

# Genetics in Prevention and Treatment of Cancer

## Introduction

Cancer prevalence is on the rise. According to the International Agency of Research for Cancer (IARC), a 50% increase in cancer rate within the next 20 years is expected (1). The prevalence of malignant cancers and cancer mortality are also on the increase. This issue is a major concern, especially in low to middle income countries where over a quarter of disease related deaths are linked to cancer (1,2). In light of the growing prevalence of cancer and its implications to modern health care, equal impetus is being paid by the scientific community to research on the disease. However, most of the research has been dedicated to studying environmental influences on cancer development, and genetic influences (or determinants) has been up until now largely overlooked. Recently, the role of genetics in the development of cancer is being more widely recognised. The advancement of genetic research and technologies is providing new possibilities for the screening, management and treatment of cancer. These new possibilities call for an evaluation of the future in cancer prevention, management and treatments as well as the vital role of genomic know-how.

This paper aims to examine the significance of a genetic role in the origins of cancer, and to discuss the application of genetics and new genetic technologies to be used in management and treatment of disease. It advocates a comprehensive approach, one which includes genetic awareness in cancer prevention and treatment.

With each passing minute, the cancer death toll is rising and more people are being diagnosed with the disease. According to the World Cancer report, 10 million new cancer cases are diagnosed annually, with over 7.1 million deaths due to cancer each year that contribute to 12.6% of the global mortality rate [1]. The Report estimates that about 22 million people worldwide are currently living with an oncological disease. Since 1990, cancer incidence has risen about 19% and cancer mortality has risen approximately 18% globally within the last decade. These numbers continue to increase.

Furthermore, countries witness a variation in the prevalence of cancer cases as well as in the types of cancer that afflict upon their populations (Table 1). These rate differences suggest underlying variations in genetic and environmental factors within these regions that possibly contribute to the onset and development of cancer.

## Genetics vs. Environment

Causal factors fall usually into two broad categories: environmental and genetic. The discussion between environment and genetics raises the age old dichotomy between nature and nurture. In population cancer research, the question repeatedly posed is—do environmental factors cause indigenous populations of a region to develop particular cancers? Or, are these individuals biologically predisposed to the disease by the virtue of their genetic makeup? For the majority of cases, neither nature nor nurture can be examined autonomously. Instead, many cases of cancer fall in the middle, experiencing the significant weight of both the environment and genes [2]. While current research has focused on the influence of the environment in cancer development, the inverse relationship between genes and environment necessitates more research in the realm of genetics. Further scientific investigation is needed to address the role of genetics in cancer. To simply look at environmental influences without acknowledging a genetic influence in cancer causation be to adopt only half of a good anti-cancer approach, this strategy is insufficient for combating cancer. Individuals are often inherently at a higher risk for cancer due to their genetic composition, and that this predisposition needs to be taken into account in conjunction with the person's lifestyle habits

when evaluating a person's overall risk for cancer. Knowledge of such a predisposition would allow the individual to make healthier lifestyle choices so as to decrease the existing risk of disease. For individuals affected by cancer, which is a significant percentage of the population, this information is critical to the prevention and avoidance of cancer.

Lifestyle and dietary habits, occupational and environmental exposures are all part of "environmental" factors that contribute to the origins and progression of cancer. In high income countries these factors more commonly include habits such as tobacco and alcohol consumption, excessive exposure to sunlight, chemicals and toxins. In low to middle income countries the culprits of cancer are frequently infectious agents such as viruses, parasites and bacteria, where the available treatment, if any, is inadequate to counter infection. In many cases untreated chronic disease can lead to cancer. Likewise, excessive exposure to asbestos is associated with lung cancer. Human papillomavirus is known to cause about 95% of cervical cancers [3]. In these scenarios, the environment seems to play a principal role in determining an individual's risk of acquiring cancer. Conversely, genetic predisposition, or certain genetic mutations that make the individual susceptible to cancer development, has been known to play a major role in many cancers. For instance, familial retinoblastoma is almost entirely dependent on genetic predisposition and the environment has very little impact.

### **The Role of Genetics in Cancer Development**

Presently the role of genetics in the development of cancer is still being unearthed. Virtually every cancer occasionally runs in families (which could reflect host or environmental factors, or both); and, each cancer type is an occasional complication of some hereditary condition, usually a rare one. So, while, most cancers have some genetic determinants, few common cancers can be largely attributed to a single major mutant gene, but for breast, colon, prostate, ovary, and lung cancer rare mutant genes that enormously increase the risk have been discovered. Consequently critics argue against extensive gene research, claiming that because the overall of population identified to have cancer linked to genetic predisposition is relatively small compared the total cancer patients, genetics is not a worthwhile study. Meanwhile, research has already established that genetic predispositions to cancer increase risk for developing cancer significantly (in some cases, a mutation on a specific gene can increase breast cancer risk by a startling 80%). Knowledge of genetic predisposition to cancer and corrective lifestyle changes can help an individual avoid the chances of developing the disease, and in some cases avoiding it all together.

Cancer cases may fall under one of three categories: inherited, familial and sporadic. Inherited cases of a dominant type include the occurrence of cancer throughout generations, frequently a result of direct germline mutation, passed successively from parent to offspring. Approximately 4% (1 to 20%, dependent of type) of cancer cases can be characterised as inherited cancers. A larger percentage of cancers are familial, and involve mutations on multiple susceptibility genes that increase an individual's risk for cancer. Familial cancers appear to run in the family, yet the frequency of the cancer does not follow the same pattern as those for inherited cancers. Because multiple genes are involved familial cancers, resulting in an irregular frequency of occurrence, it is far more difficult to predict the pattern. Usually, families with familial pattern of cancer inheritance have higher than normal prevalence, however not in a predictable pattern of incidence. Sporadic cancer cases are those where an individual randomly develops cancer in the absence of any familial pattern.

## *Susceptibility Genes*

Since many familial aggregations of cancer remain unexplained geneticists believe that many more susceptibility genes contribute to cancer development than are presently known. Especially when taking into account that all the effects of the genetic susceptibility genes for breast cancer together cannot explain all the cases of observed familial clustering. Further progress in tracking down susceptibility genes will be facilitated by the information and resources of the Human Genome Project.

The 'Human Genome Project' is expected to improve our molecular-based strategies for the identification of the genes and, thereby, improve our understanding of the genetic and environmental interactions in causing various diseases and cancer, in particular. With the human genome mapped out, scientists can more easily identify "genes of interest" (in this case relevant to cancer development), and eventually determine the functional significance of that particular gene.

Among susceptibility genes which are and will be found to be responsible for a small number of "cancer-families," will be a number of identified genes contributing to the cancer risk of a large percentage of familial aggregated forms of cancer. Three of the most studied cancers with these susceptibility genes include breast, colorectal and prostate cancer. In breast cancer, the two major genes of interest are the *BRCA1* and *BRCA2* gene. *BRCA2* acts as a tumor suppressor gene, that it is involved in regulating the cell cycle. It activates cell apoptosis, or cell death, if a cell is unable to function properly. In some breast cancer patients, the *BRCA2* site is mutated, and produces an altered protein product which is no longer capable of initiating apoptosis. Between 13 and 18 percent of breast cancers can be traced to mutations on the *BRCA1* or *BRCA2* gene. Not only do the BRCA mutations contribute to development of breast cancer, but they also have been found to have a role in ovarian cancer, and more even recently, in cancer of the fallopian tube. A 2002 study by the University of Cambridge found that in British women those over age 70 with a *BRCA1* mutation had a 36% risk for breast cancer and 28% risk of ovarian cancer [4]. Individuals with the *BRCA2* mutation had about a 69% chance of developing breast cancer and a 17% risk for ovarian cancer [4]. These rates are alarming compared to the 5% risk of breast cancers for women over 70 years of age without the BRCA mutations, demonstrating the huge increase of risk with the gene mutation [4]. An interesting trend between the BRCA mutations and frequency of cancer noted in the same research is that the risk consistently increases until a certain age, and then steadily declines [4].

Table 2 shows the prevalence of susceptibility genes of the major types of cancer.

Type of Cancer	Susceptibility Gene	Frequency in total Number of Cancer Cases
Breast	<i>BRCA 1 &amp; 2</i>	20%
	<i>TP53</i>	20%
Colorectal	<i>hMLH 1</i>	
	<i>hMLH 2</i>	
	<i>IGF2</i>	
Ovarian	<i>BRCA 1 &amp; 2</i>	10%
	<i>hMLH 1</i>	
	<i>hMLH 2</i>	
Lung	<i>CYP1A1</i>	
Prostate	<i>HPC2</i>	

### ***Testing for Germline Mutations***

Because of polymorphisms of the BRCA mutations, individuals with family members known to have had breast cancers have a greater chance for carrying the BRCA mutations. Genetic testing can confirm whether or not the individual has these mutations. Individuals are encouraged to consider genetic tests, especially a parent or sibling has a BRCA mutation. In fact, genetic testing is fairly easy to undergo, and several commercial options exist. The only issue at hand is the financial accessibility of these genetic tests. Currently the low demand for genetic testing has put pressure on the price of the service. Nonetheless, genetic tests are being developed, to make testing more efficient, accurate and more importantly affordable [5,6].

Another vivid example of the utility of genetic testing to prevent cancer is colorectal cancer. Colorectal cancer is another common inherited cancer, with notably high rates in North America. Up to 10 percent of colon cancers are attributed to genetic predisposition, with mutations occurring commonly in the *MLH1* and *MSH2* genes. These are germline mutations and which means that there is a 50 percent chance of a parent passing it to offspring. Individuals with cancer cases in their lineage are strongly encouraged to get tested.

In addition to the *MLH1* and *MLH2* risks, up to 50 percent of cancers that have been classified as sporadic cancers actually involve familial susceptibility. One of these misclassified genes is the IGF2 gene, a growth factor gene [7]. A new test has recently been developed for the IGF2, which involves taking blood samples, and looking at the DNA using biomarkers [7]. This new test is an important achievement for the scientific community and is testimony of the potential of new technology in genetic testing.

### ***Testing for Somatic Mutations***

Aside from employing genetic testing to find polymorphisms in cancer risk diagnosis, genetics can also be used in more accurately diagnosing women in cervical cancer. The standard test for cervical cancer is a pap smear, which women are recommended to undergo annually. The test examines a sample of cells from the patient, and determines whether or not cells have undergone a structural change, which would be an indication of cancer. Most recently, the American College of Obstetricians and Gynecologists made a recommendation for Digene's test, a two part exam that networks the conventional pap test with a special DNA test [8]. A Digene test is claimed to be able to more accurately determine whether or not an individual has cancer, and give an calculation of the cell's likelihood of becoming cancerous [8]. Since cervical cancer has mostly been recognized as an environmental cancer (95% of cancer cases is caused by the HPV virus), news of the Digene test serves to show that genetics can have a valuable application even in cancers that are known to be environmental.

Early testing for genetic predisposition has recently received more recognition for being part of an effective preventive care strategy. Predisposed individuals who choose a healthier lifestyle are able to evade onset of disease. Thus, individuals with a known history of cancer in the family are encouraged to get tested, especially if they have immediate family affected by cancer (noting that germline mutations have a 50% chance of being passed on).

### ***Population Screening***

While genetic testing is beneficial to the prevention of cancer at the level of the individual, population screening is also an effective way of monitoring the cancer prevalence among populations. Different regions and populations have varying prevalence for certain kinds of cancer.

In breast cancer, for example, various populations have shown coherence in the high BRCA mutation rate. A study in Tunisia [6] found that 1 out of every 16 women affected with breast cancer traced back to a mutation in the *BRCA1* gene. Studies in Finland have shown a high prevalence for a different gene mutation in connection with development of breast cancer. Instead, Finnish women have shown a high prevalence for a germline mutation in the *TP53* gene [9]. Consequently, for the Finnish, information about the BRCA mutations is not as constructive as information about the *TP53* gene. The Finnish population would benefit much more from a study catered for the needs of its population dynamics. In response to this discovery, Oulu University Hospital in Finland is now investigating the *TP53* mutations [9].

While genetic screening has proved to be cost effective against the large treatment expenses accrued by patient populations today, there are currently limitations on using such technology. Prevention is definitely cheaper than the lengthy treatments because it does not require the attainment and maintenance of costly facilities. However, at this point, implementing such a prevention program would require the consolidation of many resources and a huge initial investment which is beyond the means of most communities. Especially since genetics is still a relatively unexplored realm in cancer research and carries with it significant uncertainty, such a huge use of essential funds does not seem practical. The field of genetics should still be pursued and carefully investigated because there is a wealth of information that can be gained on the why's and how's of cancer development. Once the connection between genes and cancer is more clearly understood, and more precise screening technologies can be instigated, population screening would be a huge asset to the public health care cause. It would revolutionise cancer prevention strategies and hopefully lower overall cancer frequency.

### ***Research of Gender Disproportionalities***

While great progress is being achieved in genetic technologies and the discovery of susceptibility genes, little research has addressed the genetic dynamics in female and male cancer incidences. The following table 3 shows a disparity in prevalence between males and females for certain types of cancer. For these most common forms of cancer, as shown in the table, men seem to have a generally higher prevalence over women. These disproportionalities suggest that men and women may have different risks for different types of cancer, due to environmental factors, or inherent biological and genetic factors. Such discrepancies necessitate more research addressing the varying causes that lead to different risk between men and women for each type of cancer.

Table 3. Prevalence between males and females for certain types of cancer [1]

<b>Form of cancer</b>	<b>Male</b>		<b>Female</b>	
	(000)	% total	(000)	% total
Trachea/bronchus/lung cancers	882	3.0	331	1.2
Breast	3	0	476	1.8
Colon/rectum	317	1.1	298	1.1
Stomach	522	1.8	328	1.2
Liver	423	1.4	193	0.7
Prostate	269	0.9	...	...
Leukemia	145	0.5	115	0.4
Bladder	129	0.4	54	0.2

Current research has given little attention to gender issues in cancer. While reporting results, most publications ignore the statistical differences between men and women and some leave it out

altogether. Yet if genetic frequency and inheritance are to be carefully studied, gender must also be noted in these studies because cancer prevalences between men and women are disproportionate. Because a specific gender appears to be more susceptible to certain type of cancer, gender is also a genetic predisposition in cancer development. Men and women are predisposed to different anatomical, biochemical and genetic features (the way genes are turned on and off) that possibly plays a role in onset of disease. Studying these differences may reveal information that is beneficial to general cancer research.

### ***Growing Significance of Genes in Cancer Onset***

Cancer can be inherited and the recognition of the role of genetics in the onset and development of cancer is increasingly gaining clarity. Everyday, new genes are found to influence in development of various types of cancer, and new sites on those genes are being isolated as factors of disease. As more research becomes devoted to genetic function in carcinogenesis, the scientific community may find genes playing a larger role in cancer than previously anticipated. In fact, a publication by the International Agency of Research for Cancer found that the actual prevalence for genetic susceptibility may be two percent higher than past studies have shown, due to specificity errors in the methodology [10]. The agency conducted a blind study of a selection of genetic testing services that are commercially available and commonly used by consumers [10]. The accuracy of these services were assessed using controls with known mutations. It was found that in almost all cases, the techniques underestimated the number of mutations in a genetic sample, suggesting that many more people could be affected by predisposition than previously hypothesized [10].

Likewise, new genetic functions are being found in cancers previously attributed to environmental factors. For example in the past, public awareness campaigns have given a great deal of attention to the direct link between smoking and lung cancer, the cancer with the highest mortality rate. The campaigns cast a lot of culpability on cigarettes for being a cause to lung cancer. While these efforts effectively lowered the number of smokers and encouraged some individuals to make healthier choices in consumption, the campaigns overlooked the major component of genetic predisposition to lung cancer. More recently, researchers are slowly admitting to a genetic role in lung cancer. Researchers at the University of Nebraska have taken on a project, investigating the exact role of certain genes in lung cancer, utilizing the indispensable information from the Human Genome Project. So far, the team has found that indeed certain individuals are more genetically susceptible to carcinogenesis in the lungs, and tobacco consumption worsens the disposition [11]. This information can eventually help scientists construct a test to identify individuals with this susceptibility. Likewise, this knowledge can benefit individuals by allowing them to chose a healthier lifestyle (i.e. encourage smoking cessation) to avoid higher risk.

Even more startling are results on genetic role in cancer found by the Cancer Research UK GP Research Group (CRUK) from Oxford University [12]. With an impressive sample of over 20,000 individuals, the study showed that certain gene variations can be matched with particular personality traits. For example, variations in the human serotonin transporter gene and the dopamine receptor may be linked to certain psychologies that lead to unhealthy tendencies [12]. A truncation of the normal 5HTT-LPR can be attributed to specific moods, making individuals prone feeling depression-related symptoms [12]. The CRUK group found that these individuals are also more likely to respond to their moods by adopting negative practices. Likewise, a D4R change can make a person more inclined to indulge in unwholesome activities such as smoking and alcohol, habits associated frequently to cancer development. According to Robert Souhami, the director of the research team, these mutations leading to unhealthy behaviours are so prevalent that a change of lifestyle could probably thwart the development of about 50% of cancers [12].

Genes play a twofold role in cancer development for an individual. It not only predisposes individuals to the disease in the metabolic and biological sense, but it also predisposes individuals to certain behaviours that might enhance their risk for cancer by making them susceptible to an unhealthy lifestyle. It is important to disseminate this known information and expand the research and resources that support genetic research in cancer. Awareness of the twofold genetic component in cancer can empower individuals in to making healthy lifestyle choices. Genes have been found to have an increasing role in cancer and more discoveries will be made. It is important to utilize this information, allow predisposed individuals to apply extra caution in determining lifestyle habits, and avoiding hazardous environmental elements. Identifying the biased individuals will enable them to take preventive measures like intervening with chemotherapeutics, chemo-preventive agents, nutritional additives, vaccines or even genetic engineering.

## **Genetics and Treatment of Cancer**

Although it genes do play a role in cancer susceptibility, a role can also be given to genetics in helping to find an effective cure. Researchers have tapped into many avenues of genetic resources, and have found numerous possibilities for treatment in pharmacogenetics and a number of variations on gene therapy.

### ***Current Treatment***

The current most common treatment for cancer is surgery and chemotherapy. Yet chemotherapy is inefficient in that it does not target specific cancer cells. Chemotherapy targets dividing cells because cancer cells are in a constant state of abnormal division. This method is known to have numerous adverse side effects. Patients undergoing this treatment suffer hair loss, fatigue, and a weakening of the immune system, among other symptoms when bone marrow cells are killed [13]. Since the immune system's strength is crucial during recovery, these effects register as major setbacks to patient recovery. In addition, chemotherapy can damage reproductive organs and cells, causing sterility and long-term reproductive problem for patients. With all the major inconveniences of chemotherapy, the future of cancer treatment lies in localized treatment, of which the medical community is now seeking genetic based alternatives.

Chemotherapy not only kills healthy cells along with cancerous cells, but also fails to take into account genetic differences among individuals and consequent variations in individuals. To demonstrate, a study was conducted on *SULT1A1*, a gene known to have many polymorphisms that contribute to a reduction of enzyme activity in the metabolic pathways that processes drugs to fight breast cancer [14]. (Some multinucleotide mutations decrease enzyme function by as much as 75%) [14]. An example of this is the discrepancy in clinical responses to tamoxifen, a widely used treatment for breast cancer patients. Patients with this *SULT1A1* mutation do not respond optimally to the drug [14]. In some cases, patients are simply resistant to the drug. In others, the wrong dosage can be lethal for the patient. Side effects range in severity depending on varying abilities to metabolise the drug.

### ***Pharmacogenetics***

To improve the benefit to harm ratio of chemotherapy, the concept of pharmacogenetics must be recognized. Pharmacogenetics involves tailoring treatment to an individual's genetic characteristics to optimize drug response. Proof of principle is clear, and, one hopes that all chemotherapy dosage will be fine-tuned, taking into account the person's metabolic mutations, decreased functions, etc., to ultimately ensure that the patient receives more effective dosage for his/her condition and the genetic origins of the tumour would be targeted, as well. For those patients with the *SULT1A1*, for

example, dosage would be increased to offset the fact that the body is only able to metabolise 25% of consumed dosage.

An ongoing study in Japan is looking at Iressa, a drug that has proven to be particularly effective for lung cancer. The drug was very potent in shrinking tumor size. It has worked so well, in fact, that both the United States and Australia recently approved use of this drug. Yet despite all its powerful abilities in treating cancerous tumors, the drug has been associated with the fatalities of about 246 people and has been responsible for causing illness in another 616 patients. Despite such severe side effects, clinicians plan to continue to prescribe it because of its effectiveness. As a result, the University of Tokyo has taken on a study of the drug with the objective of screening small nuclear proteins in hundreds of genes to look for a mutation that is affiliated with these side effects. The goal is to eventually identify these mutations, develop a method to test whether or not patients will respond positively to the drug, and finally to correct the dosage if the drug is found not to be lethal for the individual. This study bears testimony to the relevance and need for pharmacogenetics.

Individual variations must be taken into account when prescribing these medications. Once an effective treatment is found, the subsequent step in science is to fine-tune it so that it is most effective not only in the general sense, but also for each individual.

Although pharmacogenetics is a far more precise treatment for individual cancer patients, it is still not a cure. Presently, patients are considered “cured” if they do not experience relapse within 5 years upon completion of chemotherapy, during which there is a high likelihood for relapse. Nor does pharmacogenetics rid the patient of this anxiety and uncertainty of relapse. A lasting cure lies in a one-time treatment, after which a patient can live safely with the assumption that the same cancer will not return. The long term solution is gene therapy, a cure that provides a single treatment correction at the source of the problem.

### ***Gene Therapy***

Several projects relating to gene therapy for cancer are in the works. One of these projects as explained in the *Chinese Medical Journal* (2002) involves a team of researchers from Shanghai Second Medical University successfully inserting a gene into human tumor cells via a retrovirus [15]. Usually tumor cells contain antigens on its surface that can separate them from normal cells. Though analogous noncancerous cells also contain these antibodies, they do so on a much smaller level. Therefore, probability of the retrovirus attaching to a noncancerous cell is low in the presence of the cancer cells. If these cancer antigens are specific, a retrovirus can be modified to contain an antibody which will bind to the antigen, enabling the virus to lodge itself on the cell and inject its viral DNA into the cell [15]. The team inserted a functional tumor suppressor gene into the viral vector, which is then incorporated into the cell when the virus injected its DNA [15]. The tumor suppressor gene was taken in by the cell and included in its DNA allowing the cell to regain the function of self-regulation and apoptosis. Researchers have found that they are able to incorporate the corrective gene into the tumorous cell, and that the retrovirus stay away from normal cells in most cases. Gene therapy in this instance is performed by a retrovirus that has been engineered to transport one specific gene.

Another study of similar principle was recently conducted in Japan. A team used an adenovirus to inject a p21 gene in esophageal squamous cancer cells. Introduction of the gene enhanced the level of a RAR $\beta$  protein, which is responsible for the inhibition of cell mitosis. Cells successfully injected with the p21 gene eventually followed through with apoptosis [16]. This experiment, similar to the previous one by the Chinese research team, demonstrates the cell's ability to inhibit

itself with apoptosis can be revived. These two experiments reveal that cell apoptosis may be restored using various genes that target specific tumor suppressor sequences. Studies conducted by the University of Mexico show that in some cases p53 reactivation is possible in certain strains of cervical cancer [17]. In normal cells, p53 halts the cell in the G1 phase, allowing the cell to use its repair mechanisms to correct the incorrect DNA before going into S phase where the DNA will be replicated. If, however, the DNA is unable to be repaired, then the p53 plays a role in initiating apoptosis, or cell death. Cells with p53 dysfunction continue to replicate even with the faulty DNA. P53 dysfunction characterizes about 50% of cancer cases, and cell proliferation goes unchecked. In cervical cancer, however, researchers believe that p53 may be simply dormant, but still functional. For wildtype cell lines, p53 transcription levels measure an increase in the presence of damaged genetic material.

The University of Mexico researchers treated several cervical cancer cell lines with NCS, an enzyme that breaks up DNA [17]. After treatment, cell viability was measured by count. Most cell lines proceeded from G1 phase of the cell cycle, although cells from a few strains were locked in the G2 phase. Furthermore, most of these cells that were fixed in G2 phase were unable to retreat from the arrest, and eventually entered cell apoptosis. Some cells, in the ViBo line, however, remained fixed in G2 phase [17]. In these specific strains, the protein product from the p53 gene significantly increased, reestablishing the cell's ability to self regulate [17]. This research provides hope of possible p53 reactivation in cancer cells, and researchers are looking into the viability of using NCS as a p53 inducer. The reactivation of a p53 gene also supports investigation of gene therapy in cancer, by demonstrating that tumor suppressor gene functions are not completely lost in cancer. This experiment is different from the previous two in that the tumor suppressor function was re-established without the introduction of a new or foreign gene.

Despite the number of different projects on gene therapy, the restoration of a tumor suppressor gene remains similar among them. There is some consensus in the scientific community that reactivation of a tumor suppressor gene may be a more effective way to eliminate cancer. The method gives back control of biological process to the cell, not by directly killing cancer cells, but by giving the cell the ability to regulate itself. This consistency is a sign of progress in cancer research, as it allows researchers to collaborate efforts in pushing the medical frontier.

Citing three deaths from gene therapy, including to children with induced leukaemia, some critics argue that gene therapy is unsafe, and will remain so in the near future. They claim that the capacity to insert genes at precise locations is a prerequisite in mutation correction, and is presently unachievable. However, this argument is only defensible when gene therapy is applied to correct the polymorphisms that predispose individuals to cancer. This is not the case with the current methods of gene therapy being studied. These therapies do not require inserting genes at precise location, as the goal is not to correct a dysfunctional polymorphism, but to insert or reactivate a tumor suppressor gene, which is turned off in about 50 % of cancer cases. Assuming that the p53 gene can still be functional in the instance of demethylation via NCS, reactivation is possible without even inserting a new gene.

Gene therapy, however, is still in its infancy stages in cancer research. The present issue of gene therapy is that it is promising in theory, but difficult to apply to in clinical procedures. It is not known how tampering with one gene will affect the function of nearby genes. Likewise, it may be a while before any type of gene therapy cancer treatment is tried clinically on humans. Thus far tests have been run primarily on mice. The human body is a lot more complex and requires many more details to be taken into consideration. The p53 reactivation, for example, was performed in cell cultures, and it will be a while before it is even taken to the next level of animal testing.

Alternatively, scientists have learned to influence genes without directly manipulating the genes. Some tumorous activity has been attributed to unusual DNA methylation [18]. In certain cancer cells, the level of methylation is found to be notably higher than noncancerous cells. This information is allowing researchers to see whether or not therapy can be applied to the methylation processes of the cell. Some researchers are trying to investigate whether or not demethylation solutions can be applied to cancer cells to restore control of mitotic activity. A study at the University of Arizona suggests that demethylation of cancerous cells and reactivation of the p53 gene may be a feasible tactic against cancer growth in the future [18].

Gene therapy has been viewed as the solution to many other common diseases, especially in diabetes where scientists have in some cases, successfully inserted specific genes into the liver. The introduction of the new gene allows the liver to assume the function of producing insulin.

While all these genetic testing technologies are available, most people do not have access to these resources, especially in low to middle income countries. Governments can strengthen their capacity to provide the adequate basis for genetic services progressively in order to lay a foundation for the increasing role of human genetics in patient care and disease prevention. To assist in this process, the Human Genetics Programme is constructing a **Genomic Resource Centre (GRC)** to provide tools for health professionals, policy makers, NGOs, and patients. The goal of the Genomic Resource Centre is to establish a consensus among the existing technologies that are available, to pull together all resources and networks of information, and to allow everyone to have access to this database. Hence, even while low to middle income countries may not have the resources to conduct extensive research on their own, the information is still available and accessible to them.

## Conclusion

The increasing evidence of genetic linkage to cancer onset and development makes it an important part of research and public health which can no longer be overlooked. While a genetic testing facilities are available, they should be made more accessible to individuals, as many would benefit immensely from this information. Governments should work to promote or subsidize the services of these facilities. By coupling awareness of genetic predispositions with choices of a healthy lifestyle, individuals will have much more authority over their health. To accomplish this, public health must deviate from the current one-track approach that solely analyses environmental factors, and take on a new strategy that cooperates genetics with environment. The aim is to significantly reduce the number of cancer cases. Concurrently, more resources need to be devoted to research in pharmacogenetics and gene therapy, where existing data shows that within these two fields lie promisingly the future treatments for cancer.

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Table 1. Deaths by Cancers in millions(1)

	AFR	AMR	EMR	EUR	SEAR	WPR	Total
Common deaths	10681	5911	4156	9703	14467	11636	56554
Neoplasms: lung/trachea/ bronchus:	544 (5,1%)a 23 (4,2%)b	1111 (18,8) 227 (20,4)	279 (6,7) 30 (10,7)	1867 (19,2) 371 (19,8)	1113 (7,7) 162 (14,5)	2202 (18,9) 399 (18,1)	7115 (12,6) 1212 (17,0)

a- % of deaths from common deaths

b- % of deaths from neoplasms