Prostate Cancer Research

Transforming research. Transforming lives.

Research Strategy

Empowering researchers to transform lives

There is an urgent need to develop new effective treatments for men with prostate cancer, particularly advanced prostate cancer, and to carry out the underpinning research to achieve this.

Our Research Strategy describes how we aim to engage and empower scientists and clinicians to achieve this goal.

Improvements in therapies have been developed in the past decade, but one man still dies of prostate cancer every 45 minutes in the UK, and 250,000 men die each year from prostate cancer world-wide. Innovative thinking and new approaches are required to solve this problem, and existing treatments need to be applied more effectively.

OUR VISION

Prostate Cancer Research recognises that many new treatment approaches, new targets and drugs need to be discovered and translated to patient benefit.

Our vision is of a world free from the impact of prostate cancer.

We understand that the probability of a scientific breakthrough and achievement of our stated goals will quicken if we broaden the base of the research we fund. Our focus is on finding therapies for advanced disease but we recognise that important research is needed to develop classification systems that can be applied when treating metastatic and non-metastatic disease. We acknowledge that clues relevant to men with advanced prostate cancer may be found in the early evolution of the disease.

We are committed to the goals of health resource equality and understand that the resources of the National Health Service are finite and would encourage research that aims to reduce the cost of prostate cancer treatment in the long term for the patients in the UK, primarily, but also around the world.

Targeting with a single drug or treatment currently does not cure the disease. Multiple treatments may need to be integrated for the treatment of a single prostate cancer patient. We are therefore committed to co-operating with other organisations to combine

approaches, to support single outstanding projects, and to promote the careers of young scientists, who can carry the research forward with ever increasing improvements in advancement of knowledge and technologies. We are committed to continually researching and reviewing at which stage scientists find it hardest to get funding, and to considering how to adjust our strategy to improve impact across the sector.

We are committed to ethically conducted research, a robust but rapid process of scientific peer review, allowing support to be quickly directed to innovative projects with fewer non-essential or administrative encumbrances.

OUR SCIENTIFIC APPROACH

Prostate Cancer Research (PCR) is dedicated to funding research that will improve the lives of and/or cure men with prostate cancer, particularly advanced prostate cancer.

Definition of Advanced Prostate Cancer

By advanced prostate cancer we mean disease that has spread outside the prostate and that may become, or is already, life threatening. We will fund research that demonstrates a clear intellectual relevance to the betterment of advanced prostate cancer patients.

Funding by Prostate Cancer Research

Our ambition is to become a world centre of excellence for prostate cancer research through funding excellent scientists and clinicians. Prostate Cancer Research scientists will be expected to carry out world leading research recognised for its originality, significance and rigour.

In assessing the scientific rigour of a proposal we follow AMRC guidelines and the norms of the sector. Areas of investigation should span one or more of the fields outlined in Table 1.

All funded teams, whatever their location, are considered to be part of the core Prostate Cancer Research group. PCR grantees are expected to work as part of a collegial academic group combining resources to target important problems relevant to men with advanced disease. Over the next two years we will work on new ways to support scientists funded by PCR. New grantees will be required to develop strategically important areas of research, to build solid links to existing groups, and to add new expertise. For a detailed list of the expectations of new members see Appendix: For New Members.

Scientific Peer Review

We know that objective peer review in reputable scientific journals is the life blood of any research activity. We are also committed to the Open Access philosophy adopted by all established research funders in the UK and elsewhere and also by the Research Excellence Framework in the UK.

Basic Science and Target Discovery

The conversion of a normal prostate cell into a life-threatening cancer cell is a complex process involving alterations in expression of thousands of many genes and changes in

multiple control pathways. We seek to support projects where there is clear evidence that the target or process under investigation is central to progression from early to advanced disease, rather than a subsidiary or supporting event. Or alternatively where a specific change in the advanced cancer cell can be used as an Achilles Heel to develop a new therapy.

Re-tasking of existing drugs is another possible strategy. Based on these principles several new treatments have been cultivated over the last decade. The new therapies relieve symptoms and prolong life, but seldom cure. There is therefore a need both:

A) to enhance existing treatments to further extend life and relieve symptoms

B) to discover and develop completely novel therapeutic approaches that have the potential to result in cancer cure

PCR currently funds the following basic science and drug discovery projects:

- Translating fundamental knowledge of stem cells and cancer biology into therapies (Dr Ahmed, Kings College. London), with particular emphasis on the Wnt pathway
- The development of a novel new way to harness immunotherapeutic properties of IL-15 (Dr Galustian, Kings College London)
- Preventing the spreading of the cancer cells by investigating the role of plexin proteins in underpinning metastasis (Dr Magali Williamson, Kings College London)
- The re-tasking of off-label Membrane Potential Regulating Compounds (ion channel and calcium store modulators) (Dr Ahmed, Kings College London)
- Driver genes and therapeutic targets in PTEN-deficient metastatic prostate cancer (Dr de la Rosa, University of Cambridge)
- Filling a critical knowledge gap in androgen receptor variant splicing to enable development of new prostate cancer therapies (Dr Gaughan, Newcastle University Centre for Cancer)
- PCR currently funds the following classification and drug targeting projects:
- Comprehensive characterisation of prostate cancer subtypes to inform precision medicine (Dr Brewer, University of East Anglia)
- Improving 17Lu-PSMA Therapy (Professor Cornelissen, University of Oxford)
- Using the prostate cancer CRISPR-Cas9 dynamic screening platform (ProCASP) to explore cellular responses to existing and emerging therapies (Dr Dev, University of Cambridge)

Classification and Drug Targeting (Personalised Medicine)

Prostate cancer is a clinically and molecularly heterogeneous disease. However no clear classification framework has been developed. The lack of a classification framework represents a major problem for the targeting of new therapies and in the development of personalised medicine. Stratifications have been proposed based on the presence of specific genetic alterations (e.g. ERG, ETV1, ETV4, FLI1, SPOP, FOXA1, and IDH1) and a number of rarer cancer subgroups have been defined (e.g. cribriform carcinoma, basal cell prostate cancer, neuroendocrine prostate cancer).

The clinical utility of these divisions in managing advanced disease is still under investigation, although the tailored targeting of patients with specific classes of genetic alteration (stratified medicine) represents a promising area of investigation, as illustrated by the use of PARP inhibitors in the treatment of patients harbouring BRCA mutation.

None-the-less there still is an urgent requirement for better classification frameworks that can used to assist targeting of therapies for advanced cancers, and for the development of linked tests that can be applied in the clinic, which we will consider funding.

Clinical Trials and Trial Support

A large number of clinical trials are underway aimed at testing new treatments for prostate cancer. Some of the major trials are shown in Table 3. We would like to support and develop links to existing clinical trials and help develop new clinical trials where this will allow the testing of discoveries made by Prostate Cancer Research projects.

We would also consider funding:

A) The development and use of model systems where these are required to test hypotheses and help devise new treatment as illustrated by our work at Cardiff

B) The development of new approaches for tracking and imaging cancer where improvements in monitoring the effectiveness of therapeutic approaches can be demonstrated, such as the use of PMSA staining for cancer imaging.

Our vision is to improve survival and quality of life for men who already have prostate cancer, and to find a cure for prostate cancer for the next generation of men. Accordingly we would consider supporting studies aimed at reducing the side effects of current therapies or focused on developing improved palliative care. In exceptional cases we would consider funding sociological and qualitative studies, particularly when they would lead to observations that could be subsequently tested in quantitative studies.

We recognise the value of biobanking samples from men with advanced disease and developing databases. We would welcome proposals where a well-defined benefit can be demonstrated and where there is an established link to existing PCR projects.

PCR currently funds the following Clinical Trials and Trial Support projects:

Models for testing new prostate cancer treatments (Professor Matt Smalley, Cardiff)

Pan-genome copy number profiling of men with advanced prostate cancer randomised to long-term androgen deprivation therapy alone or with docetaxel or abiraterone: a STAMPEDE consortium analysis of diagnostic tumour samples (Professor Attard, University College London)

The Androgen Receptor-amino terminal domain a Novel Druggable Target in the Treatment of Castrate Resistant Prostate Cancer (Professor McEwan, University of Aberdeen)

Germline and Early Disease

We would normally not fund research into early organ confined prostate cancer, germline alterations or the aetiology of prostate cancer. However, for outstanding studies where a strong link to advanced prostate cancer can be demonstrated we may make exceptions. We are specifically interested in research that will impact on the treatment of patients with advanced disease.

Partnerships and the Funding of Young Researchers

We are strongly committed to promoting the careers of young researchers.

To fulfil our goal of establishing Prostate Cancer Research as a world leading organisation for curing men with advanced prostate cancer strategic, partnerships with other organisations are welcomed. Partnerships could allow us to combine approaches or provide resources that are essential for achieving our research goals but currently missing from the PCR portfolio.

Further Information

Funding our research

PCR intends to fund research using funds raised through various fundraising activities, including events, trusts and foundations, major donors and companies.

In addition, PCR intends to partner and collaborate with other prostate cancer research and support organisations to maximise the amount of prostate cancer research that is carried out globally.

Details of grants provided by PCR

PCR intends to provide grants for research projects which are typically 3-5 years in duration.

Grants can include salary support, on costs and consumables. PCR will also be prepared to fund and support collaborations and conferences for its researchers. Additional support could be provided to improve efficiency and effectiveness of the initial grant.

Researchers supported by PCR are expected to work as part of a single collegial academic group combining resources to target important problems relevant to men with advanced disease. For a detailed list of the expectations of new members see here.

Who PCR will fund

PCR intends to fund research at highly-rated research institutions. This is assessed primarily through the Research Excellence Framework (“REF”), a periodic measurement of research quality in universities and other higher education institutions in the UK against international standards of excellence.

Applicants for major grants should at least have PhD qualification and the support of a senior researcher at their institution.

PCR intends to focus its resources on funding research in the UK initially, but would consider any research globally as the amount of research that we fund grows.

How PCR awards its grants

Initially, PCR will request interested scientists and researchers submit a short expression of interest. These will be reviewed by a Grant Review Committee and a shortlist selected. Shortlisted candidates will be asked to submit a full application which will be peer reviewed by international reviewers. Based on this, the Grant Review Committee will select successful applicants to be presented to the board for final approval. Further specific information will be provided on our website and as we launch specific funding calls.

APPENDIX

Table 1 – Science and Clinical Translation for Advanced Disease

Basic Science and Target Discovery	Prostate Cancer Classification and Drug Targeting (Personalised Medicine)
• Discovery and Development of New Drug targets • Immunotherapy • Stem Cell Research • Analytical Studies (Genomics, Proteomics, • Metabolomics) • Understanding Development and Progression • Bioinformatics Analysis of Large Datasets • New Imaging Approaches • Development of Newer and Cheaper Therapies	• New and improved Classifications based upon molecular basis of the disease • Distinguishing indolent vs aggressive cancer • Test Development • Stratified Medicine and Personalised Treatments

Clinical Trials and Trial Support	Germline and Early Disease
• New and Improved Treatments (Drugs, Radiotherapy, Immunotherapy) • Trials testing the re-tasking of Existing Drugs • Clinical Models for Drug Testing • Improved Imaging and Tracking • Reducing Side Effects • Better Palliative Care • Sociological Studies Including Qualitative Research • Biobanking and Databases	• Information Relevant to Advanced Prostate Cancer • Relationship to Environment and Diet

Table 2 - New Therapies for Advanced Prostate Cancer

The standard treatment for metastatic prostate cancer is androgen withdrawal by orchiedectomy or drug treatment. On average this controls the cancers 18 to 36 months before castration-resistant disease develops. New treatments presented in this table can prolong life through targeting of newly presenting or castration resistant disease.

Drug	Putative Method of Action	Patient Target
Docetaxel *(Taxotere, Sanofi)*	Microtubule inhibition Inhibition of AR transport	Administer with Androgen Depravation Therapy
Cabazitaxel *(Jevtana, Sanofi)*	Microtubule inhibitor Overcomes resistance to docetaxel	Second-line treatment following docetaxel
Mitoxantrone *(Novantrone, Immunex)*	Topoisomerase inhibitor	Symptom relief
Abiraterone *(Zytiga, Johnson & Johnson)*	Irreversible CYP17 inhibitor Androgen ablation	Castration recurrence
Enzalutamide *(Xtandi, Pfizer)*	Prevents AR action	Castration recurrence
Radium-223 *(Xofigo, Bayer)*	Selectively binds to areas of high bone turn over	Bony metastases
Sipuleucel-T *(Provenge)*	Autologous Cellular Immunotherapy	Castration recurrence with minimal symptoms
PARP Inhibition *(Lynparza, AstraZeneca; Rubraca, Clovis)*	Inhibits repair of single strand Inhibits repair of single strand	Cancers with BRCA1/2 DNA breaks and PALB2 mutations
Platinum-Based Chemotherapy	Induce Double Strand Breaks and Cross-linking in DNA	Cancers with DNA repair defects
Immune Checkpoint Targeting *(Keytruda, Merck)*	High mutation rate leading to enhanced immune reaction	Cancers with mismatch Repair Defects

For New Members

All funded teams, whatever their location, are considered to be part of the core Prostate Cancer Research group. PCR grantees are expected to work as part of a collegial academic group and combining both intellectual and material resources, where possible, to target important problems relevant to men with advanced prostate cancer. New grantees will be required to develop strategically important areas of research, to build solid links to existing groups, and to add new expertise. This structure differs from that of many other research charities where projects may be funded at a single or small number of institutions.

Detailed expectations may include:

1. Liaising with other PCR teams to achieve clearly defined and achievable joint goals (these may have been stated in your grant application)
2. Sharing expertise and resources to assist other PCR teams
3. Attending joint annual PCR meetings
4. Attending PCR workshops, conferences and training (virtual or in-person) where required
5. Help to publicise PCR research
6. To join fundraising groups and events to present your PCR funded work as requested by the charity
7. Develop new collaborative programs of research and consortia to address important translational questions and approaches