New tool for testing drugs for prostate cancer

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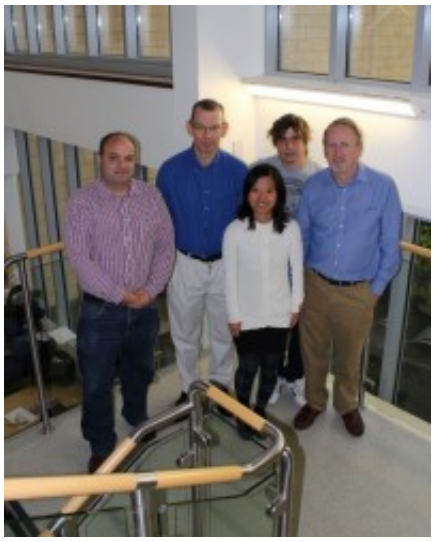

The research team (L-R: Dr Tim Woodman, Dr Matthew Lloyd, Mrs Guat Lee, Mr Maksims Yevglevskis and Professor Mike Threadgill)

Many men are growing moustaches this month as part of Movember to raise awareness and funds for improving men's health, but do you know where this money goes?

Scientists at Bath, funded by Prostate Cancer UK with support from the Movember Foundation, have developed an innovative tool to test potential drugs for prostate cancer. The researchers hope this technique will help speed up the development of new treatments for the disease, the most common form of cancer in men in the UK.

The team are studying the enzyme AMACR (also known as P504S), which is overactive in almost all prostate cancers, some bowel cancers and several other types of cancer and is thought to fuel the growth of the disease by boosting the cell's energy supply.

AMACR has been previously identified as a possible target for cancer drugs because blocking it stops the cancer cells growing. However previous attempts to develop a drug that inhibits AMACR have been slow because it is difficult to accurately measure its activity.

The Bath team has now discovered that AMACR also performs another chemical reaction that can be measured easily. The researchers now aim to develop this reaction into a convenient chemical assay that can be used by scientists assessing the effectiveness of new drugs targeted to AMACR.

Dr Matthew Lloyd, Senior Lecturer in Molecular Enzymology from the University's Department of Pharmacy & Pharmacology, explained: "AMACR helps convert a fatty acid molecule that is common in our diet, into a form that the body can easily use. Previous studies have shown that blocking this process by reducing AMACR levels causes prostate cancer cells to behave less aggressively and behave more like normal cells.

"The biological reaction is reversible and because the starting molecule and the final product are very similar it is very tricky to measure the activity of AMACR, and therefore difficult to assess whether a drug is effectively blocking it.

"Our research has found that AMACR is also able to act on another chemically related molecule in an irreversible reaction that releases a fluoride molecule which can be measured easily."

PhD student Maks Yevglevskis added: "By measuring this new reaction, we can evaluate the effectiveness of potential drug candidates accurately and easily, which will help speed up the development of new treatments in this type of cancer."

The study, published in the journal *Chemical Communications*, is funded by Prostate Cancer UK with support from the Movember Foundation and

from charitable donations from alumni and friends of the University of Bath to Cancer Research at Bath (CR@B).

Dr Matthew Hobbs, Deputy Director of Research at Prostate Cancer UK said: "There are too few treatment options for men diagnosed with prostate cancer, especially once the cancer begins to spread.

"Although this is early stage research, these results are important as they may lead to quicker, more effective and cheaper ways to develop new drugs. This could eventually prove to be an important step towards giving men with prostate cancer a better chance of survival.

"We look forward to following the next steps in this story and would like to thank the Mo Bros and Mo Sistas whose participation in Movember allowed us to fund this project."

The team has patented the technology and hope in the future to work with the pharmaceutical industry to develop a high throughput screen that will assess thousands of chemical compounds in the search for potential new cancer drugs.

More information: "The perils of rational design – unexpected irreversible elimination of fluoride from 3-fluoro-2-methylacyl-CoA esters catalysed by ?-methylacyl-CoA racemase (AMACR; P504S)" *Chem. Commun*., 2014,50, 14164-14166. DOI: 10.1039/C4CC06127F

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