Promising prostate cancer drug candidates identified

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Cancer researchers from the University of Bath have identified some promising drug candidates by using high-throughput screening methods to test tens of thousands of molecules.

The research team from the Departments of Pharmacy & Pharmacology and Chemistry are studying a protein called α-methylacyl-CoA racemase (AMACR) as a potential target for cancer treatments. Levels of AMACR protein and activity are increased by ~10-fold in all prostate cancers. Experiments have shown that reducing these levels makes cancer cells less aggressive, and their behaviour reverts to more like normal cells.

In this study the team tested more than 20,000 drug-like molecules for inhibition of AMACR using a method developed at the University of Bath. This approach, using a simple colour-change technique, allows rapid assessment of the active compounds and identification of new types of drug. The researchers identified drugs which effectively inhibit AMACR in a different way to those that have previously been developed.

The study is published in the journal *Bioorganic Chemistry*.

Lead author Dr. Matthew Lloyd said: "Although previously identified drugs are very effective in laboratory tests, in practice they are difficult to use in therapies because their properties do not allow easy distribution throughout the body. We started this study because we wanted to

identify drugs which would be easier to use therapeutically. Although the particular compounds identified in this study did not kill prostate cancer cells very effectively, it is very promising that drug-like molecules were identified."

The study was funded by Prostate Cancer UK with support from the Movember Foundation as part of their initiative to develop new treatments for prostate cancer. A large proportion of the study was performed by first author Yoana Petrova, during the summer of 2015 whilst she was a Pharmacy undergraduate at the University of Bath. This placement was undertaken as part of the Biochemical Society Summer Vacation Studentship scheme. Yoana graduated from the Department of Pharmacy & Pharmacology in the summer of 2016 and is now undertaking a Ph.D.

Simon Grieveson, Head of Research Funding at Prostate Cancer UK said: "With one man dying from prostate cancer every 45 minutes in the UK there is a desperate need to develop new and effective treatments for the disease, and that's why it's so important that we continue to fund explorative studies like this. The protein AMACR has been shown to be present in larger quantities in aggressive prostate cancer cells, and this research group have successfully developed a technique to find the protein and monitor its activity. Further to this, they have now found certain compounds that can target this protein's activity in the lab, and stop the cancer cells in their tracks. The research is still in its infancy and is some way off from clinical investigation, however this is certainly promising and we look forward to seeing how this research progresses over the coming years."

In the United Kingdom, prostate cancer is the most common male-specific cancer with 47,151 new diagnoses reported in 2015 and 11,287 deaths in 2014. It accounts for 26% of all cancers diagnosed in men, with one in eight men being diagnosed with prostate cancer in their

lifetime. Although 84% of men will survive for at least 10 years with the disease, new treatments are urgently needed especially for those men diagnosed with more advanced disease.

More information: Yoana D. Petrova et al, Identification of novel small-molecule inhibitors of α-methylacyl-CoA racemase (AMACR; P504S) and structure-activity relationships, *Bioorganic Chemistry* (2019). DOI: 10.1016/j.bioorg.2019.103264

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