RECENT ADVANCES

Applied Genomics in Obstetrics and Gynecology

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Abstract

The science of Genomics is an exciting new tool that can transform our approach to pregnancy and female reproductive health. In this article we provide a comprehensive overview of the use of genomics in different clinical aspects of obstetrics and gynecology, and their usefulness in routine clinical practice.

Keywords: Genetics, Genomics, Prenatal testing, Mutations.

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Introduction

Applied genomics in obstetrics and gynecology has revolutionized the way we understand, diagnose, and treat various conditions related to pregnancy and female reproductive health. The study of genomics involves the analysis of DNA, RNA, and protein sequences, and how they interact with each other to affect biological functions. In obstetrics and gynecology, applied genomics has helped us identify genetic variations and mutations associated with various reproductive disorders and helped us develop new diagnostic and therapeutic strategies.

Genetic Mutations

One of the most significant advances in applied genomics has been the ability to identify genetic mutations associated with inherited disorders. For example, mutations in the BRCA1 and BRCA2 genes have been linked to an increased risk of breast and ovarian cancer. Screening for these mutations in women with a family history of these cancers can help identify those at high risk and allow for early intervention and preventative measures, such as prophylactic surgery.

Infertility

Applied genomics has also improved our understanding of the genetic causes of infertility. Genetic testing can help identify chromosomal abnormalities or mutations associated with infertility in both men and women. For example, mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene have been linked to male infertility due to obstructive azoospermia, a condition where the vas deferens are blocked, preventing sperm from being ejaculated. "Y" deletion as well as sperm methylation tests can help us detect the cause of oligoteratospermia and help in improving the results. In women, mutations in genes such as FSHR, BMP15, and GDF9 have been linked to primary ovarian insufficiency, a condition where the ovaries stop functioning before the age of 40. Polycystic ovary syndrome (PCOS) is now known to be a polygenic disorder and genetic testing can help in management.

Epigenetic modifications are another cause of infertility. Epigenetic modifications refer to changes in gene expression that do not involve changes to the DNA sequence itself. Instead, epigenetic modifications occur through the addition or removal of chemical groups like methyl groups from the DNA molecule, which can affect how genes are expressed. Epigenetic modifications have been linked to many aspects of reproductive function, including oocyte maturation, fertilization, and early embryonic development.

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Prenatal Genetic Testing

Advances in DNA sequencing technologies have allowed for the non-invasive prenatal testing (NIPT) of fetal DNA from maternal blood. This testing can identify chromosomal abnormalities such as trisomy 21 (Down syndrome), trisomy 18 (Edwards syndrome), and trisomy 13 (Patau syndrome). Non-invasive prenatal testinghas replaced invasive procedures such as amniocentesis and chorionic villus sampling, which carry a risk of miscarriage. Additionally, prenatal testing has allowed for the identification of genetic mutations associated with inherited conditions such as cystic fibrosis, thalassemia, and sickle cell anemia. Genomics is also known to play a role in preeclampsia and gestational diabetes. New-born genetic testing is now preferred to conventional metabolic tests.

Gynaecological Cancers

Genomic analysis of tumor samples can help identify mutations that drive cancer growth, which can then be targeted with personalized

therapies. For example, Genomic profiling of endometrial cancer has identified several molecular subtypes of the disease, each with distinct genetic alterations and clinical outcomes. Endometrioid endometrial cancer, the most common subtype of endometrial cancer, is characterized by frequent mutations in PTEN and CTNNB1, while serous endometrial cancer has specific mutations in TP53 and frequent copy number alterations. Mutations in the PIK3CA gene have been found in up to 40% of endometrial cancers, and drugs that target this mutation have shown promise in clinical trials.

Genomic profiling of ovarian cancer has identified several molecular subtypes of the disease, each with distinct genetic alterations and clinical outcomes. For example, high-grade serous ovarian cancer, the most common subtype of ovarian cancer, is characterized by frequent mutations in TP53 and alterations in DNA repair pathways, while clear cell and endometrioid ovarian cancers have specific mutations in ARID1A and PTEN, respectively. Genomic analysis has also revealed potential therapeutic targets, such as poly ADP ribose polymerase (PARP) inhibitors, which are particularly effective in patients with BRCA mutations.

In cervical cancers, genomic analysis has shown that the integration of the HPV genome into the host genome is a critical event in the development of cervical cancer. Genomic analysis has also revealed the existence of different molecular subtypes of cervical cancer, each with distinct genetic alterations and clinical outcomes. For example, squamous cell carcinoma, the most common subtype of cervical cancer, is characterized by frequent mutations in the tumor suppressor gene TP53, while adenocarcinoma has specific mutations in the PIK3CA gene. Genomic analysis has also led to the development of novel therapies, such as immune checkpoint inhibitors, which have shown promise in the treatment of advanced cervical cancer.

Endometriosis

Applied genomics has also helped us better understand the complex interactions between genetics and environmental factors that contribute to the development of reproductive disorders. For example, a study published in the journal Human Reproduction identified a genetic variant associated with a higher risk of endometriosis. This variant was found to interact with exposure to dioxin, a toxic environmental pollutant, to increase the risk of endometriosis even further. Soon diagnostic biomarkers could be available for difficult-to-diagnose conditions like endometriosis by using miRNAs.

Logistics of Applied Genomics

The most heartening thing is the cost of genomic testing has rapidly come down and hence even in low and middle income (LMI) countries it is possible to carry out these tests routinely and help improve our diagnostic and therapeutic possibilities which will immensely benefit our patients. The glaring example is human papillomavirus (HPV) testing for both 16, 18, and other high-risk strains.

The time is not very far when every gynecologist and obstetrician will have to be well-versed with the knowledge of advances in genomics and be able to counsel patients regarding the various genetic tests and their implications.

The term "human genome epidemiology" (HuGE) denotes an evolving field of inquiry that uses systematic applications of epidemiologic methods and approaches in studies of the impact of human genetic variation on health and disease in populations.[1] The spectrum of topics addressed in human genome epidemiology range from basic to applied population-based research on discovered human genes. Human genome epidemiology can be used to assess: (A) The prevalence of gene variants in different populations; (B) The magnitude of disease risk associated with gene variants; (C) The magnitude of disease risk associated with gene-gene and gene-environment interactions; (D) The validity and impact of genetic tests for screening and prevention.[2]

Conclusion

Applied genomics has transformed the field of obstetrics and gynecology by providing new tools for the diagnosis, treatment, and prevention of reproductive disorders. Genetic testing has allowed for the identification of inherited mutations associated with cancer, infertility, and other conditions, while advances in sequencing technologies have allowed for non-invasive prenatal testing and personalized cancer therapies. As we continue to learn more about the complex interplay between genetics and environmental factors, applied genomics will continue to play an increasingly important role in improving reproductive health outcomes.

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