HUMAN TUMOR CELL LINES REPOSITORY WITH CLINICAL AND MOLECULAR CHARACTERIZATION FOR UROLOGIC ONCOLOGY RESEARCH

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Abstract

• All cell lines in the repository are derived from patients’ tissue specimen with informed consent according to tissue procurement protocols approved by the Institutional Review Board (IRB).
• The repository is managed through BioFortis’ Labmatrix (V3.5) software. The individual cell lines are described with UOB clinical annotations in both FreezerWorksUL2 and FileMaker Pro 8.1 database, which will be part of a bioinformatics network with other renal tumor tissue database at the UOB under the Labmatrix database system.
• An example of the characterization of one of our recently established cell lines is shown below, with all histologic, ultrastructural, immunologic and genetic analysis conducted.

Materials & Methods

Under NCI’s many initiatives, the Urologic Oncology Branch (UOB) has been focused on studying kidney cancer at the clinical, genetic and molecular levels. The research of more than two decades has resulted in the identification and characterization of critical genes - VHL, Met, FH, and BHD - each related to a different type of sporadic and hereditary renal cancer. Cell lines derived from these cancers are valuable tools for elucidating the mechanisms of the gene pathways.

The primary function of the renal cell carcinoma (RCC) Cell Lines Repository is to establish and manage the RCC cell lines from in vivo-derived human surgical tumor specimen and in vitro-established tumor cell lines to assist investigators with cell culture-based research models.

Results

Histologic analysis of the primary tumors

Fig. 1. Light microscopic appearance of different histologic types (A-D): kidney tumor mass samples from a patient with von Hippel-Lindau (VHL) syndrome: (A) large areas composed of mass of clear cells with enlarged, round to irregular nuclei with prominent nucleoli and abundant vacuolated cytoplasm (X400); (B) papillary lined by atypical epithelial cells with granular eosinophilic cytoplasm (X400); (C) atypical finely granular acidophilic cytoplasm (X400); and (D) histologically reminiscent foci of chromophobe renal cell carcinoma (X400).

Histologic analysis of Xenografts

Fig. 2. Morphology of UOK 257 at 55% confluence exhibits small papillary islands (A); at 90% confluence, loss of contact inhibition is evident (B). From flow cytometry, the scatterplot (C) and its one-dimensional histogram projection depict the cell cycle distribution of the tumor cell population.

Ultrastructural (Transmission EM) analysis

Fig. 3. (A) (C) Ultrastructural features of findings from cultured UOK 257 tumor cells (90-nm thin section from fixed cell pellet) (6,500). (A) Arrows indicate microvilli on one (apical) surface and basal lamina on the opposite surface. (B) Arrows indicate basal cytoplasm, junction with complex of different histologic type (200).

Genetic analysis

Fig. 4. (A) A representative metaphase spread from cell line UOK 257 at passage 18. (B) Composite karyotype of UOK 257 in near triploid, displaying multiple unbalanced translocations and deletions of chromosomes (white arrows). Inverted DAPI stained chromosomes are at the left; pseudo-colored chromosomes to the right were hybridized with spectral karyotyping (SKY) probes.

Discussion

The repository contains not only contaminant-free immortalized cell lines but also extensively-characterized DNA/RNA/Protein samples derived therefrom, both with “high quality” (in terms of biological quality of the samples and the status of ethical and legal documents associated with the samples) and related clinical and molecular annotations, and subjected to rigorous quality controls by the repository team.

Summary

Many publications have cited UOB RCC cell lines as unique source of materials. These tumor cell lines have been used as models in molecular targeting studies, in vitro and in vivo (xenograft) drug sensitivity and toxicity studies, which combines with imaging technology to immediately evaluate pre-clinical response to therapy.