Building a comprehensive and fully annotated patient derived xenograft (PDX) library mirroring cancer patient population

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Abstract

Our PDX library contains over 1,600 models derived from patients of both Asian and Western origins, covering over 20 major cancer types. Our PDX models are fully annotated with original clinical pathology diagnosis information, genomic profiling data (GeneChip and NGS), hotspot mutation data, and HLA typing info to enable immuno-oncology research. Majority PDX models have tumor growth and standard of care (SOC) treatment information. Comparing our PDXs’ genomic profiles with published patient genomic profiles in literature and TCGA data source (Guo et al, 2015 AACR #1926) revealed a high degree of similarity. Subsets of the models have been comprehensively characterized for specific relevance to specific clinical characteristics and specific drug targeting mechanisms (HuPrime® 2.0). These subsets include all clinically observed EGFR mutated NSCLC; c-MET activation diseases; FGFR driven diseases, RET-fusion driven CRC, FLT3-LITD driven AML, IDH mutated AML and CRC, RPSO-fusion driven CRC, BCR-ABL fusion disease, HER2 driven gastric and breast cancers, and ALK fusion NSCLC, etc.. We have also established numerous drug resistant models to various SOC’s of both chemotherapy and target therapies. The resistance could be de novo or induced. Models which have great metastatic potential have also been identified, enabling the study metastatic mechanisms and for identifying agents to block metastasis. A number of PDXs can grow in humanized mice (HuPrime®), where human immunity has been reconstituted in the immune-compromised mouse background to facilitate immune-oncology research.

Table 1. Summary of Patient derived HuPrime 1.0 tumor models

<table>
<thead>
<tr>
<th>Model Type</th>
<th>Colony Number</th>
<th>Total Model</th>
<th>Total Patient</th>
<th>Total Drug Treatment</th>
<th>Total Re-Engraftment</th>
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<tr>
<td>PDX</td>
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<td>4</td>
<td>2</td>
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<tr>
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<td>175</td>
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<tr>
<td>Other</td>
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<td>175</td>
<td>175</td>
<td>20</td>
<td>20</td>
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</tbody>
</table>

Figure 1. Patient derived xenograft models – HuPrime PDX platform. A. Building HuPrime PDX models and service platform. B. Core components of HuPrime pharmacology service capability.

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Figure 4. NexGen HuPrime 2.0 PDX models available for specific drug programs.

Figure 5. Large scale MCT/HuTrail studies using HuPrime 1.0 PDX models for Biomarker discovery and HuSignature™ development.

Figure 3. Development of drug resistant HuPrime PDX models by serial drug treatment and re-engraftment.

Figure 6. Proprietary HuBase 2.0 - easy data access and powerful search function.

http://hubase2.crownbio.com/