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Review Article

An Overview of Genetic Testing

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Abstract:

Since its emergence to the present day, genetic testing plays an essential role in many clinical aspects that include diagnosis, prevention and treatment. Development continues in genetic analysis as required by the latest genetic-related issues. In this review, we will discuss genetic testing techniques, the pivotal role they play in various clinical applications, and pharmacogenetic aspects of these tests.

Keywords: genetic test; pharmacogenetic; DNA

Introduction

Genetic testing is the analysis of genetic proteins such as DNA, chromosomes or RNA related to genetic or inherited diseases. [1] Genetic tests are classified into diagnostic tests and predictive tests. Diagnostic tests are competent to support the diagnosis of genetic diseases with a clear clinical picture, while prediction of future susceptibility to genetic disorders is the responsibility of predictive tests. [1,2]

Genetic studies are developing at a rapid pace, particularly in recent years. It has become an integral part of many medical fields. As its spread expands, we find that it has many techniques, such as detecting illnesses related to genetic mutations, karyotype, and phenotype. [3]

Among many applications and purposes, genetic testing has a high profile in pharmacogenetics, ancestral proof issues, and inborn metabolic disorders. [4]

In this review, we will discuss genetic testing techniques, the pivotal role they play in various clinical applications, and pharmacogenetic aspects of these tests.

Principles And Techniques of Genetic Testing

Genome study is one of the emerging specialties in general, and in the medical field in particular. Over the time, human genome investigations have made remarkable progress at the levels of diagnosis, prevention and treatment.

Back in the past, genetic analyses began with conventional cytogenic techniques where it was reported that the number of human chromosomes was 48 and continued until 1956 when Tjio and Levan corrected that misconception, the number of the chromosomes was 46. [5] Then, peripheral leucocyte culture method was combined with the fixation and staining methods that paved the way for the identification of chromosomal dysfunction related to congenital abnormalities. [6] Three years after discovering the correct number of chromosomes, the same scientists described genetic imbalances in both chromosomes (Down syndrome, trisomy 21), and sex chromosomes (Turner syndrome, monosomy X: and Kleinfelter syndrome, XXY). [7-9] In 1966, genetic analysis evolved further into possible sampling of cells derived from amniotic fluid prior to the birth of the fetus through a procedure called "amniocentesis"; through which chromosomal abnormalities can be detected during embryonic life. [10] Ten years after the last development, chromosomal structural anomalies can be seen with high resolution using high-resolution banding technique by synchronized lymphocyte cultures. [11] Seeing chromosomal aberrations with high resolution opens the way for further progress in various genetic aspects, such as: knowing the genetic causes of numerous genetic syndromes (e.g., Cri-du-Chat syndrome), the possibility of a child being born with many embryonic anomalies in balanced genetic translocations in repeated abortions. In 1902, Poveri launched the theory of somatic mutations that explained the interconnectedness between cancer and chromosomal abnormalities, where it was shown that only one genetic mutation in the responsible proteins of cellular division and growth could cause cancer. [12]

In 1982, genetic analysis progressed further and it became possible to identify chromosomal anomalies that needed accuracy exceeding 500 and 1,000 bands, fluorescence in situ hybridization (FISH) that studied those anomalies at the molecular cytogenic base. [13] Contrary to the above, a group of scientists developed FISH technique where they used nonradioactive probe in direct and indirect ways to mark specific DNA sequences. [14] Later, many methodologies based on FISH technique were developed, for example: spectral karyotyping FISH (SKY-FISH), quantitative FISH (Q-FISH), fiber-FISH, heterochromatin-M-FISH, multicolor FISH (M-FISH), combined binary ratio labeling FISH (COBRA-FISH), centromere-specific M-FISH (cenM-FISH). [15-21]

One of the most prominent roles played by diagnostic clinical FISH tests is the detection of subtelometric errors (deletion and duplication) that are directly responsible for mental disability and many congenital defects.

Unfortunately, FISH techniques were not characterized by low cost and time saving. Therefore, array-based comparative genomic hybridization technique has been developed that has adopted the concept of comparing the hybridization between normal DNA and amplified tumor DNA in metaphase environment. [22-24] It enabled scientists to identify subtelometric errors with higher resolution. By contrast, the technique of comparing genome variation did not have the ability to detect the recessive disease genes, mosaic aneuploidy, uniparental disomy (UPD), or heterochromatic rearrangements. Because of this, it became inevitable that a higher resolution method would be developed and the result was the integration of SNB and CGH arrays. [25] The combined arrays technique is precisely superior 10 to 15 times than FISH technique, and the substrate is only DNA without needing metaphase chromosomes. [26]

At the beginning of the 1990s, polymerase chain reaction (PCR) emerged, which revolutionized the world of molecular genome techniques and made it easier to make millions of copies of specific DNA sequences. [27] Restriction fragment length polymorphism (RFLP) and single-strand confirmation polymorphism (SSCP) are the most used methods for diagnosing genetic mutations, yet they were unable to identify all mutations. This was skipped by Maxam-Gilbert chemical sequencing technology, which relied mainly on the chemical modulation of DNA followed by division in certain bases. [28] The latter did not last long because it cannot handle long PCR fragments, and its chemical risks. Maxam-Gilbert chemical sequencing technique was quickly replaced by a manual Singer sequencing method that centered around the concept of dideoxynucleotide chain termination. [29]

With the emergence of the Human Genome Project in the United States of America that demonstrated the entire sequence of the human genome and which in turn included about 25 thousand genes did not stop there. [30,31] The effect was extended to reveal new mutations associated with genetic diseases. Singer's manual technique was not commercial those developments in terms of cost and time which necessitated the development of a massively parallel sequencing (MPS) technique that opened the door for the diagnosis of many diseases, such as: malignant tumors, metabolic neurological diseases, and mental disability. [31]

Clinical Applications of Genetic Testing

As explained in the definition of genetic testing, it encompasses a broad spectrum of age groups. Genetic testing purposes also multiply to include crucial aspects in clinical medical applications, such as: prevention, diagnosis, and treatment.

Diagnostic genetic tests are often performed to confirm a disorder in a patient with a clinical picture likely to return to a genetic disease. DNA-based technologies are now the prevailing techniques for diagnosing Duchene muscular dystrophy by detecting the deletion of dystrophin gene. [32] The result of DNA tests is the point between merely a genetic diagnosis or the continuation of a biopsy. 30% of Duchenne muscular dystrophy patients may have a negative result due to the fact that the technique used (DNA-based techniques) may not detect the deletion of Dystrophin gene. [32] This proportion of patients falls under the umbrella of heterogeneity of alleles, which means that there are many different mutations in the same gene and all lead to the same disease. [33]. For example: mutations in BRCA 1 and BRCA 2 genes are closely associated with breast and ovarian cancers. [34]. Also, patients with thyroid medullary carcinoma with mutations in the oncogene RET shows that cancer is part of MEN-2. 85% to 95% of relatives of thyroid medullary carcinoma patients have positive results by testing RET oncogene mutations. [35-37] On the other hand, genetic disorders can occur as a result of only one mutation in specific genes, such as in sickle cell anemia, where a particular single mutation in the beta-globulin gene ensures that adult hemoglobin converts to hemoglobin S. [38] Usually, the genetic diagnosis of this disease is done through hemoglobin electrophoresis as can the use of DNA-based techniques. However, DNA-based techniques have the added advantage of being diagnostic in the prenatal period. [39]

In terms of chromosomal disorders diagnosis where the defect is in the form of translocation, deletion, duplication, loss of chromosomal segment, presence of additional chromosome, or rearrangement of chromosomes, genetic cytogenic tests are optimal. [40,41] FISH and fluorescent DNA probes technique related to it enables investigator to identify chromosomal micro-mutations and deletions, such as: 22q11 deletion syndrome which cause congenital heart disease, learning difficulties, and palate anomalies. [42-44]

In addition to the diagnostic value, genetic tests offer a prognostic benefit for genetic diseases. When genetic pathogenic mutations are detected in a family member, the rest of the household is likely to be at a different risk of developing the disease. This allows for preventive action. This concept is clearly in the case of mutations in the oncogene RET that lead to thyroid medullary carcinoma. The presence of these genetic mutations requires direct testing of other family members and thyroidectomy in those who share the genetic mutation with the original patient. [45,46] Also, the offspring of Huntington's disease patients (autosomal dominant disorder causing motor and mental illness) are recommended to conduct genetic tests. Because there are mutations related to the disease, children are 100% susceptible to Huntington. [47] Unfortunately, until now there are no precautionary measures for this category. A pre-test consultation is therefore required to avoid negative psychological and societal effects. [47] In addition to medical reasons, genetic tests can be performed for personal decisions related to having children. In the case of autosomal recessive and X-linked diseases, the role of genetic testing is to identify the cases of carrier state. The incidence of genetic diseases varies depending on the type of defect. In autosomal recessive diseases (e.g.sickle cell anaemia) the rate of inheritance of the disease to the offspring is 25% provided that both mother and father are carriers of the disease. In the case of X-linked recessive disorders, carrier women can inherit 50% of each son. The precaution that can be followed when confirming a carrier state in the parents is to council them with the need for prenatal genetic testing that entails making a decision towards such pregnancy.

Doctors usually note that patients' response to the drug is different, some appear to respond at odds with expectations, and others may experience severe side effects. [48] We can attribute this variation among patients to the genetic factor, the enzymes responsible for drug metabolism, and lifestyle.

Cytochrome P450 is an enzyme containing heme responsible from metabolizing many compounds inside and outside the body. [49,50] Although it is controlled by approximately 57 cytochrome genes, CYP3A4, CYP2D6, and CYP2C9 are the most prominent ones in drug metabolism. [51] Cytochrome P3A5 is a component of the Cytochrome P3 group and is present in the kidneys, intestines, prostates, and liver. Also, it plays a reductive role in drug metabolism, so it can lead to varying responses among patients. [52] In the other hand, CYP2C9 and CYP2C19 genes act as an enzyme inhibitor leading to a declining metabolism of a range of drugs including sulfonyluria, warfarin, and phenytoin. The expression of these genes in some patients calls for reducing the doses of drugs affected by them, especially, warfarin whose accumulation leads to serious adverse consequences. [53]

Drug genetics play a pivotal role in the metabolism of many drugs, for example: azathioprine is an immunosuppressant used to treat autoimmune diseases and in organ transplantation. An enzyme thiopurine S-methyltransferase (TBMT) is responsible for his metabolism, which is made up of three non-functional alleles TPMT*2, TPMT*3A, and TPMT*3C. The prevalence of these alleles varies according to the ethnic group as the latter is the most prominent among Africans, while the second is the most common among Caucasians. [54] In cases of kidney transplant, these alleles can be associated together with azathioprine -related marrow suppression, but the category of patients with TPMT*3A high expression are subjected to life-threatening marrow failure. This requires reducing the dose of azathioprine when used for kidney transplant patients of Caucasian ethnicity. [55]

Also, asthma patients with mutations in 5-lipoxygenase-promoter region show a weaker response to lipoxygenase inhibitors. [56] The same concept applies to anti-hypertension, especially ACE inhibitors. Some patients with ACE insertion/deletion mutations have shown therapeutic responses different from those of patients they lack. [57] However, knowing the patient's pharmacogenetic and its association with the pharmacokinetic has become a given that must be considered to detail the drug at a dose that gives the best results with the least possible side effects.

Ethical Consideration of Genetic Testing

Since genetic tests will not stop at the point of confirming a diagnosis, but will go beyond to influence preventive and personal medical decisions, it is essential to provide comprehensive counselling to individuals or families who will undergo such tests. When genetic counselling is related to the development of clinical therapeutic plans, recommendation-based genetic counselling is the most appropriate. [58] If genetic testing has to be repeated here, no genetic counselling is required every time. However, genetic counselling is better not directed (i.e. the patient's ownership of all aspects of the disease that help him or her to make the appropriate decision of his or her own volition without giving recommendations), in cases of childbearing, and untreatable diseases. [59,60] Before taking the patient's consent to a genetic test, it is necessary to take into account the psychological, familial, and social effects that may result from it and to take the necessary precautions towards them. [61] In addition to the trade-off between the predictive value of the genetic test and its negative effect.

Conclusion

Since its emergence to the present day, genetic testing plays an essential role in many clinical aspects that include diagnosis, prevention and treatment. Development continues in genetic analysis as required by the latest genetic-related issues.

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References

1. Rayas AL, Jimenez JD. (2022). PRINCIPLES OF GENETIC TESTS. Fast Facts on Genetics and Genomics for Nurses: Practical Applications 2:159.
2. Catto AJ, Carter AM. (2003). Genetic principles and techniques. Stroke Genetics. 1:31.
3. Brezina PR, Kutteh WH. (2015). Clinical applications of preimplantation genetic testing. Bmj. 19;350.
4. Grosse SD, Khoury MJ. (2006). What is the clinical utility of genetic testing? Genetics in medicine. ;8(7):448-50.
5. Tjio J. H. and Levan A., (1956). The chromosome number of men, *Hereditas*. **42**, 1-6.
6. Moorhead P. S., Nowell P. C., Mellman W. J., Battips D. M., and Hungerford D. A., (1960). Chromosome preparations of leukocytes cultured from human peripheral blood, Experimental Cell Research. 20, 3, 613-616,
7. Lejeune J., Gautier M., and Turpin R., (1959). Etude des chromosomes somatiques de neuf enfant mongoliens, *Comptes Rendus*. **248**, 1721-1722.
8. Ford C. E., Jones K. W., Polani P. E., De Almeida J. C., and Briggs J. H., (1959). A sex-chromosome anomaly in a case of gonadal dysgenesis (turner′s syndrome), *The Lancet*. **273**, 7075, 711-713,
9. Jacobs P. A. and Strong J. A., (1959). A case of human intersexuality having a possible *XXY* sex-determining mechanism, *Nature*. **183**, 4657, 302-303,
10. Steele M. W. and BregW. R.Jr., . (1966). Chromosome analysis of human amniotic-fluid cells, *The Lancet***1**. 7434, 383-385, 2-2.0-0014021719.
11. Yunis J. J., (1976). High resolution of human chromosomes, *Science*. **191**, 4233, 1268–1270,
12. Boveri T., (2008). Concerning the origin of malignant tumours by Theodor Boveri. Translated and annotated by Henry Harris, *Journal of Cell Science*. **121**, 1, 1-84,
13. Langer-Safer P. R., Levine M., and Ward D. C., (1982). Immunological methods for mapping genes on Drosophila polytene chromosomes, *Proceedings of the National Academy of Sciences of the United States of America*. **79**, 14, 4381-4385,
14. Langer P. R., Waldrop A. A., and Ward D. C., (1981). Enzymatic synthesis of biotin-labeled polynucleotides: novel nucleic acid affinity probes, *Proceedings of the National Academy of Sciences of the United States of America*. **78**, 11, 6633-6637.
15. Schröck E., du Manoir S., Veldman T., Schoell B., Wienberg J., Ferguson-Smith M. A., Ning Y., Ledbetter D. H., Bar-Am I., Soenksen D., Garini Y., and Ried T., (1996). Multicolor spectral karyotyping of human chromosomes, *Science*. **273**. 5274, 494-497,
16. Martens U. M., Zijlmans J. M. J. M., Poon S. S. S., Dragowska W., Yui J., Chavez E. A., Ward R. K., and Lansdorp P. M., (1998). Short telomeres on human chromosome 17p, *Nature Genetics*. **18**, 1, 76-80.
17. Florijn R. J., Bonden L. A. J., Vrolijk H., Wiegant J., Vaandrager J.-W., Baas F., Den Dunnen J. T., Tanke H. J., Van Ommen G.-J. B., and Raap A. K., (1995). High-resolution DNA Fiber-Fish for genomic DNA mapping and colour bar-coding of large genes, *Human Molecular Genetics*. **4**, 5, 831-836,
18. Bucksch M., Ziegler M., Kosayakova N., Mulatinho M. V., Llerena J. C., Morlot S., Fischer W., Polityko A. D., Kulpanovich A. I., Petersen M. B., Belitz B., Trifonov V., Weise A., Liehr T., and Hamid A. B., (2012). A new multicolor fluorescence in situ hybridization probe set directed against human heterochromatin: HCM-FISH, *Journal of Histochemistry & Cytochemistry*. **60**. 7, 530-536,
19. Speicher M. R., Ballard S. G., and Ward D. C., Karyotyping human chromosomes by combinatorial multi-fluor FISH, *Nature Genet*. (1996). *ics*,. 4, 368-375,
20. Tanke H. J., Wiegant J., van Gijlswijk R. P. M., Bezrookove V., Pattenier H., Heetebrij R. J., Talman E. G., Raap A. K., and Vrolijk J., (1999). New strategy for multi-colour fluorescence in situ hybridisation: COBRA: Combined binary ratio labelling, *European Journal of Human Genetics*. **7**, no. 1, 2-11,
21. Nietzel A., Rocchi M., Starke H., Heller A., Fiedler W., Wlodarska I., Loncarevic I. F., Beensen V., Claussen U., and Liehr T., (2001). A new multicolor-FISH approach for the characterization of marker chromosomes: Centromere-specific multicolor-FISH (cenM-FISH), *Human Genetics*. **108**, 3, 199-204,
22. Solinas-Toldo S., Lampel S., Stilgenbauer S., Nickolenko J., Benner A., Döhner H., Cremer T., and Lichter P., Matrix-based comparative genomic hybridization: Biochips to screen for genomic imbalances, *Genes, Chromosomes and Cancer*. (1997) **20**, no. 4, 399-407.
23. Pinkel D., Segraves R., Sudar D., Clark S., Poole I., Kowbel D., Collins C., Kuo W.-L., Chen C., Zhai Y., Dairkee S. H., Ljung B.-M., Gray J. W., and Albertson D. G., (1998). High resolution analysis of DNA copy number variation using comparative genomic hybridization to microarrays, *Nature Genetics*. **20**, 2, 207-211.
24. Albertson D. G. and Pinkel D., (2003). Genomic microarrays in human genetic disease and cancer, *Human Molecular Genetics*. **12**, no. 2, 145-152,
25. de Leeuw N., Dijkhuizen T., Hehir-Kwa J. Y., Carter N. P., Feuk L., Firth H. V., Kuhn R. M., Ledbetter D. H., Martin C. L., van Ravenswaaij C. M. A., Scherer S. W., Shams S., Van Vooren S., Sijmons R., Swertz M., and Hastings R., (2012).

Diagnostic interpretation of array data using public databases and internet sources, *Human Mutation*. **33**, no. 6, 930-940,

26. Le Scouarnec S. and Gribble S. M., (2012). Characterising chromosome rearrangements: recent technical advances in molecular cytogenetics, *Heredity*. **108**, 1, 75-85,
27. Saiki R. K., Scharf S., Faloona F., Mullis K. B., Horn G. T., Erlich H. A., and Arnheim N., (1992). Enzymatic amplification of beta-globin genomic sequences and restriction site analysis for diagnosis of sickle cell anemia, *Biotechnology*. **24**, 476-480.
28. Maxam A. M. and Gilbert W., [57] (1980). Sequencing end-labeled DNA with base-specific chemical cleavages, *Methods in Enzymology*., 499-560,
29. Sanger F., Nicklen S., and Coulson A. R., (1977). DNA sequencing with chain-terminating inhibitors, *Proceedings of the National Academy of Sciences of the United States of America*. **74**, 12, 5463-5467,
30. Lander E. S., Linton L. M., Birren B. et al., (2001). Initial sequencing and analysis of the human genome, *Nature*. **409**, 860-921.
31. Brenner S., Johnson M., Bridgham J., Golda G., Lloyd D. H., Johnson D., Luo S., McCurdy S., Foy M., Ewan M., Roth R., George D., Eletr S., Albrecht G., Vermaas E., Williams S. R., Moon K., Burcham T., Pallas M., DuBridge R. B., Kirchner J., Fearon K., Mao J.-I., and Corcoran K., at all, (2000). Gene expression analysis by massively parallel signature sequencing (MPSS) on microbead arrays, *Nature Biotechnology*. **18**, no. 6, 630-634,
32. Korf BR, Darras BT, Urion DK. (2000). Dystrophinopathies [includes: Duchenne muscular dystrophy (DMD, pseudohypertrophic muscular dystrophy), Becker muscular dystrophy (BMD), and X-linked dilated cardiomyopathy (XLDCM)]. Seattle: GeneClinics,
33. Grody WW. (1999). Cystic fibrosis: molecular diagnosis, population screening, and public policy. Arch Pathol Lab Med; 123:1041-1046.
34. Brody LC, (1998). Biesecker BB. Breast cancer susceptibility genes: BRCA1 and BRCA2. Medicine (Baltimore); 77:208-226.
35. Weisner GL, Snow K. Multiple endocrine neoplasia type 2 [includes: MEN 2A (Sipple syndrome), MEN 2B (mucosal neuroma syndrome), familial medullary thyroid carcinoma
36. Raue F. (1998). German medullary thyroid carcinoma/multiple endocrine neoplasia registry. Arch Surg; 383:334-336.
37. Kebebew E, Ituarte PH, Siperstein AE, Duh QY, Clark OH. (2000). Medullary thyroid carcinoma: clinical characteristics, treatment, prognostic factors, and a comparison of staging systems. Cancer; 88:1139-48.
38. Ashley-Koch A, Yang Q, Olney RS. (2000). Sickle hemoglobin (HbS) allele and sickle cell disease: a HuGE review. Am J Epidemiol; 151:839-845.
39. Cao A, Galanello R, Rosatelli MC. (1998). Prenatal diagnosis and screening of the haemoglobinopathies. Baillieres Clin Haematol; 11:215-238.
40. Crow JF. (2000). Two centuries of genetics: a view from halftime. Annu Rev Genomics Hum Genet; 1:21-40.
41. Capone GT. (2001). Down syndrome: advances in molecular biology and the neurosciences. J Dev Behav Pediatr; 22:40-59.
42. Pergament E. (2000). New molecular techniques for chromosome analysis. Baillieres Best Pract Res Clin Obstet Gynaecol; 14:677-690.
43. McDonald-McGinn D, Emanuel BS, Zackai EH, Children's Hospital of Philadelphia. 22q11 Deletion syndrome. [Includes: Shprintzen syndrome, DiGeorge syndrome (DGS), velocardiofacial syndrome (VCFS), conotruncal anomaly face syndrome (CTAF), Caylor cardiofacial syndrome.
44. De Decker HP, Lawrenson JB. (2001). The 22q11.2 deletion: from diversity to a single gene theory. Genet Med; 3:2-5.
45. Wells SA Jr, Skinner MA. (1998). Prophylactic thyroidectomy, based on direct genetic testing, in patients at risk for the multiple endocrine neoplasia type 2 syndromes. Exp Clin Endocrinol Diabetes; 106:29-34.
46. Niccoli-Sire P, Murat A, Baudin E, et al. (1999). Early or prophylactic thyroidectomy in MEN 2/FMTC gene carriers: results in 71 thyroidectomized patients. Eur J Endocrinol; 141:468-74
47. Harper PS, Lim C, Craufurd D. (2000). Ten years of presymptomatic testing for Huntington's disease: the experience of the UK Huntington's Disease Prediction Consortium. J Med Genet; 37:567-71.
48. Evans WE, McLeod HL (2003) Pharmacogenomics—drug disposition, drug targets and side effects. N Engl J Med 348:538-549
49. Caraco Y (2004) Genes and the response to drugs. N Engl J Med351:2867–2869
50. Van Schaik RHN (2004) Implications of cytochrome P450 polymorphisms on the toxicity of antitumor agents. Ther DrugMonitor 26:236-240
51. Daly AK (2004) Pharmacogenetics of the cytochrome P450. Curr Top Med Chem 4:1733–1744
52. Lamba JK, Lin YS, Schuetz EG, Thummel KE (2002) Genetic contribution to variable human CYP3A mediated metabolism. Adv Drug Deliv Rev 54:1271-1294
53. Llerena A, Dorado P, O'Kirwan F, Jepson R, Licinio J, Wong ML (2004) Lower frequency of CYP2C9*2 in Mexican-Americans compared to Spaniards. Pharmacogenomics J 4:403–406
54. Krynetski E, Evans WE (2003) Drug methylation in cancer therapy: lessons from the TPMT polymorphism. Oncogene 22:7403-7413
55. Formea CM, Myers-Huentelman H, Wu RL, Crabtree J, Fujita S, Hermming A, Reed A, Howard R, Karlix JL (2004) Thiopurine S-methyltransferase genotype predicts azathioprine-induced myelotoxicity in kidney transplant recipients. Am J Transpl 4:1810-1817
56. Drazen JM, Yandava CN, Dube L, Szczerback N, Hippensteel R, Pillari A, Israel E, Schork N, Silverman ES, Katz DA, Drajesk J (1999) Pharmacogenetic association between ALOX5 promoter genotype and the response to anti-asthma treatment. Nat Genet 22:168-170
57. Arnett DK, Claas SA (2004) Pharmacogenetics of antihypertensive treatment. Drug Dev Res 62:191-199
58. Cummings S. (2000). The genetic testing process: how much counseling is needed? J Clin Oncol;18: -:60-64.
59. (1975). Genetic counseling. Am J Hum Genet; 27:240-242.
60. Michie S, Smith JA, Heaversedge J, Read S. (1999). Genetic counseling: clinical geneticists' views. J Genet Couns; 8:275-287
61. Hubbard R, Lewontin RC. (1996). Pitfalls of genetic testing. N Engl J Med; 334:1192-1194

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