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Recruiting the Human Pathological Specimen Scientifically and Rightly for Cancer Molecular or Biological Researches

By Xu Han-You

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Methods: In this article, the author researched and provided facts and examples obtained from studies conducted in high grade institutes in China and others that the quality control of recruiting the human pathological specimens in cancer genetics researches are not treated with attention. In order to mend these problems, different methods for the recruiting of the human pathological specimen better have been created.

Findings: At least some research projects have not paid attention to the quality control of recruiting the human pathological specimens in cancer genetics researches in high grade institutes from China and others.

Keywords: recruiting the human pathological specimen; cancer research; genetics; research promotion; quality control; S T R E G A.

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Recruiting the Human Pathological Specimen Scientifically and Rightly for Cancer Molecular or Biological Researches

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Findings: At least some research projects have not paid attention to the quality control of recruiting the human pathological specimens in cancer genetics researches in high grade institutes from China and others. The research creates and provides 7 methods and directions on how to recruit the human pathological specimens scientifically and rightly. The most important method to recruit the human pathological specimen well is that, before recruiting the human pathological specimens in cancer patients, the histories of X-ray examinations, the examinations of the computed tomography, the chemo-therapy and the other treatment methods should be considered carefully. Because the X-ray, chemo-therapy and other radiation may heavily damage the structure of chromosomes and genes. So we must consider these things before the genome-wide association study and other cancer molecular or biological researches began.

Interpretation: If the cancer molecular or biological researches consider and reference these viewpoints before their researches. The bad situation of quality control of recruiting the human pathological specimens could be changed into better. So that the quality of the cancer researches could be promoted and enhanced a lot. The cancer prevention and treatment could be better. The author proposed to add an extension of the S T R E G A statement.

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I. Introduction

Recruiting the human pathological specimen scientifically and rightly should be very important for medical and biological researches. It is known to all medical and biological researchers that up to now, lots of recruiting the human pathological specimen have been done and lots of researches have been recruiting the human pathological specimen, including clinical and basic researches. Many high quality journals have published lots of research articles which recruited the human pathological specimen, especially the cancer researches.

As more and more cancer genetics researches have been done by recruiting the human pathological specimen. And more and more these kinds of researches are under way. Also, more and more cancer genetics researches are going to be done by recruiting the human pathological specimen. The quality control in the cancer genetics researches is the most important aspect. One of the important factors of the quality control is the quality control of recruiting the human pathological specimens which are used in these research projects for cancer genetics researches. As the genome-wide association study applies more and more human pathological specimens of cancer patients. Recruiting the human pathological specimens scientifically and rightly is the top agenda of the research quality control. But there is little report about the method of recruiting the human pathological specimens scientifically and rightly for cancer molecular or biological research in the cancer genetics research articles. Which expresses that it is imperative to pay more and more attention to this problem. In this review, I research and provide the fact that there are at least some research projects that have not paid attention to the quality control of recruiting the human pathological specimens in cancer genetics researches in high grade institute in China and others. And provide the methods and directions on how to recruit the human pathological specimens scientifically and rightly.

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II. The Fact of no Quality Control of Recruiting the Human Pathological Specimens in China

a) Some research projects searched have not quality control of recruiting the human pathological specimens in China

In one of the top cancer institute of China, the cancer genetics researches have no quality control of recruiting the human pathological specimens. But the articles of their researches have been published on the Nature Genetics and other high level cancer related journal. For example, in the research of Chen Wu, *et al* [1], they conducted a genome-wide association study (GWAS) and a genome-wide gene-environment interaction analysis of esophageal squamous-cell carcinoma (ESCC) in 2,031 affected individuals (cases) and 2,044 controls with independent validation in 8,092 cases and 8,620 controls. They identified nine new ESCC susceptibility loci, of which seven, at chromosomes 4q23, 16q12.1, 17q21, 22q12, 3q27, 17p13 and 18p11, had a significant marginal effect ($P = 1.78 \times 10-39$ to $P = 2.49 \times 10-11$) and two of which, at 2q22 and 13q33, had a significant association only in the gene–alcohol drinking interaction. The Nature Genetics published an article that involved 10123 cases of esophageal squamous-cell carcinoma sample and 10664 control sample. There is not any clear method report on how recruiting the human pathological specimens of 10123 cases of esophageal squamous-cell carcinoma (ESCC) sample. Also, there is not any clear method report on how recruiting the human specimens of 10664 control sample and also they say nothing of the quality control of recruiting the human pathological specimens. Even the genome-wide of the 10123 cases of esophageal squamous-cell carcinoma sample had been attacked or have been attacked by X-ray, chemo-therapy and other radiations or damages from repeated treatments and examinations. Furthermore, the history facts of X-ray, chemotherapy and other radiations or damages from examinations in 10664 control sample are confused. So it is much too easy to arouse the questions that if their research finding of nine new ESCC susceptibility loci have been caused by X-ray, chemo-therapy and other radiations or damages from repeated treatments and examinations applied on the ESCC patients before the research recruiting the human pathological specimens of 10123 cases of esophageal squamous-cell carcinoma.

In this top cancer institute of China, the other similar researches present the same situations or problems with no quality control of recruiting the human pathological specimens. The researches are studies of Chen Wu, et al. [2], research of Gao, Y. et al. [3] and Christian C Abnet, et al. [4], Meiying Li. et al.[5].

In an other institute, one of the research presents also the similar situation. In the research of Zi-Jiang Chen, et al [6]., they conducted genome-wide association study identified susceptibility loci for polycystic ovary syndrome on chromosome 2p16.3, 2p21 and 9q33.3. In their study, they only recruited from Han Chinese women presenting in reproductive and gynecology clinics in several collaborating hospitals. In all subjects from whom peripheral blood samples were obtained, they recorded such anthropometric variables as age, body height, weight and menstrual cycle, as well as selected endocrine and biochemical parameters. All polycystic ovary syndrome cases were diagnosed according to the Revised 2003 Consensus on Diagnostic Criteria and Long-term Health Risks Related to Polycystic Ovary Syndrome. But no quality control of recruiting the human pathological specimens was done. The quality control of recruiting the human pathological specimens in this study is excluding the damages of venous peripheral blood lymphocytes samples caused by X-ray or other physical and chemicals.

b) Some research projects searched have not quality control of recruiting the human pathological specimens in other country

It is the fact that the methods of the cancer genetics researches and genome-wide association study (GWAS) are all referenced methods of foreign countries, even in the top institutes in China. So the worse situation that no quality control of recruiting the human pathological specimens in China is infected each other among the foreign institutes and the institutes of China. This important aspect is supported by the fact that the top biological journal, the Nature Genetics, has been constantly publishing the research articles with no quality control of recruiting the human pathological specimens from China and foreign institutes.

At present, even the so called highest level in the world about the Pan-cancer analysis of whole genomes (PCAWG) also has shortcomings in recruiting cancer specimens. Because the research has only paid attention to the samples come from treatment-naive, primary cancers. But they have not scientifically and rightly paid attention to if their samples come from treatment-naive, primary cancers had diagnosis X-ray and other diagnosis damages to the genes of the samples [7]. And lots of researches have been referencing the samples doing as what the PCAWG has done.[8, 9].

c) Some research projects searched have not quality control based on S T R E G A and other international guidelines.

According to the guidelines of S T R E G A (Strengthening the Reporting of Genetic Associations), [10, 11]. the Consolidated Standards of Reporting Trials (CONSORT) [12, 13], and the Strengthening the

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Reporting of Observational studies in Epidemiology (STROBE) Statement [14, 15], some research projects searched in China have not quality control based on these international guidelines. Especially, these research projects have not population stratification about the disease risks. Their genome-wide association studies also have not either family-based designs or methods such as genomic control and principal components analysis to control for stratification. They say nothing about the research designs or methods to control the stratification of risk factors in research, diagnosis and treatment of the cancer patients, especially the risk factors of radiation and chemicals.

III. Methods and Directions on how to Recruit the Human Pathological Specimens Scientifically and Rightly

As the situation that no quality control of recruiting the human pathological specimens in China and other countries are severe. It is imperative to mend and change the bad situation at once. Because I am a medical professional and researcher. I can not help but do the research on these things. So the methods and directions on how to recruit the human pathological specimens scientifically and rightly have been researched as follows.

a) The time to recruit human pathological specimens in cancer patients and normal control groups should be in the same period. Because the human pathological specimens are easy to lose their structure of chromosomes and genes.
b) The position, where the human pathological specimens in cancer patients are recruited, should be the same as the normal control groups. Because the molecular pathology or molecular histopathology are different in various position from cancer patients and normal control groups.
c) The past human pathological specimens in cancer patients should not be used for cancer genetics research. Because the past human pathological specimens in cancer patients must be changed by environment and its own changes can develop as time goes on.
d) The top important thing is that before recruiting the human pathological specimens in cancer patients, the histories of X-ray examinations, examinations of the computed tomography, chemo-therapy and other treatment methods should be considered carefully. Because the X-ray, chemo-therapy and other radiation may heavily damage the structure of chromosomes and genes. So if we did not consider these things before the genome-wide association study and other cancer molecular or biological researches began. There was no way to do the scientific researches.
e) As radiotherapy is the most important therapy for cancer patients. The human pathological specimens from the cancer patients are often interfused with the heavy radiations. How to research scientifically and rightly on these pathological specimens are more important than finding new susceptibility loci in cancer patients.
f) The fixation, staining preparation, section and preservation of the specimens are also important. So the method for fixation, staining preparation, section and preservation of the specimens should be the same between the cancer patients and normal control groups.
g) The health examination of cancer patients and normal control groups by X-ray, computed tomography and other examinations should also be considered carefully before research.

IV. Discussion

The rapidly evolving evidence on genetic associations is crucial to integrating human genomics into the practice of medicine and public health. Genetic factors are likely to have an impact on the occurrence of numerous common diseases, and therefore identifying and characterizing the associated risk, or protection, will be important in improving understanding of etiology and potentially for developing interventions that might be based on genetic information.

The number of publications on gene-disease associations has increased tremendously, with the number each year having more than doubled between 2001 and 2007, with more than 30,000 published articles during that time. Articles on genetic associations have been published in about 1500 journals, in several languages.

Although there are a number of similarities between genetic association studies and “classical” observational epidemiologic studies of lifestyle and environmental factors, the former present several specific challenges including an unprecedented volume of new data and the likelihood of very small individual effects. Genes may operate in complex pathways with gene-environment and gene-gene interactions. Moreover, the current evidence base on gene-disease associations is fraught with methodological problems. These include inadequate statistical power; flawed study design; suboptimal study conduct and biased analyses; lack of standardization among studies; selective reporting of “positive” results; and poor or incomplete reporting of results even from well-conducted studies [10, 11].

Hopefully, the CONSORT, STROBE, and S T R E G A have highlighted the importance of quality control in recruiting the human pathological specimens on cancer clinical molecular diagnostic tests and basic molecular or biological researches.

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V. Conclusion

In order to mend the problems which there is no quality control of recruiting the human pathological specimens on cancer genetics and other biological researches in China and other countries at present. The methods how to do the better and recruit the human pathological specimen well have been created.

The research has found that at least some research projects have not paid attention to the quality control of recruiting the human pathological specimens in cancer genetics researches in high grade institute in China and others. The research creates and provides 7 methods and directions on how to recruit the human pathological specimens scientifically and rightly. The most important method to recruit the human pathological specimen well is that, before recruiting the human pathological specimens in cancer patients, the histories of X-ray examinations, the examinations of the computed tomography, the chemo-therapy and the other treatment methods should be considered carefully. Because the X-ray, chemo-therapy and other radiation are heavy damage to the structure of chromosomes and genes. So if we did not consider these things before the genome-wide association study and other cancer molecular or biological researches began. There was no way to do the scientific researches.

If all the genome-wide association study and other cancer molecular or biological researches consider and reference my viewpoints before their researches. The bad situation of quality control of recruiting the human pathological specimens could changed into better. So that the quality of the cancer molecular or biological researches could be promoted and enhanced a lot. The advancing of the cancer prevention and treatment could be great.

This work may be referenced to be an extension of the S T R E G A statement and should be used to guide the research designs or methods to control the stratification of risk factors in the processes of diagnosis and treatment of the cancer patients, especially the risk factors of radiation and chemicals and to recruit the human pathological specimens rightly on cancer clinical molecular diagnostic tests and basic molecular or biological researches.

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Conflict interest statement:

There is no conflict of interest for this paper.

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