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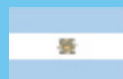
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Genetic counseling in post-genomic era: Don't pretend to know the meaning of a gene mutation if you don't know

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Abstract

In this post-genomic era, more and more susceptibility loci of many possible genetic diseases are published. As our knowledge about these susceptibility loci is limited and partial, we should be very careful and responsible when patients seek genetic counseling about these possible genetic diseases. We should apply Confucius's principle about knowledge and information to genetic counseling, and tell the truth to our patients about what we know and what we do not know. Like many other cancers, breast cancer is a very complicated, multifactorial disease; genetic factors, lifestyles and eating habits, environmental factors, and viral infections might be involved in breast cancer; hence, it is difficult to figure out the real etiology of breast cancer. It is not crystal clear that a person who carries mutations of the breast cancer 1, early onset and/or breast cancer 2, early onset genes would eventually get breast cancer in her/his lifetime. No person should undergo a preventive double mastectomy, unless we know the etiology of breast cancer someday.

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Key words: Genetic counseling; Genetic disease; Susceptibility loci; Breast cancer 1, early onset and breast cancer 2, early onset genes; Preventive double mastectomy

Core tip: Many susceptibility loci of possible genetic diseases are published. As our knowledge about these susceptibility loci is limited and partial, we should be very careful and responsible when patients seek genetic counseling about these possible genetic diseases. Currently, I have not seen any solid evidence in support of the linkage between breast cancer and breast cancer 1, early onset (*BRCA1*) or/and breast cancer 2, early onset (*BRCA2*); and it is not crystal clear that a person who carries mutations of the *BRCA1* and/or *BRCA2* genes would eventually get breast cancer in her/his lifetime. No person should undergo a preventive double mastectomy, unless we know the etiology of breast cancer someday.

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INTRODUCTION

You either know it or you don't, don't pretend to know it if you don't, this is the proper attitude toward knowledge-Confucius (551–479 BC).

Nenad *et al*^[1] raised concerns about genetic counseling in post-genomic era. Nowadays, it seems we have known so many susceptibility loci of many possible genetic diseases already, and more and more such susceptibility loci will be published in the future. More than 2000 years ago Confucius told us that we should handle information and knowledge very carefully and responsibly, the same attitude and spirit should be applied to genetic counseling in post-genomic era.

Firstly, we should indicate and list all those clearly established genetic diseases, such as Down syndrome^[2], sickle cell anemia^[3,4], Fanconi anemia^[5], and hemophilia^[6].

We know these genetic diseases relatively well, patients can have their better choices after receiving genetic counseling.

Secondly, we should also analyze and study the literature, in order to indicate and list all possible genetic diseases, such as some certain breast cancers^[7-12], autism^[13,14], some types of obesity^[15], and diabetes^[16-18]. As our knowledge about these susceptibility loci is limited and partial, we should be very careful and responsible when patients seek genetic counseling about these possible genetic diseases. We should tell them frankly what we know and what we do not know, and try our best to help them to make their hard decisions.

Thirdly, we should be able to tell patients that what diseases are definitely not genetic diseases, such as bacterial, parasitic, and viral infections, even though many congenital infections like toxoplasmosis, rubella, hepatitis B, syphilis, herpes, cytomegalovirus, and human immunodeficiency virus can be transmitted from mother to child during pregnancy, delivery or breastfeeding^[19].

Recently, actress Jolie^[20] underwent a preventive double mastectomy. I personally disagree with this action.

IS BREAST CANCER A GENETIC DISEASE DUE TO MUTATIONS OF BREAST CANCER 1, EARLY ONSET OR/AND BREAST CANCER 2, EARLY ONSET GENE?

Breast cancer 1, early onset (*BRCA1*) gene is located on chromosome 17q^[7-9], and breast cancer 2, early onset (*BRCA2*) gene is located on chromosome 13q^[10-12]. Besides *BRCA1* and *BRCA2*, there are some other susceptibility loci of breast cancers^[21-25].

A phenotype (trait) can be determined by one allele (dominant) or by two alleles (recessive). As we know, there are different types of genetic diseases. Some are autosomal-recessive genetic diseases like cystic fibrosis, sickle-cell anemia, and fanconi anemia (except Fanconi anemia subtype B); some are autosomal-dominant genetic diseases like Huntington's disease; Fanconi anemia subtype B, Duchenne muscular dystrophy, and Wiskott-Aldrich syndrome are X-linked recessive genetic diseases^[26], and Rett syndrome^[27,28], X-linked vitamin D-resistant rickets^[29] are X-linked dominant genetic diseases.

If some breast cancers were autosomal-complete dominant genetic diseases, then all of the carriers of *BRCA1* or/and *BRCA2* gene mutations should have breast cancer too. But from the published data, we could not conclude that was true, because only some of those carriers developed breast cancer in their lifetimes^[8,30-32]. We need to know whether breast cancer is an autosomal-incomplete dominant genetic disease. On the other hand, if some breast cancers were autosomal-recessive genetic diseases, then we need to confirm this is true: both of her/his parents of a breast cancer patient who carries the homozygous genes of *BRCA1* or/and *BRCA2* mutations

should be carriers or patients of *BRCA1* or/and *BRCA2* gene mutations. Homozygosity mapping should be performed to clarify this unclear problem^[33-40].

Currently, I have not seen any solid evidence in support of the linkage between breast cancer and *BRCA1* or/and *BRCA2*; and it is not crystal clear that a person who carries mutations of the *BRCA1* and/or *BRCA2* genes would eventually get breast cancer in her/his lifetime^[31,32].

CONCLUSION

Like many other cancers, breast cancer is a very complicated, multifactorial disease; genetic factors, lifestyles and eating habits, environmental factors such as radiation, toxic chemicals^[41,42], and viral infections^[43] might be involved in breast cancer; hence, it is difficult to figure out the real etiology of breast cancer. For a complex disease, a true linkage is so hard to find^[44], therefore, we should perform honest and strict epidemiological and genetic studies to evaluate the real risk of *BRCA1* and *BRCA2* gene mutations. While Angelina Jolie's natural breasts are gone already, we do not want to see more persons follow her to undergo such a preventive double mastectomy in the future, unless we are very clear and sure about the genetic link between some types of breast cancer and the mutations of *BRCA1* and *BRCA2* genes.

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