

Patient-Derived Tumor Organoids: Characterization and Functional Applications

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Introduction

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, Weill Cornell Medicine, Stanford University, 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, currently providing 337 fully characterized 2-D and 3-D cancer models derived from over 28 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.

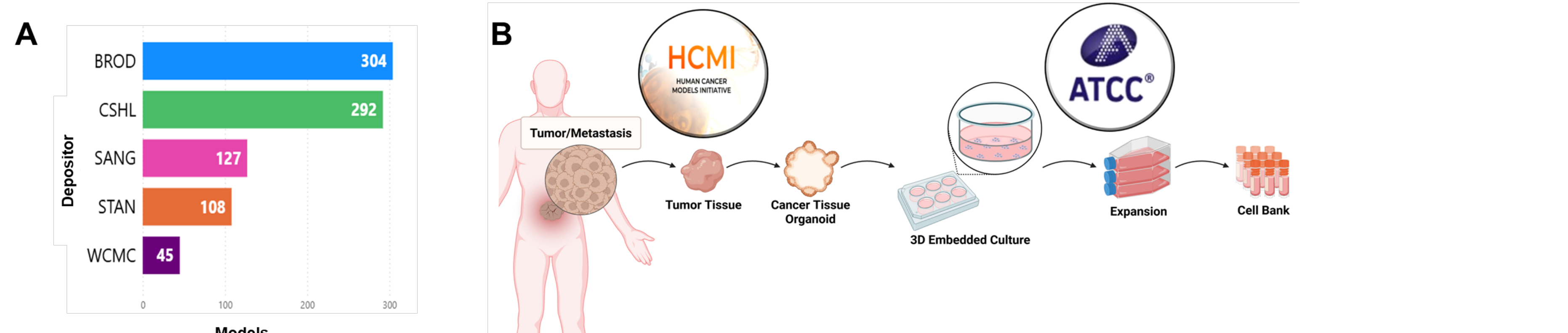


Figure 1: The Human Cancer Models Initiative (HCMI). (A) Model distribution by depositor within the HCMI portfolio. (B) ATCC initiates the production pipeline and generates cell banks from this material. Figure created with BioRender.com.

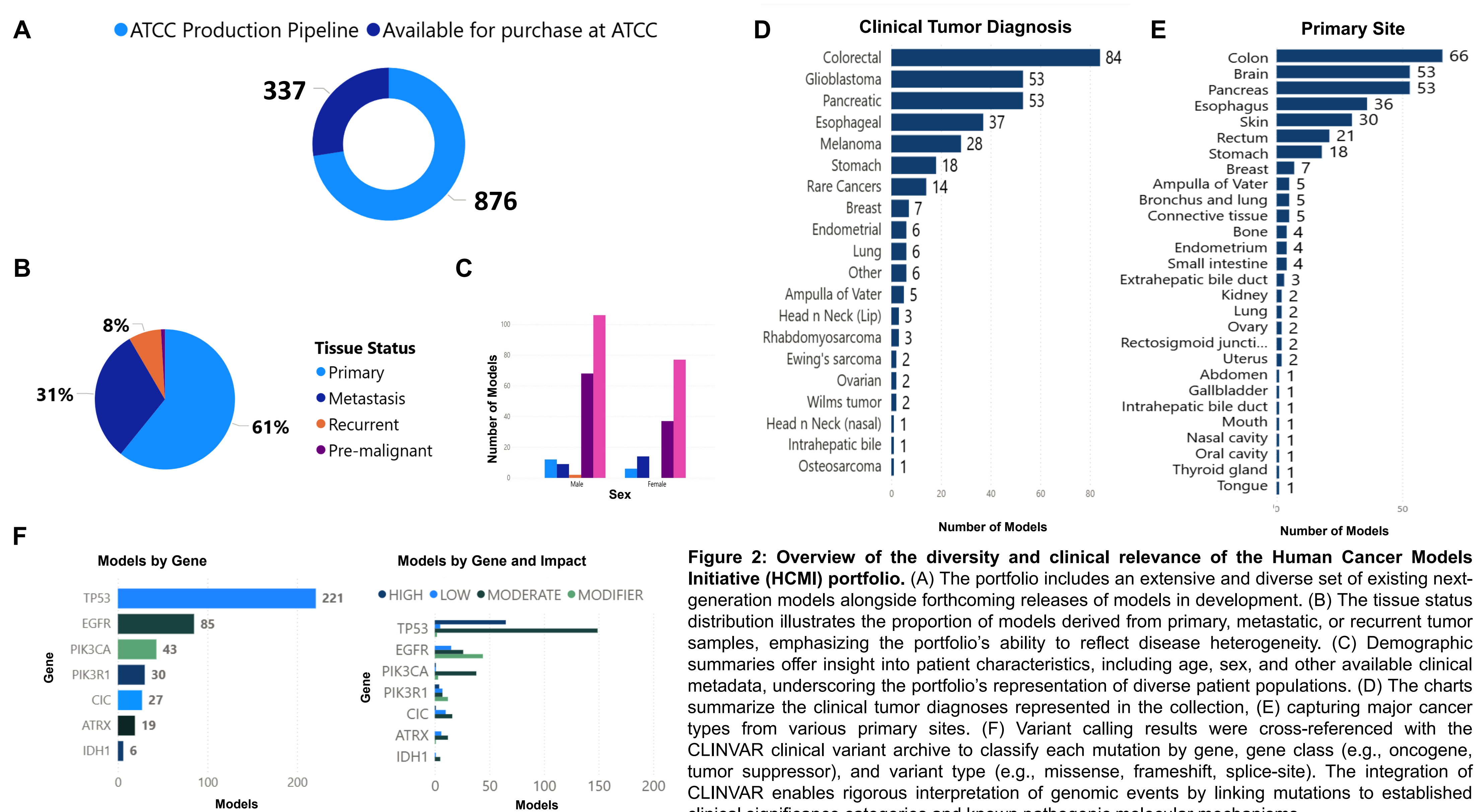


Figure 2: Overview of the diversity and clinical relevance of the Human Cancer Models Initiative (HCMI) portfolio. (A) The portfolio includes an extensive and diverse set of existing next-generation models alongside forthcoming releases of models in development. (B) The tissue status distribution illustrates 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. (F) 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.

Manufacturing Workflow

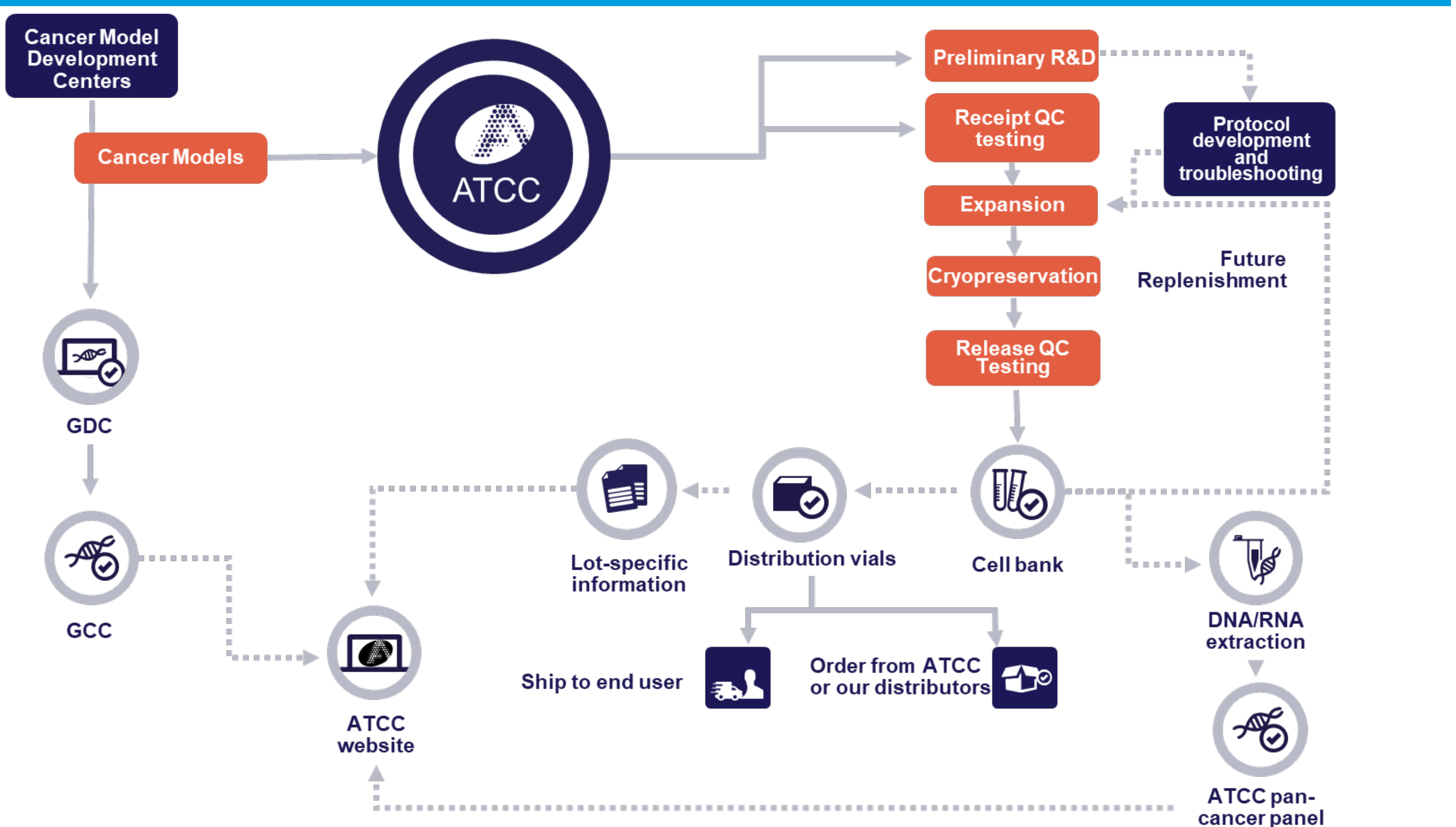


Figure 3: Our production workflow outlines the end-to-end process for manufacturing and cell banking process for HCMI models. This workflow visually walks through key stages in preliminary R&D and model generation protocol development at their respective academic/institutional sites, transitioning then 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 Colorectal Models

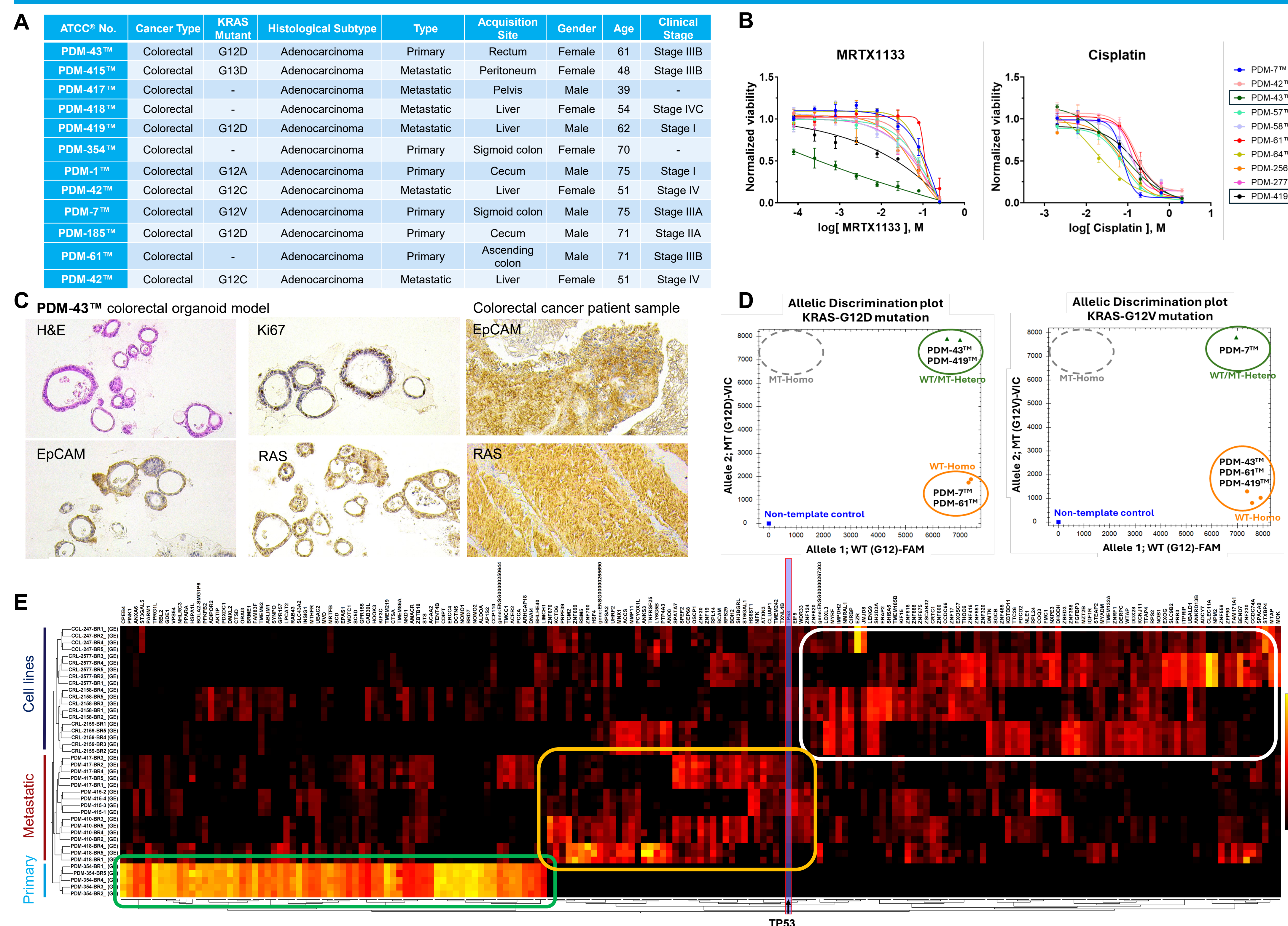


Figure 4: Colorectal cancer organoid model characterization. (A) List of colorectal cancer models that show unique KRAS mutations. (B) The KRAS G12D mutant organoid model PDM-43™, as seen also from the allelic discrimination plot. (C) ATCC® PDM-43™ histopathology as compared to colorectal cancer patient samples showing H&E, Ki67, EpCAM, and RAS markers. (D) These models exhibited marked sensitivity to the KRAS G12D inhibitor MRTX1133, demonstrating a pronounced cytotoxic response relative to KRAS wild-type or alternate-KRAS-mutation organoids. (E) Heatmap shows gene expression pattern across the cell models. Red-induced, Black-reduced. ATCC® provides Organoid Growth Kit 1A (ATCC® ACS-7100™)/Organoid Growth Kit 1D (ATCC® ACS-7103™) for colorectal organoid culture. *For relevant growth media components and instructions, visit ATCC's website for model-specific information. (Green box – primary colorectal organoids, Yellow box – metastatic colorectal organoids, and White box – colorectal cancer cell lines)

HCMI Pancreatic Models

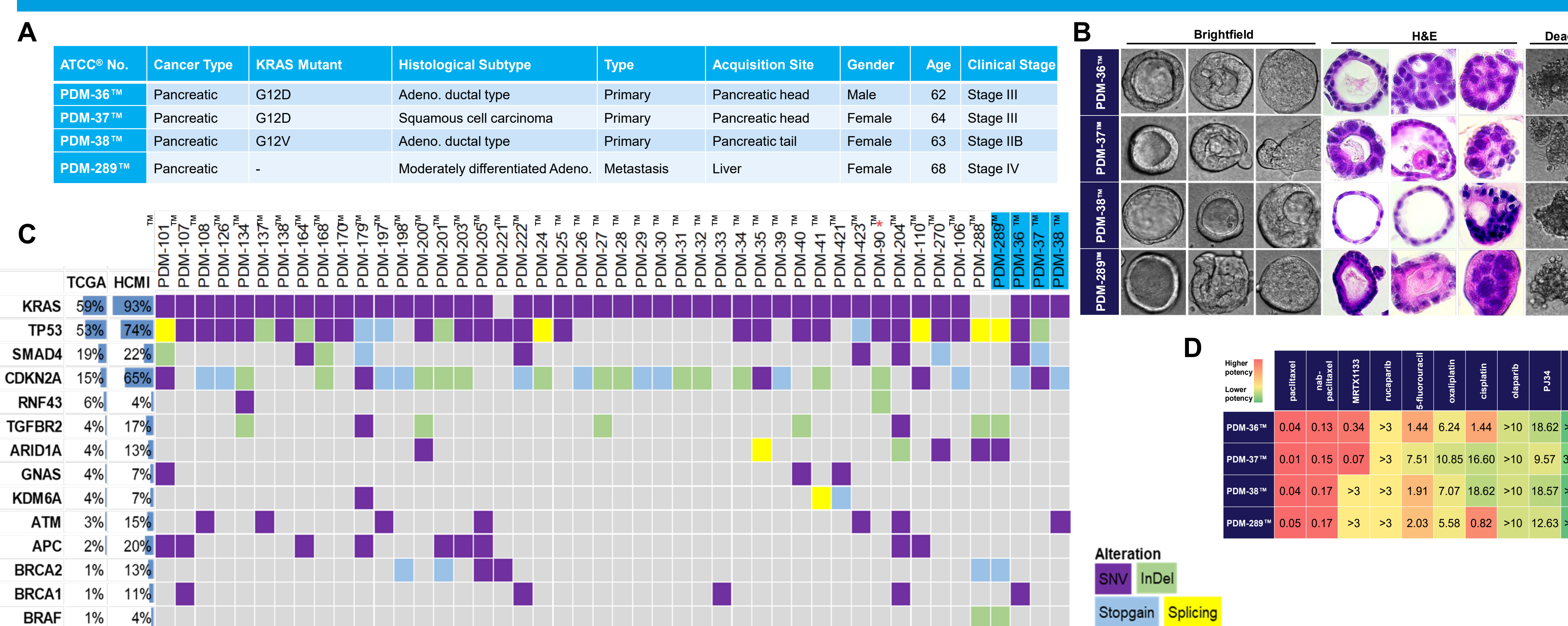


Figure 5: Drug sensitivity and characterization of pancreatic organoid models. (A) List of pancreatic cancer organoids (PCOs) that displays KRAS mutation status and clinical characterization. (B) Morphology in brightfield and H&E stained pancreatic cancer organoid models. (C) Oncoplot highlighting the most frequently mutated genes and selected somatic driver mutations in pancreatic cancer patient-derived organoid models (n=46). Percentage and data bar indicate prevalence of mutation in this cohort as well as The Cancer Genome Atlas (TCGA) pancreatic cancer cohort (n=179). (D) Two KRAS G12D mutant organoid models (ATCC® PDM-36™ and ATCC® PDM-37™) exhibit marked sensitivity to the KRAS G12D inhibitor MRTX1133, demonstrating a similar differential sensitivity for KRAS G12D mutant models in contrast with non-KRAS G12D mutant models as previously seen in colorectal organoid models. This selective drug response across multiple models and tissue types underscores the capacity of HCMI cancer organoids to support the development of advanced model therapeutics. ATCC® provides Organoid Growth kit 1B (ATCC® ACS-7101™) and Wnt-3A producing line (ATCC® CRL-2647™) for pancreatic organoid culture. * ATCC® PDM-90™ has an additional N2 max supplement – see instruction on our website for kit components.

Conclusion

- The HCMI Portfolio offers a robust collection of patient-derived cancer models
- Advanced cell 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

