OPEN ACCESS Freely available online

ISSN: 2161-1041
Hereditary Genetics: Current Research

Commentary

Preimplantation Genetic Testing for Lower-Penetrance Cancer Pathogenic Variants

Xiaoqing Wang*

Department of Urology, Shanghai Jiao Tong University, Shanghai, China

DESCRIPTION

Advances in genetic technology have given individuals at risk for hereditary cancers new tools to make informed reproductive choices. Preimplantation Genetic Testing (PGT), originally developed to detect high-penetrance genetic mutations associated with diseases like cystic fibrosis and Huntington's, is now being applied to a broader spectrum of genetic variants, including those linked to cancer. However, a unique set of challenges arises when considering PGT for lower-penetrance cancer pathogenic variants, where the risk is increased but not guaranteed, and often influenced by a combination of genetic and environmental factors.

This article delves into the role of PGT in detecting lower-penetrance cancer variants, the ethical and clinical considerations it entails, and its potential benefits and limitations for at-risk individuals.

Understanding lower-penetrance cancer pathogenic variants

Lower-penetrance cancer pathogenic variants refer to genetic mutations that moderately elevate the risk of cancer but do not make its development inevitable. These variants are distinct from high-penetrance mutations, such as *BRCA1* and *BRCA2* mutations, which carry a high likelihood of leading to cancers like breast and ovarian cancer. Lower-penetrance mutations might increase cancer risk by two to five-fold, often influenced by lifestyle and environmental factors.

Examples include certain variants associated with colorectal cancer (such as MUTYH) and prostate cancer. For individuals with these variants, the lifetime cancer risk is increased but remains variable, often depending on gene-gene interactions and individual lifestyle choices. This variation complicates the decision-making process around using PGT, as the probability of cancer development is not definitive.

Preimplantation Genetic Testing (PGT) and its application in cancer

PGT is a reproductive technology that involves screening embryos for specific genetic conditions before implantation. It is typically used in conjunction with *In vitro* Fertilization (IVF), where embryos are generated and subsequently tested for genetic mutations. PGT can identify embryos carrying pathogenic variants, allowing parents to choose embryos that do not carry the specific mutation, thereby reducing the genetic cancer risk for the future child.

For high-penetrance cancer mutations, PGT is increasingly common as it significantly reduces the risk of children inheriting mutations that would likely lead to cancer. However, PGT for lower-penetrance mutations raises more complex questions, as the mutation may not always lead to cancer, and the level of risk may not justify the procedure's emotional and financial costs.

Clinical considerations for PGT in lower-penetrance cancer mutations

Risk assessment and counseling: Genetic counselors play a crucial role in helping prospective parents understand the relative risk posed by lower-penetrance cancer mutations. Unlike high-penetrance mutations, where risk predictions are clearer, the variability in lower-penetrance mutations requires careful interpretation of how environmental and lifestyle factors might affect risk.

Weighing the benefits: For some families, the peace of mind that comes from reducing cancer risk is sufficient to justify PGT. While PGT can prevent the transmission of specific genetic risks, it does not eliminate all potential health risks, as cancer is multifactorial and influenced by numerous non-genetic factors.

Costs and accessibility: PGT is a costly procedure, often not covered by insurance, especially for lower-penetrance mutations where the clinical justification may be less compelling. For many, the financial burden of IVF and PGT, along with the uncertain benefit, becomes a significant consideration.

Correspondence to: Xiaoqing Wang, Department of Urology, Shanghai Jiao Tong University, Shanghai, China; E-mail: wangxiaq2254@163.com

Received: 06-Nov-2024, Manuscript No. HGCR-24-27449; **Editor assigned:** 08-Nov-2024, PreQC No. HGCR-24-27449 (PQ); **Reviewed:** 22-Nov-2024, QC No. HGCR-24-27449; **Revised:** 07-Jul-2025, Manuscript No. HGCR-24-27449 (R); **Published:** 14-Jul-2025, DOI: 10.35248/2161-1041.25.14.307

Citation: Wang X (2025) Preimplantation Genetic Testing for Lower-Penetrance Cancer Pathogenic Variants. Hereditary Genet. 14:307.

Embryo selection and ethical implications: Lower-penetrance cancer mutations bring ethical challenges around embryo selection. Embryo selection based on minor or uncertain risks could lead to an increased societal focus on genetic "perfection," where even low risks are selected against. This slippery slope has implications for future generations and may shape societal views on acceptable levels of genetic risk.

Potential benefits of PGT for lower-penetrance mutations

Despite the challenges, PGT for lower-penetrance mutations can provide benefits. Some families with a history of certain cancers, such as colorectal or prostate cancer, may feel strongly about reducing any inherited cancer risk. Even if the risk is lower, avoiding the mutation in future generations might offer emotional relief and a sense of control over familial health history. Additionally, as genetic research advances, our understanding of risk factors for these lower-penetrance mutations will likely improve, enabling more refined predictions and personalized risk assessments.

Limitations and the future of PGT in lower-penetrance cancer risks

PGT for lower-penetrance mutations is not without limitations. Given the multifactorial nature of cancer, excluding a single gene variant does not eliminate the risk of cancer, as other genetic and environmental factors may still play a role. Moreover, as PGT becomes more widely available, the decision to use it for lower-penetrance mutations raises concerns about over medicalization and potential stigmatization of genetic variation.

Looking forward, advancements in genomic technology and greater insights into gene-environment interactions may allow for more accurate risk assessments, potentially leading to more informed choices regarding PGT for lower-penetrance mutations. Precision medicine approaches could help families make choices based on comprehensive risk profiles, balancing genetic predispositions with lifestyle and environmental factors.

CONCLUSION

PGT for lower-penetrance cancer pathogenic variants offers a promising option for families with a genetic predisposition to cancer, though it raises nuanced ethical and clinical questions. While the decision to use PGT for such variants is deeply personal, thorough counseling and risk assessment are essential to ensure informed and balanced choices. As science progresses, so too will our understanding of these variants, enabling individuals and families to make increasingly precise and tailored reproductive decisions.