Repository and Inventory of Human Renal Tumor Cell Lines for Urologic Oncology Research

- Establishment and Characterization of the First Fumarate Hydratase (-/-) Hereditary Leiomyomatosis Renal Cell Carcinoma Cell Line


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Abstract

The Human Renal Tumor Cell Line Repository is established by NCI-Urologic Oncology Branch (UOB) and provides scientists with the cell lines as both in vitro and in vivo models for studying kidney cancer at the preclinical, genetic, cytogenetic, and molecular levels, for accelerating discoveries of the regulatory pathways and functions of disease genes. The primary function of the repository is to establish and maintain the cell lines from in vitro generated human operative tumor specimen and in vitro established tumor cell lines to assist investigators with cell culture based research models. All cell lines in the repository are derived from patients’ tissue specimen with informed consent according to the tissue procurement protocol approved by the Institutional Review Board (IRB). The repository is managed via BioForts software. All the cell lines are described with UOB patient clinical annotations cited from CRIS and the repository is linked to Labmatrix™ database, which is a part of a bioinformatics network with tissue bank recording system available to the UOB tissue procurement core facility. The repository not only provides extensively multi-level-characterized, contaminant-free, immortalized cell lines, with a clearly invaluable resource for the cancer research, but also ethical and legal documents associated with the cell lines and related clinical annotations, both having been subjected to rigorous quality controls by the UOB repository team.

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, PTEN 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.

Results

Histopathologic and Ultrastructural analysis of HLRCC tumors and xenograft derived from UOK 262 cells

![Image](https://www.nationalcancerinstitute.nih.gov/research-ioc/)

Fig. 1: Hematoxylin-eosin staining of tumor tissue from a patient with HLRCC and from a tumor xenograft: (A) Right renal tumor tissue; (B) Right renal lymph node; (C) Xenograft derived from cells taken from patient’s lymph node (UOK-262-A-FRH); (D) Xenograft derived from UOK 262 cells (as FF).

Fig. 2: Electron micrographs of mitochondria from normal human renal cortical epithelial (HRCE) cells (A & B), and from HLRCC tumor cells, UOK262 (C & D). Mitochondria of tumor cells are ectopic and show disruption of internal membrane cristae. Magnification indicated as a scale bar on each image.

UOK 262 cells display higher Glycolysis rate and lost their mitochondrial respiration capability

![Image](https://www.nationalcancerinstitute.nih.gov/research-ioc/)

Fig. 4: In vitro growth of UOK 262 and 786-O cells in 0.5g/L, 2.5g/L, 5g/L, and 10g/L D-glucose. The cells’ proliferation and survival were glucose dependent.

Characteristics of invasion of UOK 262 cells

![Image](https://www.nationalcancerinstitute.nih.gov/research-ioc/)

Fig. 7. In vitro real-time assay of the invasive potential of UOK 262 cells. UOK 262 is more invasive than 786-O whole normal HRCE cells are not invasive.

Summary

We have maintained an efficient and stable production system by subculturing for the long-term use with fingerprinted genetic background and productivity. Many publications have cited UOB tumor cell lines (such as UOK 257) as unique source of materials. Recently molecular targeting studies have become valuable approaches, by using cell lines as excellent model (such as UOK 262), both in vitro and in vivo model for chemosensitivity and toxicity studies, which incorporates with imaging to immediately evaluate pre-clinical response to therapy. The cell line models could be the basis and ideal platform for identifying effective anticancer compounds that target tumorspecific, metabolic changes caused by cellular or genetic alterations. The repository not only provides extensively multi-level-characterized, contaminant-free cell cultures of immortalized cell lines, which is clearly invaluable resource for the cancer research, but also ethical and legal documents associated with these lines and related clinical annotation, both subjected to rigorous quality controls by the UOB repository team.