Prostate cancer and a possible link with schizophrenia

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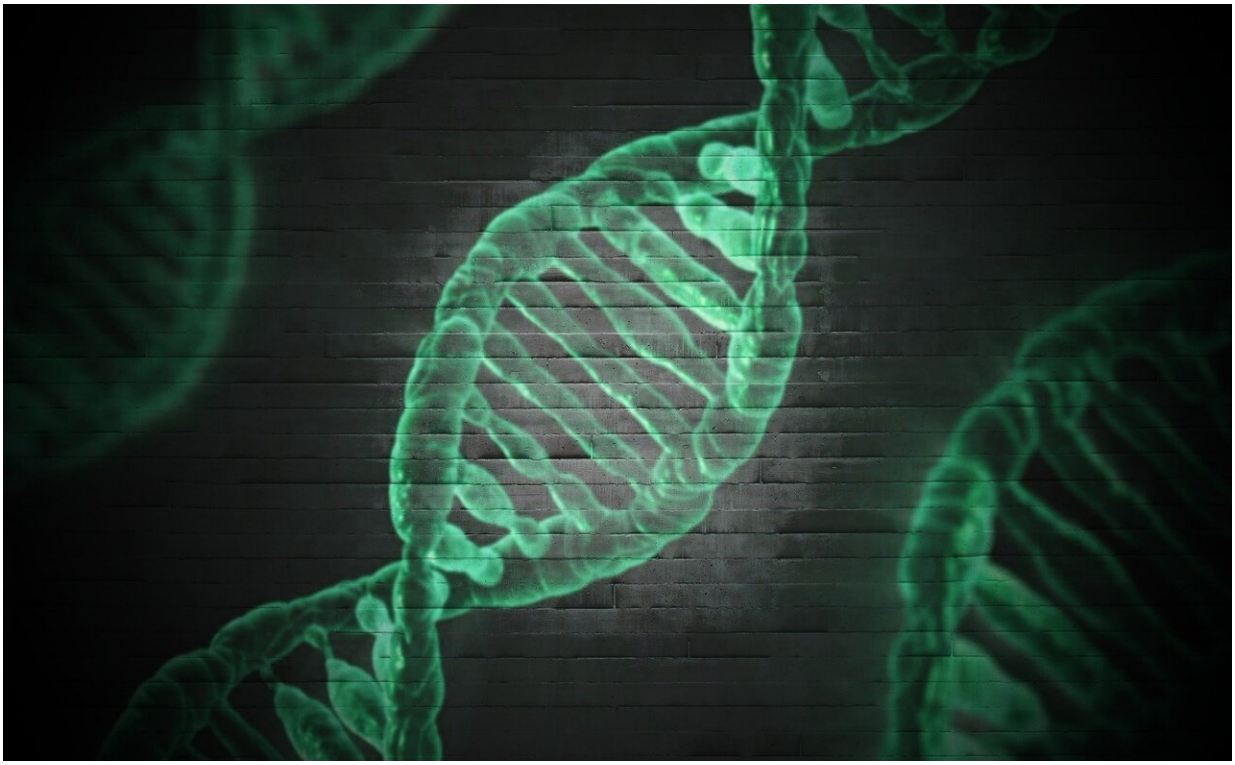

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Oncotarget published "The presence of polymorphisms in genes controlling neurotransmitter metabolism and disease prognosis in patients with prostate cancer: a possible link with schizophrenia" reported that polymorphisms of neurotransmitter metabolism genes were

studied in patients with prostate cancer (PC) characterized by either reduced or extended serum prostate-specific antigen doubling time corresponding to unfavorable and favorable disease prognosis respectively.

The following gene polymorphisms known to be associated with neuropsychiatric disorders were investigated:

- A. The STin2 VNTR in the serotonin transporter SLC6A4 gene;
- B. The 30-bp VNTR in the monoamine oxidase A MAOA gene;
- C. The Val158Met polymorphism in the catechol-ortho-methyltransferase COMT gene;
- D. The promoter region C-521T polymorphism and the 48 VNTR in the third exon of the dopamine receptor DRD4 gene.

The STin2 12R/10R variant of the SLC6A4 gene and the -521T/T homozygosity of the DRD4 gene tended to be overrepresented in PC patients with unfavorable disease prognosis.

These gene variants are regarded as protective against schizophrenia, and the observed trend may be directly related to a reduced PC risk described for schizophrenia patients.

These results warrant further investigation of the potential role of neurotransmitter metabolism gene polymorphisms in PC pathogenesis.

Dr. Vladimir N. Anisimov from The Petrov National Medical Research Center of Oncology said, "The importance of complex networks of heterotypic interactions between multiple distinct cell types (both malignant and normal) and regulatory circuits has now become widely recognized."

The traditional tumor-centric view focused exclusively on malignant cell

populations has largely been replaced with a concept of tumor microenvironment, the latter being regarded as a "dynamic interaction arena in which tumor cells interact with the extracellular matrix, resident and recruited cells, and soluble factors".

Although there is a general consensus that chronic stress and depression tend to result in an impairment of the immune responses and might facilitate cancer initiation and progression, while the risk of developing some cancers appears to be decreased in patients with schizophrenia.

Pancreatic Cancer is not only the second most common cancer in men, but this is also a condition characterized by a wide variation of severity that ranges from indolent to highly aggressive disease.

The latter feature of PC makes tumor growth monitoring a very important prerequisite for successful disease management, and repeated measurement of the concentration of a blood biomarker of PC, prostate-specific antigen, is generally accepted as an important prognostic tool for routinely monitoring patients with this condition.

It was noted above that psychiatric disorders may be associated with a seriously altered PC risk, but little is known about possible influences of patients' genetic background both on this phenomenon and on disease prognosis when PC is already present.

The Anisimov Research Team concluded in their *Oncotarget* Research Output that oncological conditions are known to occur less frequently in schizophrenia patients, and this phenomenon primarily affects men, being especially pronounced for PC.

Interestingly, PC has recently emerged as a cancer, development of which strongly depends on neurogenic regulatory pathways provided by nerves growing as an important TME component.

Furthermore, neurotransmitters, such as serotonin and dopamine, are now regarded as major factors modulating neoplastic growth through influences on angiogenesis and neoplastic cell proliferation.

The results presented in this paper indicate that the presence of certain polymorphic variants of the SLC6A4 and DRD4 genes related to serotonin and dopamine signaling pathways respectively appears to correlate with PC prognosis.

Further larger studies are needed for clarifying the role of neurotransmitter metabolism gene polymorphisms in PC pathogenesis.

More information: Gennady M. Zharinov et al, The presence of polymorphisms in genes controlling neurotransmitter metabolism and disease prognosis in patients with prostate cancer: a possible link with schizophrenia, *Oncotarget* (2021). DOI: 10.18632/oncotarget.27921

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