Aggressive prostate cancer incidence in New Zealand—“united we fall, divided we stand”

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PROSTATE CANCER (PCa) IS ONE OF THE MOST SIGNIFICANT NON-SKIN CANCER MALE HEALTH CONCERNS WORLDWIDE,1 WITH AT LEAST ONE IN SIX PCa PATIENTS ESTIMATED AT BEING AT RISK OF DEVELOPING AGGRESSIVE PCa.2 This makes the identification of a strong predictive biomarker and/or treatment of this disease a priority, especially from the New Zealand perspective. The Australia/New Zealand region records the highest rates for age-standardised men with PCa, relative to the population of men worldwide.2,3

Although age, ethnicity and family history are among the most widely accepted risk factors for PCa, nothing concrete has yet been achieved to clinically alter the outcome.4 Other basic underlying components that connect these three factors remain lifestyle and nutrition. With progressing age, lifestyle changes; different individuals across various ethnicities enjoy different kinds of lifestyle; and certain families also have very personalised lifestyle factors, such as the amount and kind of meat eaten. Environmental factors play a major role in the expression of genes and the encoded proteins. Hence, work was started in identifying the most relevant external conditions in New Zealand for their potential effects on the high incidence rate of aggressive PCa.1,4–7

There are certain environmental, nutritional and lifestyle conditions prevalent in New Zealand, such as low levels of selenium in soil,9 deficiency of Vitamin D,9 high intake of fatty foods10 and rate of obesity,11 high percentage of tobacco smokers11 and ageing population12 that may combine in as yet unknown ways to increase the risk of aggressive PCa locally. We have been undertaking a holistic approach to understand the gene by environment interaction(s) and the risk of aggressive PCa in a cohort including New Zealand men of self-declared European ethnicity with different clinically diagnosed grades/stages of PCa, and gender matched healthy controls within a similar age range (Ethics reference NTY05/06/037 by Northern B Ethics Committee, New Zealand, previously, Northern Y Ethics Committee, New Zealand).

Our results have identified a number of single nucleotide polymorphisms (SNPs) statistically significantly associated with a risk of PCa and aggressive PCa. SNPs are
increasingly becoming strong biomarker candidates to identify susceptibility of PCa (among other cancers). Very interestingly, a number of these genes are related directly and/or indirectly to selenium metabolism, Vitamin D metabolism, obesity and fat metabolism, inflammation and inflammatory pathways, metabolism of tobacco constituents as well as being involved with androgen metabolism, mismatch repair and oncogenesis. PCa is a common but complex disease, involving a number of aspects of genetics such as failure of mismatch repair genes and over-expression of oncogenes, but it will be naïve to forget about the impact of external factors. Current research focus is on the identification of potential and universal biomarkers for aggressive PCa. But it is also well established that we are what we eat, and local external factors such as consumption of red meat, duration of exercise and consumption of dietary supplements will need to be examined. This will aid us in understanding how the progression of PCa can be checked; especially bearing in mind the prevalent health and lifestyle factors in New Zealand.

Although genome-wide association studies are used for the identification of the direct role SNP association plays as risk for aggressive PCa, and the various environmental conditions mentioned above have also been related to various non-communicable health diseases, our results indicate that SNP interactions with demographic and lifestyle factors could also add to the allelic effect of producing a modified risk of a disease. Those SNPs that have come up statistically significantly associated with the risk of aggressive PCa in our studies could be indicating a unique situation for New Zealand men with PCa. Our belief now is that a uniform multifactor approach will add value towards current clinical practices in improving diagnosis and along with detailed patient history is vital for combatting certain cases of aggressive PCa, which may be influenced by region-specific lifestyle factors as well as of universal genetic factors. In other words, some SNPs important for the progression of PCa may be triggered by local conditions. It is possible that local conditions also play a part for other chronic diseases as well.

The nature of PCa onset is being unraveled with further development of techniques for genomic analysis, with greater access through affordability and accuracy being key drivers of this trend. We propose that the model of patient health should unite the nature and nurture of pathologies in patients equally, and thus the risk of cancers, including PCa, should be region-specific rather than global to take into account local external factors. By identifying such local factors, preventative education programs can also be started to help reduce the risk of PCa as well as encourage early diagnosis of PCa before it becomes aggressive. Such programs may vary from population to population, taking into account lifestyle and nutritional differences. To conclude, we believe that physicians, nutritionists and dieticians, researchers, geneticists and statisticians should be “united” in their approach to tackling PCa, which is to discuss and follow preventative measures on a local, “divided” basis.
Competing interests:
Nil.

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