Hereditary Prostate Cancer: From Gene Discovery to Clinical Implementation

ABOUT THE LECTURE

Prostate cancer demonstrates a high degree of heritability which has prompted the search for genetic factors contributing to this common disease. In general, family-based studies using linkage analysis have not been successful in identifying rare, highly penetrant gene mutations associated with hereditary prostate cancer (HPC). One exception is the discovery of *HOXB79* as a prostate cancer susceptibility gene based on fine-mapping of a candidate linkage region on chromosome 17q21-22. Our laboratory team identified a recurrent *HOXB79* mutation (G84E) occurring in a subset of chromosome 17q 21-22 linked families. Additional studies conducted by us and others have shown that 1) the *HOXB79* G84E mutation is more common in men with early-onset and/or a positive family history of prostate cancer, 2) the mutation is specific for prostate cancer risk, 3) the G84E mutation accounts for ~5% of HPC worldwide, and 4) the mutation occurs on a common haplotype consistent with a founder effect. More recently, studies of men with metastatic prostate cancer have led to the recognition that germline mutations in DNA repair genes (BRCA1/2, ATM, etc.) may occur in 5-10% of men with advanced prostate cancer. This finding is important for patients because of prognostic and therapeutic implications (responsiveness to platinum and PARP inhibitors) and for family members. Finally, GWAS has resulted in the identification of over 100 SNPs associated with prostate cancer. These markers may be useful alone or in combination with rare mutations to help clarify prostate cancer risk in conjunction with other clinical tests. In summary, while we have made significant strides in characterizing the germline mutational landscape of prostate cancer, opportunities still exist for gene discovery as well as translating this information into clinical management of patients.

Speaker: **Prof Kathleen A. Cooney, MD MACP**
Chair, Department of Medicine
Duke University School of Medicine

Host: **Prof Patrick Casey**
Senior Vice Dean, Research
Duke-NUS Medical School

Date: **Tuesday, 6 August 2019**

Time: **12.00 PM - 1.00 PM**
(Light refreshments will be served at 11.30 AM)

Venue: **Duke-NUS Medical School**
Amphitheatre, Level 2

Contact Person: **Ms Kathleen Chan, Duke-NUS Research Affairs Department**
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ABOUT THE SPEAKER

Dr. Kathleen Cooney specializes in the care of men with advanced prostate cancer, and she investigates the genetic epidemiology of prostate cancer. She earned her MD from the University of Pennsylvania, and trained in Internal Medicine and Hematology/Oncology at the University of Michigan (UM). She was chair of Internal Medicine at the University of Utah and division chief of Hematology/Oncology and deputy director of the Comprehensive Cancer Center at UM. She joined Duke University in 2018.

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