Link between prostate cancer and vitamin A may lead to improved treatment

September 5 2012

(Medical Xpress)—Cancer scientists at the University of York have shown a link between prostate cancer and vitamin A for the first time.

Professor Norman Maitland, who was awarded £2.15m by Yorkshire Cancer Research a year ago to continue his groundbreaking research into prostate cancer, has found that a prostate specific gene is under the control of retinoic acid – a derivative of vitamin A.

The discovery, which is published in the scientific journal Nucleic Acids Research, means that it will now be possible to test whether retinoic acid, if given therapeutically, can force prostate cancer stem cells to develop into more specialised cells – a process known as differentiation - which could kill them or render them more susceptible to chemotherapy.

All-trans retinoic acid therapy (ATRA) is already used in another cancer – acute promyelomcytic leukaemia (APL) – and has been hugely successful in improving survival rates from 0% to 80%.

Nearly 41,000 men are diagnosed with prostate cancer every year in the UK, and although around 80% survive for five years or more, 10,000 men die annually.

Professor Maitland, Director of the YCR Cancer Research Unit in the Department of Biology, said: "It has been known for many years that low vitamin A in samples of blood is associated with prostate cancer, but nobody knew the mechanisms involved. We have revealed a functional

biological link between retinoic receptor expression and our laboratory models of prostate cancers.

"Specifically, the gene we have investigated – the prostate transglutaminase (TGP) – is one of the most prostate-specific genes known from the 28,000 in the human genome. We have shown that the TGP gene is controlled by the retinoic acid signalling pathway.

"When retinoic acid gets into a prostate cancer cell, it binds to one of three receptors in the nucleus of the cell. This binding then triggers a sequence of molecular events inside the nucleus which results in the TGP gene being turned on or off. We have shown that the same situation also applies to a number of other genes. All of these genes then tell the cell how to behave – to divide for example."

In a separate review article published in Nature Reviews Urology, Professor Maitland argues that differentiation therapies have previously been misused in cancer treatments, but that used in lower doses, they could be a realistic treatment option.

He said: "Onocologists have been using agents such as retinoic acid as toxins. What we need to do is use them at lower doses so that they change the properties of the susceptible cells. However, they may affect normal stem cells and some cells may react unpredictably, so we need to investigate what happens before we try the treatment on patients. This will now form part of our experimental approach in York."

Provided by University of York