Project title: Elucidating Relationships Between The Gut Microbiome And Lethal Prostate Cancer (PCa) Biology.

Project Summary:
PCa is the commonest cancer in men, a common cause of cancer mortality globally, and is increasing in incidence (Sartor & de Bono NEJM 2018). PCa aetiology remains poorly understood although inflammation has been implicated as has androgen receptor (AR) signalling in light of early genomic rearrangements at AR binding sites (de Bono et al, Nature Reviews Cancer 2020). Defective homologous DNA repair is also implicated, as having extrinsic factors including gut microbiome generated metabolites. We have recently reported that PCa sufferers accumulate androgen-generating microbiota (AnGM) which can fuel PCa growth. Studies by our collaborators have also reported that AR signaling induces double strand DNA breaks (Haffner et al, Nature Genetics 2010). We have recently identified microbiota metabolites through metagenomic studies and volatile organic compound (VOC) analyses of PCa sufferers. In this project, the candidate will work with a multidisciplinary team to elucidate relationships between gut microbiome metabolites and PCa AR signaling, inflammation and DNA damage, overseeing an ongoing clinical trial (NCT06126731) of multiple antibiotics followed by probiotics that involves collection and analyses of serial stool metagenomic studies, plasma metabolomic analyses, tumour biopsies and VOCs. The candidate will be expected to work both in laboratory and clinic, oversee analyses conducted at both The ICR and Imperial and collaborating laboratories.

Aims:

- To elucidate dysbiosis-associated biochemical pathways in PCa sufferers, comparing these with healthy controls, and determining their clinical relevance.
- To correlate changes in microbiota and microbiota derivatives including breath and plasma metabolomic signatures in PCa sufferers following antibiotic and probiotic therapy in the PROMIZE clinical trial (NCT06126731).
- To assess the impact of PCa dysbiosis associated metabolites on PCa biology in preclinical *in vitro* and *in vivo* PCa model studies.

Supervisory Team: Prof Johann de Bono is a clinician-scientist at The ICR/RM with a strong track record in prostate cancer translational and clinical research. **Prof Julian Marchesi** is a Professor of Digestive Health at Imperial College and is a leading expert in the gut microbiome and its impact on human health and disease. **Dr Jia Li** is a Reader in Biological Chemistry at Imperial College and a Co-Lead of the Section of Nutrition in the Department of Metabolism, Digestion, and Reproduction and leads microbiome metabolomic efforts.
Clinical Specialities: The suitable candidate will be planning/undergoing training in medical or clinical oncology or urology with a primary interest in prostate cancer.