Patient-Derived Tumor Xenograft (PDX) Models for Oncology Research

Charles River's portfolio consists of hundreds of fully characterized, proprietary patient-derived tumor xenografts (PDXs) representing all the major tumor histotypes. Our wide range of models and expertise ensures clients' research is truly translationally relevant, speeding entrance to the clinic.

Our PDX portfolio features:
- Subcutaneous, orthotopic, and disseminated models
- Extensive molecular and pharmacological characterization
- Integrated drug discovery approach using the same PDX model (and/or the corresponding PDX-derived cell line) in different assay systems: 2D in vitro/3D ex vivo screening assays and subsequent in vivo efficacy tests
- Identification of biomarkers which may help to predict tumor sensitivity to anti-cancer agents and to define target patient populations
- PDX model platform using humanized mice in standard or single mouse trial (SMT) format
- Ongoing addition of new PDX models which are obtained through international collaborations with major hospitals and universities

To establish our PDX models we implant patient tumor explants directly into mice, either subcutaneously (solid tumors) or intratibially (hematological cancers), without any in vitro culture on plastic. PDX models preserve important characteristics of the original patient tumor such as heterogeneous histology and tumor architecture, molecular alterations, and sensitivity to anti-cancer agents. As a consequence, preclinical pharmacological profiling of novel anticancer agents using PDX models may allow predictions of responders and response rates in the clinic and improve the design of clinical trials.
An Integrated Portfolio:

- Tumor Compendium for model selection
- 2D in vitro assays
- 3D ex vivo assays
- PDX in vivo models
  - Subcutaneous, orthotopic, and disseminated
  - Humanized models available
  - Single mouse trial format available

Figure 1: Charles River’s portfolio consists of hundreds of fully characterized PDXs representing all the major tumor histotypes.

Online Tumor Model Database

Our online compendium of tumor model characterization data allows clients to search by features of interest to facilitate tumor model selection for 2D in vitro cell line screening, for 3D ex vivo colony assays, and for in vivo efficacy tests. Search parameters include tumor histology, mRNA expression level, gene copy number alteration and whole exome sequencing mutation profiles. Search criteria can be used individually and in combination. The wealth of information we have collected on each PDX model guides our suggestions as to which PDX models are suited best to help our clients to reach their goals.

2D In Vitro and 3D Ex Vivo Assays

Our extensive in vitro portfolio is the foundation of a comprehensive screening approach. With over 400 publicly available human tumor cell lines and proprietary cell lines derived from more than 80 of our PDX models (for 2D assays), as well as ex vivo explants from over 300 PDX models (for 3D assays), we can devise the best strategies for the preclinical profiling of novel anti-cancer agents, utilizing carefully chosen combinations of tumor histologies, molecular subtypes, and drug sensitivity profiles. Along with molecular profiles, PDX-derived cell lines and PDXs in 2D and 3D assays, respectively, are cost and time-effective tools for selecting appropriated PDX models as well as conditions for in vivo efficacy studies.

PDX In Vivo Models

For the in vivo profiling of anti-cancer agents targeting tumor cells directly PDX models are implanted into immunodeficient mice. In vivo work with agents activating the immune system to fight cancer is performed in PDX-bearing immunodeficient mice, i.e., the initially immunodeficient mice are engrafted with a human hematopoietic cells enabling the establishment of a human immune system. This approach makes it possible to study the interaction of IO anticancer agents with both human tumor cells and human immune cells in the same organism. PDX model selection for the in vivo testing of immunoncology agents relies on additional criteria such as the immune landscape of PDX models. Final read-outs of in vivo efficacy tests with IO agents are not just tumor volume and tolerability data as for non-IO agents but also changes in the immune system triggered by the test agents which are the basis of tumor inhibition and are assessed by flow cytometry, immunohistochemistry and other analyses.

Driven by PDX models and/or PDX-derived cell lines in vitro, ex vivo, and in vivo, along with bioinformatics approaches to data analysis, our integrated preclinical profiling approach leads to more relevant data, speeding up preclinical research and enabling better design of clinical trials.