

NOV **WED**
27 **10** **30**
AMSummerlee
Science Complex
SSC 2315

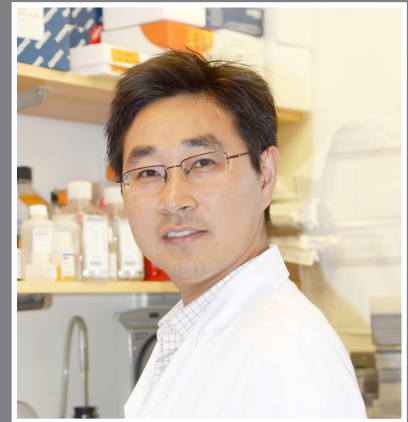
DR. HANSEN HE

SENIOR SCIENTIST, PRINCESS MARGARET CANCER CENTRE, UNIVERSITY HEALTH NETWORK

MCB HOST: DR. WEI ZHANG

Decode the noncoding cancer genome

More than 98% of the human genome is noncoding, which gives rise to almost 3 million regulatory regions and thousands of noncoding RNAs. Hundreds of prostate cancer (PCa) risk-associated SNPs are enriched in noncoding *cis*-regulatory elements (CREs) with their *modi operandi* still being elusive. Here, we performed a CRISPRi essentiality screen of these risk-associated CREs (rCREs) in PCa cell lines. The most essential rCRE regulates the oncogene *MYC* and long noncoding RNA *PVT1* and is overlapped with the SNP rs11986220. Suppression of this CRE reduces cellular proliferation and tumorigenesis. However, the function of this CRE is dependent on variable CTCF deposition at an intervening site, which forms an insulator loop blocking the CRE-*MYC* interaction. Conceivably, the causal effect of rs11986220 is also dependent on CTCF deposition at this site resulting in an underestimation of its genotype-*MYC* association using population-wide eQTL analysis approach. We detect rs11986220 as a *MYC* eQTL in prostate tissues only in individuals with low CTCF binding. Hence, our findings suggest that rs11986220 confers risk for PCa synergistically with low CTCF binding, warranting a paradigm shift in current approaches of assessing risks conferred by genetic predispositions.



All welcome to attend
Light refreshments will be served

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