Murine PTEN Null Prostate Cancer Model

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BACKGROUND

In the western world, prostate cancer remains the most common malignancy and the second-leading cause of cancer-related deaths in men. The PTEN gene (phosphatase and tensin homologue deleted on chromosome 10) has been well characterized as a tumor suppressor gene, and its malfunction/deletion has been linked to numerous cancer types, including prostate. Mutations or deletions of PTEN have been found in 30% of primary prostate cancers and 63% of malignant cases, ranking it as one of the most common determinants of prostate tumor progression. PTEN-controlled signaling pathways are therefore promising targets for therapeutic strategies, though significant problems in producing animal models have prevented serious gains toward this end. Lack of PTEN leads to embryonic lethality and heterozygote PTEN animals do not undergo normal prostate cancer development. A significant need remains for a workable PTEN-null prostate cancer animal model system.

INNOVATION

UCLA researchers have developed a prostate cancer model in mice by deleting the PTEN tumor suppressor gene. The deletion is tissue-specific and leads to PTEN loss specifically in the prostate. This model recaptures the disease progression seen in human prostate cancer and is non-responsive to androgen-ablation therapy. Studying the consequences of PTEN loss in prostate cancer in vivo was not possible before this innovation. Additionally, this is the first and only animal model where the initiating oncogenic event is not androgen-dependant. This PTEN-null model has been utilized by UCLA researchers to successfully identify several down-stream targets of PTEN, including known signature genes associated with human cancer metastasis. UCLA researchers have also established a PTEN-null prostate cancer cell line from this animal model (UC Case No. 2005-007), as well as an isogenic PTEN-fibroblast cell line (UC Case No. 2005-059), and embryonic fibroblast and stem cell lines that lack Pten (UC Case No. 2005-060).

APPLICATIONS

This model is suitable for examination of prostate tumor development from initiation to metastasis, as well as androgen-independent growth. This innovation can be utilized in gene expression profiling related to prostate cancer progression and metastasis, which may lead to identification of novel targets and biomarkers for cancer diagnostics and therapeutics. The mechanism of resistance to androgen-ablation therapy could also be studied using this model.

The embryonic cell lines derived from the PTEN-null model can be used in multiple ways from PTEN characterization to diagnosis and therapeutic development, as well as generation of animal models. The isogenic cell line has potential for use in elucidating the specific role of PTEN in cell proliferation, migration, and differentiation.

RELATED MATERIALS


PATENT STATUS

Patent Pending

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- A Method for In Vivo Visualization of Mutated Mouse Cells
- PTEN Null Cell Lines
- Adipose Tissue-specific PTEN Knockout Mice
- Genetically Engineered Mice Lacking a Tumor Suppressor Gene in the CNS