, RNA seq, etc.)
- Quality control by our veterinary pathologists
- Diagnostic testing (human pathogen panel)
- Cryopreservation for future use
- Development into organoids
- Development into cell lines
- Flow cytometry

How are PDX and CDX models stored?

In order to utilize the valuable PDX models for future academic research, we cryopreserve tumor tissue from PDX models. We bank as much tissue from low passages as possible. Our efficient cryopreservation methods allow the recovery of cryopreserved PDX models with a 90% take rate. Some cancer types are more sensitive to freezing than others, and during the course of live-model development we always aim to test viability from frozen.

I want to run a preclinical study on my PDX model. Can you help?

We can run your pharmacokinetic (PK) and pharmodynamic (PD) in vivo studies using PDX, CDX and allograft platforms. Our team has experience with many types of preclinical treatment studies, including studies of inhibitor efficacy, dosing efficacy and dosing requirements, combined chemotherapy efficacy and dosing requirements, and T-cell therapy and cytokine response.

In a typical PK or PD experiment using a novel therapeutic compound, we implant cohorts with PDX or CDX models and begin treatment when the tumor reaches a target size. We offer all standard drug delivery methods. Throughout the dosing period we collect data on tumor dimensions, body weight and any clinical observations twice a week. We can also collect blood, perform irradiation treatments and coordinate mouse imaging. Post-treatment tumors (and other tissues) can be collected for your team's downstream analysis (including flow cytometry, gene expression analysis and histology). By overseeing these studies, our team can shorten the gap between the preclinical and clinical phases and speed up your tumor research.

Treatment administration methods include:

- Oral gavage
- Ad libitum water bottle
- Intraperitoneal injection
- Subcutaneous injection
- Intravenous injection
- Intradermal injection
- Intratumoral injection
- Targeted irradiation
- Whole body irradiation

What if I need extra help planning or administering my PDX experiments?

We provide customer service and support throughout the project, starting with your expectations and outlining potential risks.

Our experienced team can also offer input on the growth rates of established PDX models, associated risks and tolerability for efficacy study designs, flexible options for dosing, frequency of formulation and any additional logistics for sourcing of materials and animals. We help you select the experimental route best tailored to your research goals.

For added convenience we have our own IACUC protocol under which we perform all PDX services. The protocol encompasses all surgical procedures, mouse monitoring and tumor measurements. We can also help you address all relevant regulatory requirements, including IACUC, Department of Defense and Environmental Health & Safety regulations.