



Prostate Cancer: The Importance of Nutrition in Prevention and Treatment

Dr Anait S. Levenson

PROSTATE CANCER: THE IMPORTANCE OF NUTRITION IN PREVENTION AND TREATMENT

Prostate cancer is a leading cause of illness and death in men around the world, and to date, no prevention strategies have been discovered. **Dr Anait S. Levenson** and a team of cancer researchers from Long Island University in the United States of America are working to advance our understanding of how and why prostate cancer develops. Their important work also demonstrates how compounds found in foods such as grapes and blueberries may help prevent the development and progression of cancer.

Understanding Prostate Cancer

Cancer is a leading cause of death worldwide. In the United States of America, 1,898,160 new cancer cases and 608,570 cancer deaths were projected for 2021 but the reality for prostate cancer was even starker – an alarming increase was seen for both new cases and deaths.

There is currently no treatment available to prevent this type of cancer and 30% of men with risk factors placing them under active surveillance for prostate cancer develop more aggressive disease requiring intensive treatment such as surgery and hormone therapy (chemical castration), which have devastating effects on the individual and their quality of life.

As a result, scientists and healthcare professionals are dedicated to further understanding the pathways leading to prostate cancer and discovering new ways to prevent this disease. Dr Anait S. Levenson from Long Island University in the United States of America is one of the scientists driving a new understanding of the impact of diet on prostate cancer

progression and prevention.

Understanding the underlying pathways of cancer progression is key to being able to optimise diagnostics, improve treatment and develop new medicines. Dr Levenson and her team are particularly interested in the molecular and genetic mechanisms of prostate cancer development and progression. To date, the team's research has focussed on the MTA1 protein, an epigenetic molecule which is highly expressed in several types of cancer, including prostate cancer.

It is now known that MTA1 is involved in multiple stages of prostate cancer including inflammation, tumour growth and invasion. In addition to regulating survival pathways through various epigenetic modulations, MTA1 can impact molecules called microRNAs (miRNAs for short) which control multiple cancer development pathways, including enhancing cancer progression and the ability of the cancer cells to spread (a process known as metastasis). Dr Levenson and her team highlighted the role of MTA1 in prostate cancer progression by studying mice genetically

modified to overproduce MTA1. Their research showed that mice with higher levels of MTA1 were more likely to develop cancerous prostate cells than mice with normal MTA1 levels.

Diet and Cancer Prevention

Although the link between a person's diet and cancer risk is complicated, data have linked a diet high in dairy and fats with an increased risk of prostate cancer. More recently, diets high in certain fruits, vegetables, and soy foods have been associated with a decreased risk of prostate cancer.

As prostate cancer is an age-related and slow-growing disease likely influenced by nutrition, the use of diet for prevention and as an intervention alongside conventional treatment has huge potential. Nutrition-based intervention is a particularly exciting prospect given that there are currently no other preventative actions or treatment options available.

Most modern medicines are based on naturally occurring compounds.

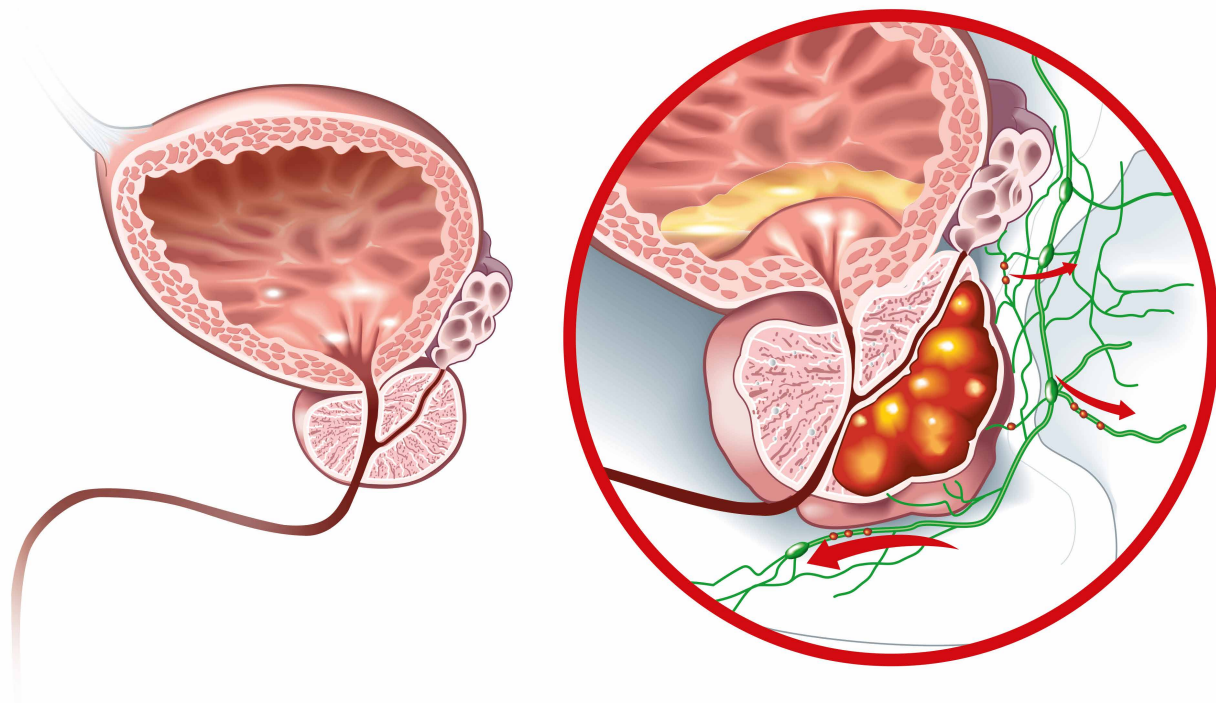


Illustration of healthy prostate and cancerous prostate



Grapes and blueberries contain high levels of stilbenes

Currently, scientists around the world are investigating the effects of diets high in these compounds as well as how these natural compounds can be modified to make more effective medicines.

Dr Levenson's team is currently investigating the preventive and therapeutic potential of naturally occurring compounds called polyphenols, which are found in plant-based foods such as fruits, vegetables, tea and dark chocolate. Previous studies have linked diets high in these compounds with a lower risk of developing cancer.

Importantly, Dr Levenson's research has focused on a type of polyphenol produced by certain plants when under environmental stress. These polyphenols, called stilbenes, are known to have antioxidant, anti-inflammatory, antimicrobial and anti-tumour properties. There are over 400 types of natural

stilbenes which can be found in foods such as grapes (including wine), blueberries and peanuts.

Dr Levenson's team is currently working on resveratrol (which comes from grapes and is probably the most well-known stilbene), pterostilbene (which comes from blueberries), and gnetin C (which comes from the melinjo plant, commonly used in Indonesian food).

While the exact mechanisms underlying the beneficial effects of stilbenes are not yet completely understood, Dr Levenson's team has shown how stilbenes can protect against prostate cancer by targeting MTA1 and altering miRNAs, leading to tumour-suppressing genes being turned on and thus, cancer progression and inflammation pathways being slowed down.

Stilbenes in Practice

In 2013–15, Dr Levenson's team treated prostate cancer cells in the lab with resveratrol (a polyphenol found in grapes and wine) and pterostilbene (a polyphenol found in blueberries). They discovered that these compounds suppressed the growth rate of tumour cells and that pterostilbene was more potent than resveratrol in inhibiting MTA1.

Following on from this, the team treated mice which were genetically modified to overproduce MTA1 with a pterostilbene-supplemented diet. They found that the mice with higher levels of MTA1 were more likely to develop cancerous prostate cells than mice with normal MTA1 levels. They also discovered that the mice who had eaten a pterostilbene-supplemented diet had



reduced levels of MTA1, and certain miRNAs, and subsequently, showed fewer cancerous prostate cells.

In 2020, the team added grape powder (which contains both resveratrol and pterostilbene) to the diet of mice who were genetically predisposed to developing prostate cancer. They found that the mice who were treated with grape powder had lower levels of tumour-causing miRNAs and that these mice had less abnormal prostate cell growth.

Less is known about gnetin C, a resveratrol dimer, most commonly found in the melinjo plant, which is part of Indonesian cuisine. In an impressive series of experiments, Dr Levenson's team treated mice with prostate overexpressing MTA1 with gnetin C, resveratrol, and pterostilbene, and found that gnetin C was much more efficient at slowing tumour progression than either of the other two compounds.

By analysing the prostate tissue, the team could see that gnetin C slowed the progression of prostate cancer by reducing cell division, inflammation, and the formation of new blood vessels and by inducing cell death (apoptosis). These studies highlight the role that MTA1 and miRNAs play in prostate cancer development and demonstrate that dietary stilbenes can reduce prostate cancer progression.

Dr Levenson's findings have exciting implications for the future of prostate cancer prevention and treatment. The team's latest findings show how including more stilbene-containing foods in our diets may help protect both the general population and 'at risk' patients from prostate cancer. In a recent publication, Dr Levenson stated 'A substantial portion of prostate cancer cases could be prevented by applying effective "prostate cancer-specific diets" that contain bioactive dietary polyphenols and micronutrients'.

The Future of Stilbenes

Whilst there have not yet been any human trials on the effect of stilbenes on prostate cancer development, the future of these compounds is bright as the evidence increases to support their use to prevent and treat cancer. These natural dietary compounds have been shown to protect against prostate cancer in mice, and remarkably, they have been shown to make drug-resistant cancer cells in the laboratory sensitive to treatment again. Whilst the significant amounts of stilbenes in foods such as blueberries and grapes may help to prevent cancer from developing, the ability to modify these natural substances into potent anticancer drugs is a thrilling development in the quest to provide better outcomes for cancer patients.



Meet the researcher

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Dr Anait S. Levenson obtained her medical degree from the Second Moscow State Medical Institute and then went on to receive a PhD in Clinical Immunology from the Institute of Tuberculosis, Moscow. Dr Levenson's interests lie in cancer research and pharmacology. Her research group focuses on understanding the molecular and genetic pathways leading to prostate cancer progression and metastasis, as well as investigating the potential of natural dietary compounds known as stilbenes for cancer prevention and treatment. Dr Levenson is an internationally recognised leader in nutritional cancer chemoprevention, and she has published over 60 journal articles and seven book chapters. She is an active member of several leading professional societies including the American Association for Cancer Research, the New York Academy of Sciences, and the American Council for Medicinally Active Plants where she served as President for two years (2020–2022).

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Thanks are also given to the numerous students, laboratory members and collaborators who have supported this research over the years

FUNDING

National Institutes of Health/National Cancer Institute
Department of Defence Prostate Cancer Research Program
The California Table Grape Commission

FURTHER READING

R Hemani, I Patel, N Inamdar, et al., [Dietary Pterostilbene for MTA1-Targeted Interception in High-Risk Premalignant Prostate Cancer](https://doi.org/10.1158/1940-6207.CAPR-21-0242), Cancer Prevention Research, 2022, 15(2), 87–100. DOI: <https://doi.org/10.1158/1940-6207.CAPR-21-0242>

P Parupathi, G Campanelli, RA Deabel, et al., [Gnetin C Intercepts MTA1-Associated Neoplastic Progression in Prostate Cancer](https://doi.org/10.3390/cancers14246038), Cancers, 2022, 14(24), 6038. DOI: <https://doi.org/10.3390/cancers14246038>

T Joshi, Patel I, Kumar A, et al., [Grape powder supplementation attenuates prostate neoplasia associated with Pten haploinsufficiency in mice fed high-fat diet](https://doi.org/10.1002/mnfr.202000326), Molecular Nutrition & Food Research, 2020, 64(16), e2000326. DOI: <https://doi.org/10.1002/mnfr.202000326>

S Dhar, A Kumar, L Zhang, et al., [Dietary pterostilbene is a novel MTA1-targeted chemopreventive and therapeutic agent in prostate cancer](https://doi.org/10.18632/oncotarget.7841), Oncotarget, 2016, 7(14), 18469–84. DOI: <https://doi.org/10.18632/oncotarget.7841>

SDhar, AKumar, AMRimando, et al., [Resveratrol and pterostilbene epigenetically restore PTEN expression by targeting oncomiRs of the miR-17 family in prostate cancer](https://doi.org/10.18632/oncotarget.4877), Oncotarget, 2015, 6(29), 27214–26. DOI: <https://doi.org/10.18632/oncotarget.4877>

