Washington University Human in Mouse Patient-Derived Xenograft (PDX) Collection
A Curated Collection of Human Breast Cancer PDX Models

WHY USE PDXS FOR PRECLINICAL RESEARCH?

PDXs are the most clinically relevant preclinical models available to support cancer drug discovery and development programs. This is because tumor tissue is harvested from a patient and then directly implanted into an immunocompromised mouse (see schematic below).

This contrasts with traditional xenografts, which rely on cancer cell lines grown on plastic for prolonged periods, causing key features to tend to drift from those of the original disease. PDXs are considered the most predictive for how drugs will perform in the clinic, since they closely recapitulate the genetic and phenotypic properties of the tumor from which they were derived. PDXs can be passaged and expanded in mice to ensure a future supply while simulating cancer progression.

Initially described by Li et al. (2013), Washington University Human in Mouse (WHIM) human breast cancer PDX models are a curated collection available to support research, drug discovery, and compound validation. These PDXs are available as suspended cells or frozen chunks and include general patient and tumor characteristics (e.g., age, smoking status, tumor location, mutation status, diagnosis, treatments, hormone receptor status) and model-specific information for many PDXs (e.g., RNAseq, whole genome sequencing, proteomic profiles, passage number, estradiol responsiveness, fulvestrant selective estrogen receptor degrader resistance).
POPULAR WHIM PDXs

WHIM human breast cancer PDX models are available to meet specific research requirements, and they are available based on several attributes, including the following:

- Molecular subtype,
- Mutation status (most common mutations), and
- Treatment resistance and sensitivity.

Inotiv is the exclusive supplier of WHIM human breast cancer PDX models. The most popular WHIM PDXs are those sourced from metastatic tumor sites in the brain, skin, right rib, or liver. Several popular WHIMs and their molecular characteristics are shown below.

<table>
<thead>
<tr>
<th>WHIM</th>
<th>ER STATUS</th>
<th>PR STATUS</th>
<th>HER2 STATUS</th>
<th>PS3 GENOTYPE</th>
<th>WHOLE GENOME SEQUENCED</th>
<th>EXOME SEQUENCED</th>
<th>RNASEQ</th>
<th>GENE EXPRESSION (MICROARRAY DATA) AVAILABLE</th>
<th>PAM50 SUBTYPE</th>
<th>PRIMARY TUMOR</th>
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<tbody>
<tr>
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<td>-</td>
<td>-</td>
<td>-</td>
<td>SI665 insertion</td>
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</table>

DOSING CAPABILITIES

Inotiv provides expert dosing services (non-GMP) for preclinical therapeutic screens in PDXs, which typically require subcutaneously implanting 100–300mm³ cells to establish and be enrolled into a treatment study.

While the most commonly requested regimen is once daily oral dosing, Inotiv also offers daily intravenous, intraperitoneal (IP), and subcutaneous injection options at no additional charge. Inotiv provides additional services, including terminal bleeds, tumor processing, body weight, and histological and pathological analyses.
CASE STUDY: DRUG RESPONSES IN WHIM6 PDXs

A standard of care (SOC) dosing study was performed in PDX mouse models established using the “WHIM6” tumor line, derived from a triple negative breast tumor that is sensitive to alkylating agents (e.g., cyclophosphamide) and anthracyclines (e.g., doxorubicin).

Four groups of athymic nude mice (Hsd:Athymic Nude-Foxn1nu) were implanted with 1.5 x 10^6 WHIM6 cells. Tumors were measured twice weekly until a median volume of 100–300 mm^3 was reached. The mice were then randomized and normalized by tumor volume into treatment groups (see table). Dosing occurred weekly for three weeks.

As shown below (left plot), the WHIM6 PDXs responded to SOC treatments similarly to the response observed in the parental human tumor (i.e., sensitive to cyclophosphamide). As shown in the right plot, body weight was maintained for all treatment groups for more than 60 days, while the saline group maintained weight for only 40 days before having to be sacrificed.

WHIM PDX models effectively simulate the response patients may have to various drugs, providing insight on the best way to move forward with a treatment. Recapitulating human disease with PDX tumor cell lines has become a staple in breast cancer therapy development.

REFERENCES


Learn more about how you can work with highly characterized PDX breast cancer models: inotivco.com/whim-pdx-models