

ATCC's Human-Relevant Cancer Models for Mechanism-Based Toxicity and Drug Response Profiling

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Human Cancer Model Initiative (HCMI)

The Human Cancer Models Initiative (HCMI) is a global collaboration led by the National Cancer Institute (NCI), with partners including Cancer Research UK, the Wellcome Sanger Institute, Hubrecht Organoid Technology, and NCI-funded institutions such as the Broad Institute and Cold Spring Harbor Laboratory. The initiative develops next-generation, patient-derived cancer models that better capture the genomic and phenotypic complexity of human tumors compared to traditional cell lines. ATCC® is the sole distributor of the HCMI portfolio, providing more than 300 fully characterized 2-D and 3-D cancer models derived from over 18 tissue types, including colorectal, pancreatic, brain, and esophageal cancers as well as rare cancers like Wilms tumor and Ewing's sarcoma. These models reflect diverse clinical backgrounds and retain high genomic fidelity, preserving over 80% of oncogenic drivers and maintaining transcriptional and epigenetic landscapes comparable to patient tumors. By offering clinically relevant models with available sequencing data and patient metadata through the HCMI portal, this work supports improved preclinical testing, biomarker discovery, precision oncology research, and studies of tumor heterogeneity and health disparities.

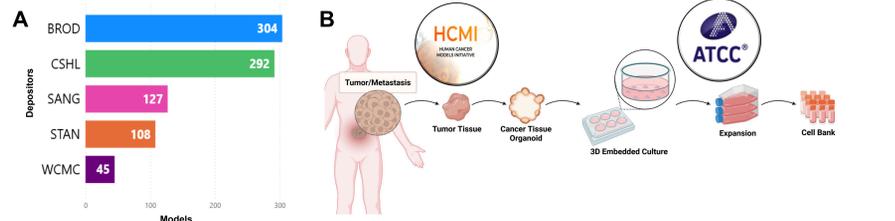


Figure 1: The Human Cancer Models Initiative (HCMI). (A) Institutes involved with depositing HCMI organoid/spheroid models at ATCC. (B) ATCC initiates the production pipeline and generates cell banks from this material. Figure created with BioRender.com.

Production Workflow

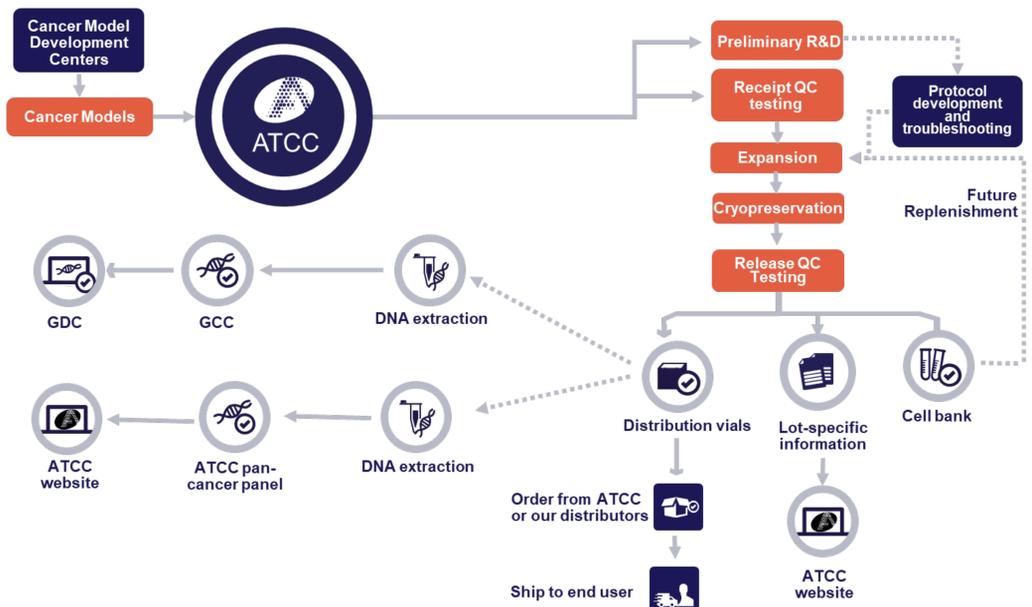


Figure 2: Our production workflow outlines the end-to-end process for manufacturing and cell banking process for HCMI models. This workflow visually walks through key stages from preliminary R&D and model generation protocol development at their respective academic/institutional sites. Transitioning to accessioning, expansion, quality testing, cryopreservation of cell banks, and eventual distribution and shipment to end users by ATCC. This workflow also presents ATCC's role in quality control, DNA analysis, comparative analysis with GDC data generation, and future replenishments, emphasizing the rigorous steps involved in releasing high quality cancer models to the research community.

HCMI Portfolio Breakdown

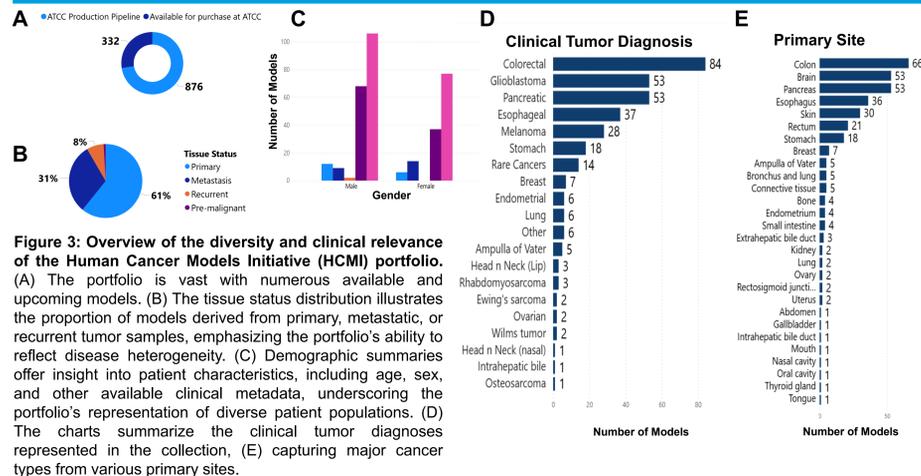


Figure 3: Overview of the diversity and clinical relevance of the Human Cancer Models Initiative (HCMI) portfolio. (A) The portfolio is vast with numerous available and upcoming models. (B) The tissue status distribution illustrates the proportion of models derived from primary, metastatic, or recurrent tumor samples, emphasizing the portfolio's ability to reflect disease heterogeneity. (C) Demographic summaries offer insight into patient characteristics, including age, sex, and other available clinical metadata, underscoring the portfolio's representation of diverse patient populations. (D) The charts summarize the clinical tumor diagnoses represented in the collection, (E) capturing major cancer types from various primary sites.

Genomic Signatures

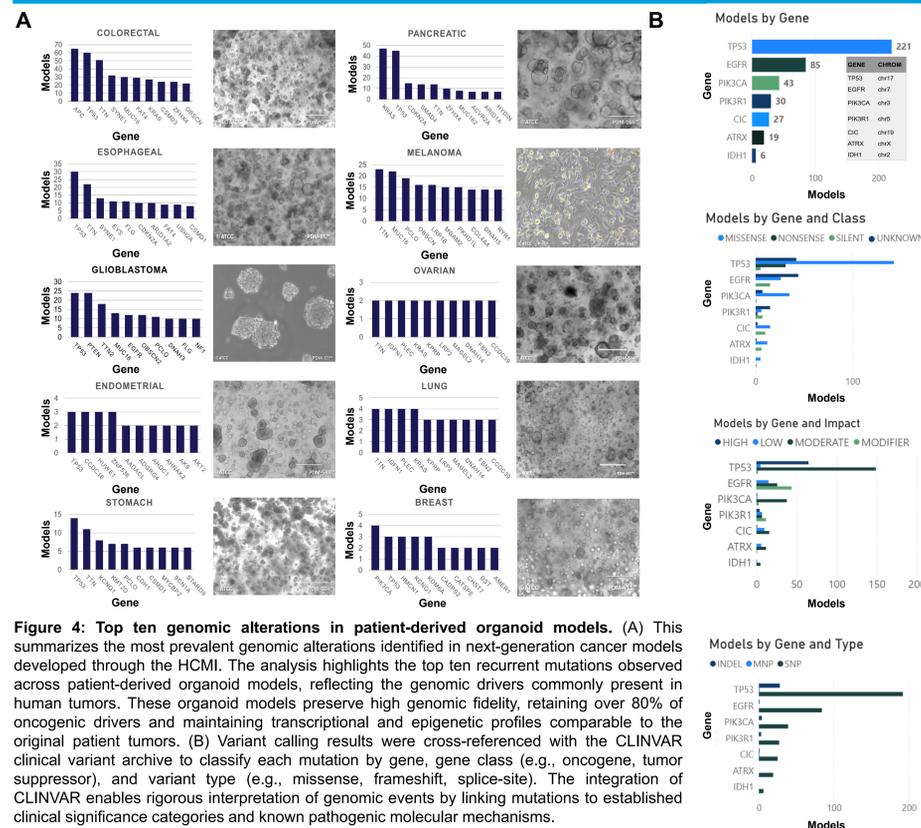


Figure 4: Top ten genomic alterations in patient-derived organoid models. (A) This summarizes the most prevalent genomic alterations identified in next-generation cancer models developed through the HCMI. The analysis highlights the top ten recurrent mutations observed across patient-derived organoid models, reflecting the genomic drivers commonly present in human tumors. These organoid models preserve high genomic fidelity, retaining over 80% of oncogenic drivers and maintaining transcriptional and epigenetic profiles comparable to the original patient tumors. (B) Variant calling results were cross-referenced with the CLINVAR clinical variant archive to classify each mutation by gene, gene class (e.g., oncogene, tumor suppressor), and variant type (e.g., missense, frameshift, splice-site). The integration of CLINVAR enables rigorous interpretation of genomic events by linking mutations to established clinical significance categories and known pathogenic molecular mechanisms.

Assessing Colorectal Organoids

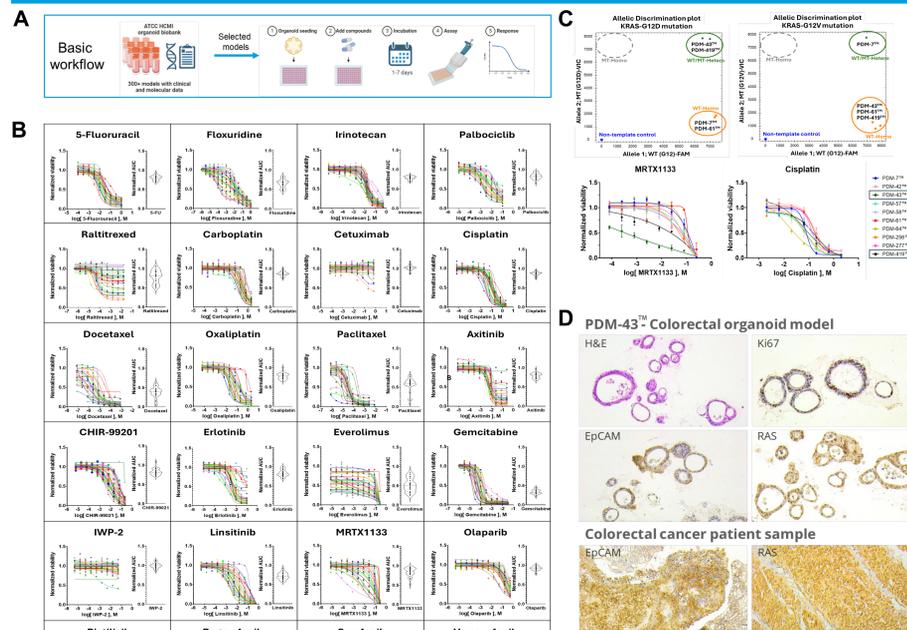


Figure 5: Drug sensitivity and characterization of KRAS-mutant colorectal organoid models. (A) Compound screening was performed on colorectal cancer organoids (CCOs) (workflow created with biorender.com). (B) Cell viability assays revealed clear, dose-dependent reductions in viability across treatments, with area-under-the-curve (AUC) values summarized as a violin plot to illustrate variability and drug-response distributions within the CCO cohort. (C-D) The KRAS G12D mutant organoid PDM-43, as seen also from the allelic discrimination plot, exhibited marked sensitivity to the KRAS G12D inhibitor MRTX1133, responding to G12D inhibitor MRTX1133, demonstrating a pronounced cytotoxic response relative to KRAS wild-type or alternate-KRAS-mutation organoids. This robust and selective drug response underscores the capacity of PDM-43™ to faithfully recapitulate KRAS G12D dependency, mirroring therapeutic vulnerabilities observed in patient tumors.

List of KRAS-variants in HCMI colorectal cancer organoids

| KRAS variant | ATCC # | Name | Tissue Status | KRAS variant | ATCC # | Name | Tissue Status |
|--------------|---------|-------------------|---------------|--------------|---------|---------------------|---------------|
| G12C | PDM-42 | HCM-SANG-0265-C18 | Metastasis | A146T | PDM-256 | HCM-CSHL-0247-C18-A | Primary |
| G12C | PDM-45 | HCM-SANG-0268-C18 | Primary | A146T | PDM-277 | HCM-CSHL-0247-C18-B | Metastasis |
| G12D | PDM-185 | HCM-CSHL-0238-C18 | Primary | A146T | PDM-40 | HCM-SANG-0284-C18 | Primary |
| G12D | PDM-226 | HCM-BROD-0025-C16 | Primary | G12A | PDM-1 | HCM-CSHL-0056-C18 | Primary |
| G12D | PDM-276 | HCM-CSHL-0461-D12 | Pre-malignant | G12A | PDM-46 | HCM-SANG-0269-C18 | Primary |
| G12D | PDM-43 | HCM-SANG-0266-C20 | Primary | G12S | PDM-513 | HCM-WCMC-0671-C18 | Primary |
| G12D | PDM-47 | HCM-SANG-0270-C20 | Primary | G12V | PDM-408 | HCM-CSHL-0582-C18 | Metastasis |
| G12D | PDM-49 | HCM-SANG-0272-C20 | Primary | G12V | PDM-44 | HCM-SANG-0267-D12 | Primary |
| G12D | PDM-6 | HCM-CSHL-0062-C18 | Primary | G12V | PDM-7 | HCM-CSHL-0063-C18 | Primary |
| G12D | PDM-96 | HCM-CSHL-0143-C20 | Primary | G13D | PDM-415 | HCM-CSHL-0659-C18 | Metastasis |
| G12S | PDM-103 | HCM-CSHL-0164-C20 | Metastasis | G13D | PDM-104 | HCM-BROD-0001-C18 | Metastasis |
| G12S | PDM-190 | HCM-CSHL-0244-C20 | Primary | Q61H | PDM-62 | HCM-SANG-0286-C20 | Primary |

Conclusions

- The HCMI Portfolio offers a robust collection of patient-derived cancer models.
- Models enable more predictive and mechanistic drug-response profiling
- HCMI ensures consistency and scientific quality
- Overall portfolio advances precision oncology and supports the development of next-generation cancer therapeutics.



Explore HCMI Models



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