

## Scientists find new role for P53 genetic mutation -- initiation of prostate cancer

June 7 2012

---

A team of UC Davis investigators has found that a genetic mutation may play an important role in the development of prostate cancer. The mutation of the so-called p53 (or Tp53) gene was previously implicated in late disease progression, but until now has never been shown to act as an initiating factor. The findings may open new avenues for diagnosing and treating the disease.

The study was published online in the journal [Disease Models & Mechanisms](#) and will appear in the November 2012 print edition in an article titled, "Initiation of prostate cancer in mice by Tp53R270H: Evidence for an alternate molecular progression," and is available online.

"Our team found a molecular pathway to prostate cancer that differs from the current conventional wisdom of how the disease develops," said Alexander Borowsky, associate professor of pathology and laboratory medicine and principal investigator of the study. "With this new understanding, research can go in new directions to possibly develop new diagnostics and refine therapy."

Prostate cancer is the leading cancer diagnosis in men in the United States. Although it is curable in about 80 percent of men with localized disease, the rate is much lower if the cancer is highly virulent and has spread beyond the prostate gland.

The investigators developed a mouse model genetically engineered to have a mutation in the "tumor suppressor" gene, p53, specifically in the

cells of the prostate gland. These mice were significantly more likely to develop prostate cancer than control mice without the mutation, and provided the first indication that the p53 mutation could be involved in the initiation of prostate cancer. They also note that the mutation of p53 in the prostate differs from loss or "knock-out" of the gene, which suggests that the mechanism is more complicated than simply a "loss of tumor suppression" and appears to involve an actively oncogenic function of the mutant gene.

The p53 gene encodes for a protein that normally acts as a tumor suppressor, preventing the replication of cells that have suffered DNA damage. Mutation of the gene, which can occur through chemicals, radiation or viruses, causes cells to undergo uncontrolled cell division. The p53 mutation has been implicated in the initiation of other malignancies, including breast, lung and esophageal cancers.

Other studies have associated p53 mutation with [disease progression](#) in prostate cancer, but this is the first to find that it can have a role in the early initiation of prostate cancer, as well.

Until now, understanding of the role of p53 was that mutation occurred exclusively as a late event in the course of prostate cancer. Based on the findings in the new mouse model that the researchers developed, p53 mutation not only can initiate prostate cancer but might also be associated with early progression toward more aggressive forms of the disease.

[Genetic mutations](#) can initiate cancers in a variety of ways. Those include promotion of uncontrolled cell growth and loss of the gene's normal cell growth-suppressor functions. Exactly how the p53 mutation promotes the initiation and progression of prostate cancer remains to be clarified and is a focus of current research by the UC Davis team. They also are trying to gain an understanding of how the p53 mutation affects

the effectiveness of standard treatments for prostate cancer, such as radiation and hormone therapy.

Another application of the discovery could be the development of a new diagnostic test for prostate cancer based on the presence of the p53 mutation as a biomarker.

"Knowing that prostate cancer can develop via [p53](#) mutation opens new opportunities for researchers in the field," said Borowsky. "This is a game-changer in the understanding of [prostate cancer](#)."

Provided by Queen's University Belfast

Citation: Scientists find new role for P53 genetic mutation -- initiation of prostate cancer (2012, June 7) retrieved 24 April 2024 from <https://medicalxpress.com/news/2012-06-scientists-role-p53-genetic-mutation.html>

<p>This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.</p>
--