Improved treatment for prostate cancer through new PET imaging technology

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Prostate cancer kills over 10,000 men annually in the UK alone. Detecting prostate cancer typically starts through a blood test or biopsy, after which patients are referred for PET/CT imaging so radiologists can

see their tumor and any metastasis to decide on the best course of treatment. Positron Emission Tomography (PET) imaging is central to managing prostate cancer, although the production of radiotracers for PET imaging is usually complex and time-consuming which limits availability for patients.

Faced with this significant unmet need, King's researchers engineered a simple and quick-to-produce kit called "Galliprost," which improves the synthesis of radiotracers in PET imaging.

PET imaging relies on radiotracers such as gallium-68 to identify cancer cells. However, traditional methods of synthesizing gallium-68 radiotracers are complex and time intensive.

The key to this problem lies in the engineering of the chelating agents, which bind the gallium-68 to a biomolecule vector.

A suitable template for design emerged from an earlier body of work by Professor Robert Hider, Emeritus Professor at the School of Cancer & Pharmaceutical Sciences. Professor Hider had been working to develop hydroxypyridinones HOPOS as a treatment for β-thalassemia, a genetic blood disorder. It affects 330,000 infants per year globally and children only survive with transfusion of normal red blood cells. However, these frequent transfusions lead to a toxic build-up of iron and without treatment to remove excess iron patients die by their mid-twenties. Professor Hider worked in collaboration with Zhejiang University to produce the iron-chelating HOPO Deferiprone, now a standard treatment for β-thalassemia with a lifespan extension of 45 years on average for the 50,000 people treated each year.

Professor Hider's HOPOs also offered a solution for radiotracers, based on the chemical similarities between iron and gallium—the HOPOs were able to bind gallium just as well as iron. Working with Professor Phil

Blower, Head of Department of Imaging Chemistry and Biology, a tris(hydroxypyridinone) ligand (THP) was linked to PSMA, a molecule that binds to prostate cancer, to enable fast and efficient gallium-68 radiolabelling of a prostate cancer imaging agent. The radiolabelling could be done conveniently in five minutes instead of the several hours required for previous methods.

This formulation allows the tracer to be produced on site, in a manner suitable for frontline healthcare staff, without complex procedures or costly infrastructure.

A sterile kit—Galliprost—was subsequently engineered for producing the tracer quickly under clinical conditions. The Galliprost tracer has been clinically evaluated at King's and its partner NHS Trust in more than 1,500 prostate cancer patients, showing that it meets both its key aims of impacting patient management (about one third of patients had treatment decision changed as a result of the scan) and being very easily synthesized in the hospital setting.

The screening service was established in partnership with Guy's and St Thomas' Hospitals in 2017. More than 1,000 patients have benefited at Guy's and St Thomas' hospitals alone. This cost-efficient and effective treatment has provided cost savings of between £600 and £1,500 per patient.

The work by King's has also had led to world-wide distribution. In 2019, Theragnostics entered a commercial partnership with GE Healthcare to provide global distribution, preparation and further development of Galliprost. Theragnostics reported data from a phase two clinical study demonstrating that one third of newly diagnosed prostate cancer patients—and over 50% of patients with biochemically recurrent disease—had their treatment plans modified as a result of a GalliProst scan. The change in patient management increased to 75% in a post-

radical radiotherapy setting.

The HOPO chelator applications are not restricted to prostate cancer. By linking the HOPOs to molecules other than that target other diseases, the concept can be extended to develop imaging agents for other cancers. The team are developing these new agents, as well as working with Dr. Rick Southworth to explore the use of HOPOs to protect patients receiving cancer chemotherapy against heart disease which can be a side-effect of treatment.

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