

# Genetic testing for lung cancer risk

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## About this booklet

This brochure is designed to give you information to help you decide whether you want to take a genetic test for lung cancer risk. It includes information on genes and genetic testing.

To understand what a genetic test is, it first helps to understand a bit about genes. This is explained on the next page.

## Page 2

# What are genes?

Inside each of your trillions of cells is your unique set of 46 chromosomes. Chromosomes contain DNA, which contains genes.

Genes contain the information needed by the cell to make proteins. So, you can think of a gene as a recipe for making a protein. The recipe is written in a special code. The code contains only four letters (*A, C, G, T*).

Proteins do all the jobs needed to keep the cell and the body alive and well. Some proteins send messages to the brain. Some proteins build teeth and bone. Other proteins digest your food.

Variations in genes affect how proteins do their job properly. For example, sometimes there is an 'A' in place of a 'C'. Sometimes part of a gene is missing, or in the wrong place. And sometimes whole genes are missing. This can mean the protein doesn't work properly or isn't made at all.

## What are genetic tests and what are they used for?

Genetic tests detect variations in genes. They provide information about one's genetic makeup, and can sometimes be used to see whether an individual has an increased likelihood of developing a health condition.

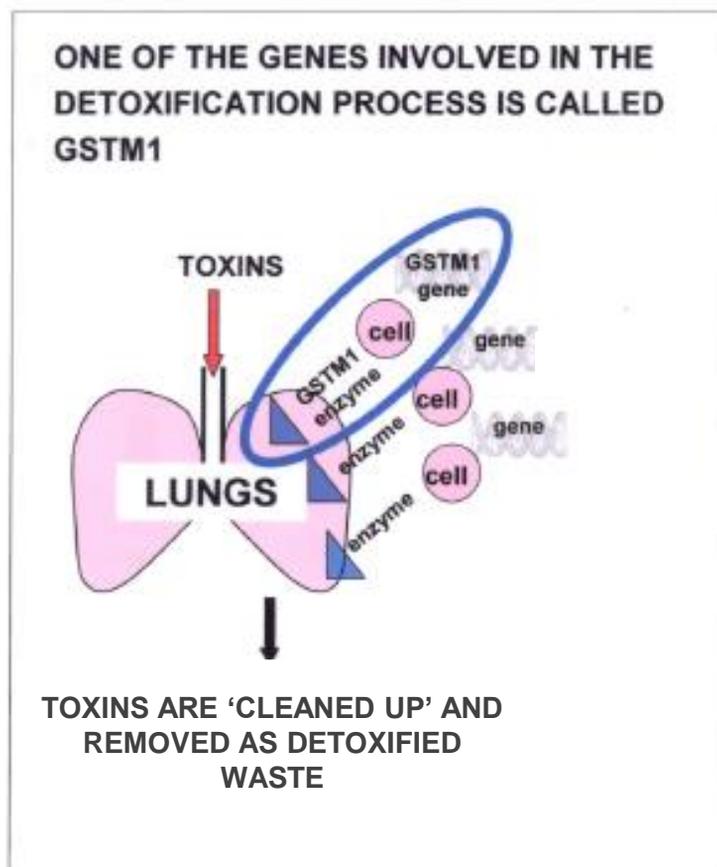
Genetic tests are available now for certain types of cancer. In most cases, learning that you have a particular gene variation does not automatically mean that you will get the health condition; it means only that you have a higher than average risk of developing the health condition.

## The *GSTM1* gene and the *GSTM1* enzyme

One of your genes is called the '*GSTM1* gene'. This gene contains information your cells use to make the *GSTM1* enzyme.

### What is the *GSTM1* enzyme?

Every day, toxins enter your body in small amounts from the environment. To protect itself, your body makes hundreds of enzymes that break down and flush out these harmful toxins. The *GSTM1* enzyme is one of these 'cleaning up' enzymes. *GSTM1* and these other enzymes work a bit like detergent, breaking down the toxins and flushing them out (you can see some examples of toxins that are in cigarettes on the next page). This process is shown in the picture below.



## Cigarette smoke contains thousands of harmful toxins

**Benzo(a)pyrene** A chemical that damages your genes so that your body can not stop the growth of tumors that can lead to lung and other cancers.

### A few other chemicals that you should know about:

**Arsenic**, a poison used to kill rats, and DDT used to kill insects are just two of the chemicals that you breathe in when you smoke. Each time you smoke these chemicals get carried to every cell in your body. Cigarette smoke also contains about 4,000 other harmful chemicals. At least 50 are known to cause cancer.

**Nicotine** The chemical that causes addiction. It speeds up the heart rate and closes down blood vessels and raises blood pressure.

**Carbon monoxide (CO)** A poisonous gas that makes it harder for the blood to carry oxygen to the body's organs. CO makes the heart work harder to get enough oxygen, which can lead to heart disease.

**Hydrogen cyanide** A poisonous gas that makes the lungs less able to stretch. This makes it harder for the lungs to fill up with and exhale air, and can lead to shortness of breath and emphysema.

**Acetone**  
Paint stripper

**\*Naphthylamine**  
Used to make dye and rubber

**Methanol**  
Rocket fuel

**\*Pyrene**  
Smoke of burning garbage

**Napthalene**  
Mothballs

**\*Cadmium**  
Used in car batteries

**Carbon Monoxide**  
Car Exhaust

**\*Benzo(a)pyrene**  
Made by burning insecticide

**\*Vinyl Chloride**  
Used to make plastics

**Hydrogen Cyanide**  
Poison used in gas chambers

**\*Toluidine**  
Used as a base in dyes

**Ammonia**  
Floor cleaner

**Urethane**  
Used to make adhesives

**Toluene**  
Industrial solvent

**Arsenic**  
Art poison

**Phenol**  
Found in fertilizer

**Butane**  
Lighter fuel

**\*Polonium-210**  
Used in nuclear weapons production

**DDT**  
Insecticide

\* Known cancer-causing substances

Adapted from a poster by the National Anti-Smoking Society of Fiji

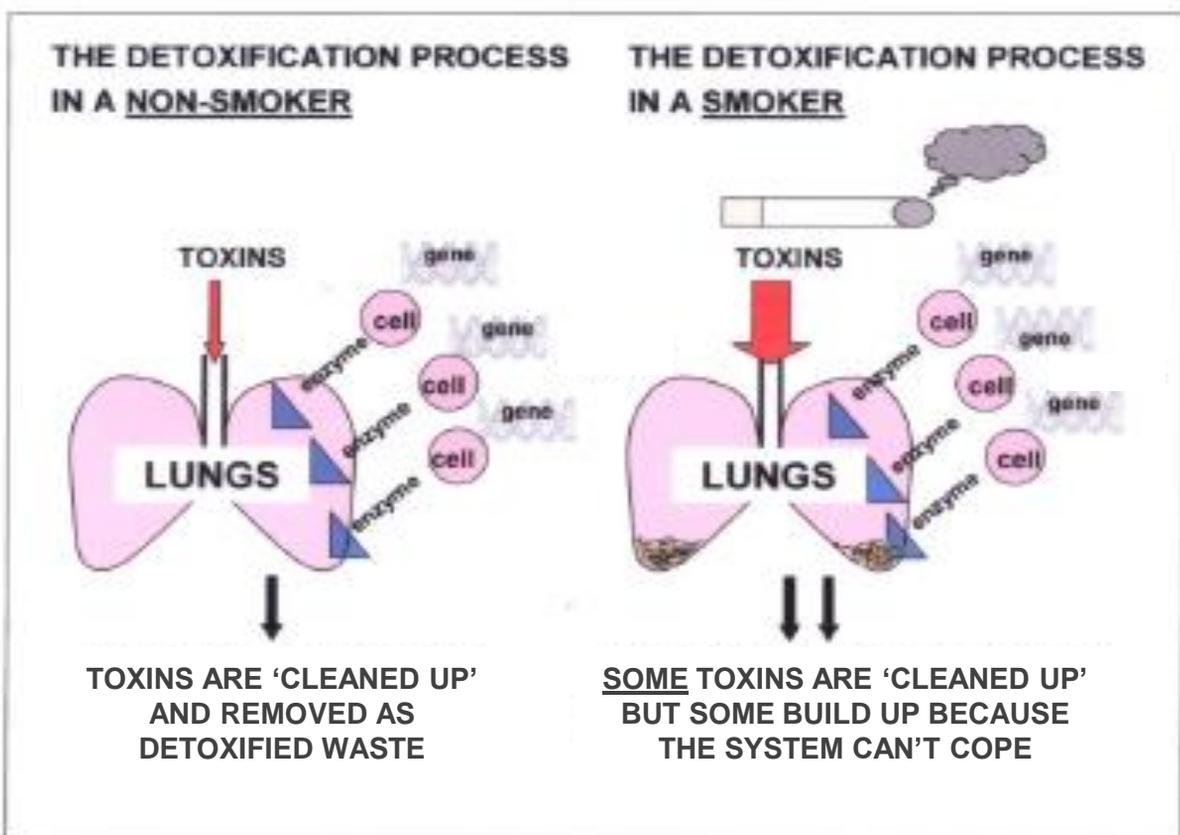
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## Toxin overload!

The left side of the figure below shows how the process of breaking down toxins works in a non-smoker. Small amounts of toxins from the environment enter the lungs (and the rest of the body). But these toxins are continually cleaned up by the enzymes produced by genes, keeping the lungs clear and healthy.

However, as illustrated on the previous page, when you smoke cigarettes, you take thousands of harmful toxins into your body. The 'clean up' enzymes can help to clear out some of the toxins in cigarette smoke. However, the large number of toxins may overload the system and may not all be 'cleaned up' (right side of the figure below). The diagram below on the right shows this. The build up of toxins in your lungs can eventually lead to lung cancer.

Cigarette smokers who do not have these "clean up" enzymes working properly may have even greater toxin overload.



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## Smoking, toxins and lung cancer

Although healthy cells in your body usually divide and multiply in a controlled and orderly way, repeated exposure to toxins in cigarette smoke can turn these healthy cells into abnormal cells. These abnormal cells get out of control, and divide and multiply too fast. Lung cancer occurs when healthy cells in your lungs become abnormal and get out of control.

The toxins in cigarettes make cigarette smoking the leading cause of lung cancer. Nine out of 10 patients with lung cancer are or have been cigarette smokers. Smokers who quit smoking lower their chances of getting lung cancer by up to 70%.

Lung cancer is a very serious disease. It kills more people in the United States than any other cancer, and most patients with lung cancer die within one year of their diagnosis. About 160,000 people every year die from lung cancer.

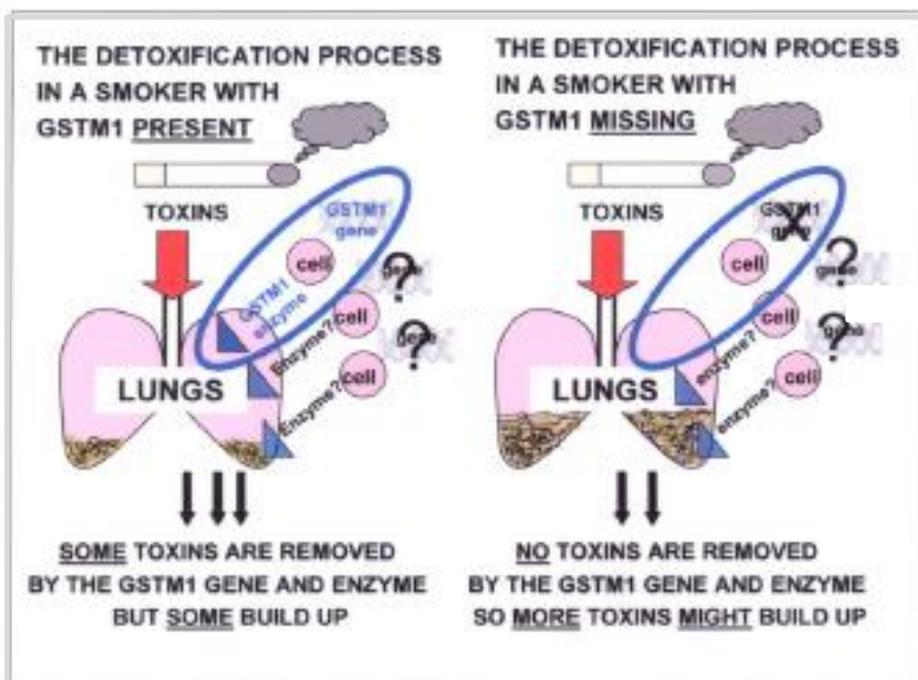
Symptoms of lung cancer include: extreme shortness of breath, a cough that won't go away, bloody phlegm, hoarseness and difficulty swallowing, poor appetite, chest pain from fluid build-up, bone tenderness and pain, severe constipation that can lead to nausea, and vomiting and belly pain.

## Some people are missing the *GSTM1* gene

Some people (between 30% and 50% of the US population) are missing the *GSTM1* gene. On the left in the diagram below you can see what happens when a smoker has the *GSTM1* gene. Some toxins are removed by the *GSTM1* enzyme but lots of toxins still build up.

The diagram on the right shows what happens when a smoker does not have the *GSTM1* gene. Because the cells are not making the *GSTM1* enzyme, smokers who are missing the *GSTM1* gene may be clearing out fewer of the toxins in cigarette smoke.

So, knowing whether a person has the *GSTM1* gene present or missing can tell us about the body's ability to 'clean up' toxins from cigarette smoke. This information does not tell us anything about the presence or absence of any of the other genes that help to clean up toxins.



## *GSTM1* and lung cancer risk

In research studies, smokers with lung cancer have been found to be more likely to be missing the *GSTM1* gene than smokers who do not have lung cancer. This suggests that people who are missing the *GSTM1* gene have a higher risk of developing lung cancer than people who have the *GSTM1* gene present. What this translates to in terms of the number of smokers expected to get lung cancer based on having the *GSTM1* gene present or missing is provided later in this booklet on pages 13 and 14.

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## What are we testing?

In this study, we are testing a saliva sample to see if people have the *GSTM1* gene. Knowing whether you have the *GSTM1* gene is the same as knowing whether you have the *GSTM1* enzyme.

The genetic test for *GSTM1* is a 'genetic susceptibility test'. This means that the test result tells you a little bit about your chances of getting lung cancer in the future.

It is important to remember that this test has not been shown to improve health. It can only be offered in research studies.

We are interested in whether people will find this kind of information about their personal genetic risks of smoking-related diseases useful or not and how it affects their decisions about smoking.

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## Genetic test procedure

Genetic testing for *GSTM1* is completely painless, and can be done by swishing a mouthwash thoroughly for 45 seconds, and then spitting it back into a plastic tube. This collects enough DNA to send to the labs and they can then test it to see whether you have the *GSTM1* gene present or missing.

## What happens after the genetic test?

Two weeks after taking the genetic test, you will be asked to return to a study site on campus to get your result. During this session, you will be shown your test result on a computer by a health educator.

There are two possible results from the *GSTM1* genetic test: 'GSTM1 gene missing' or 'GSTM1 gene present'. These are explained in more detail on the next couple of pages.

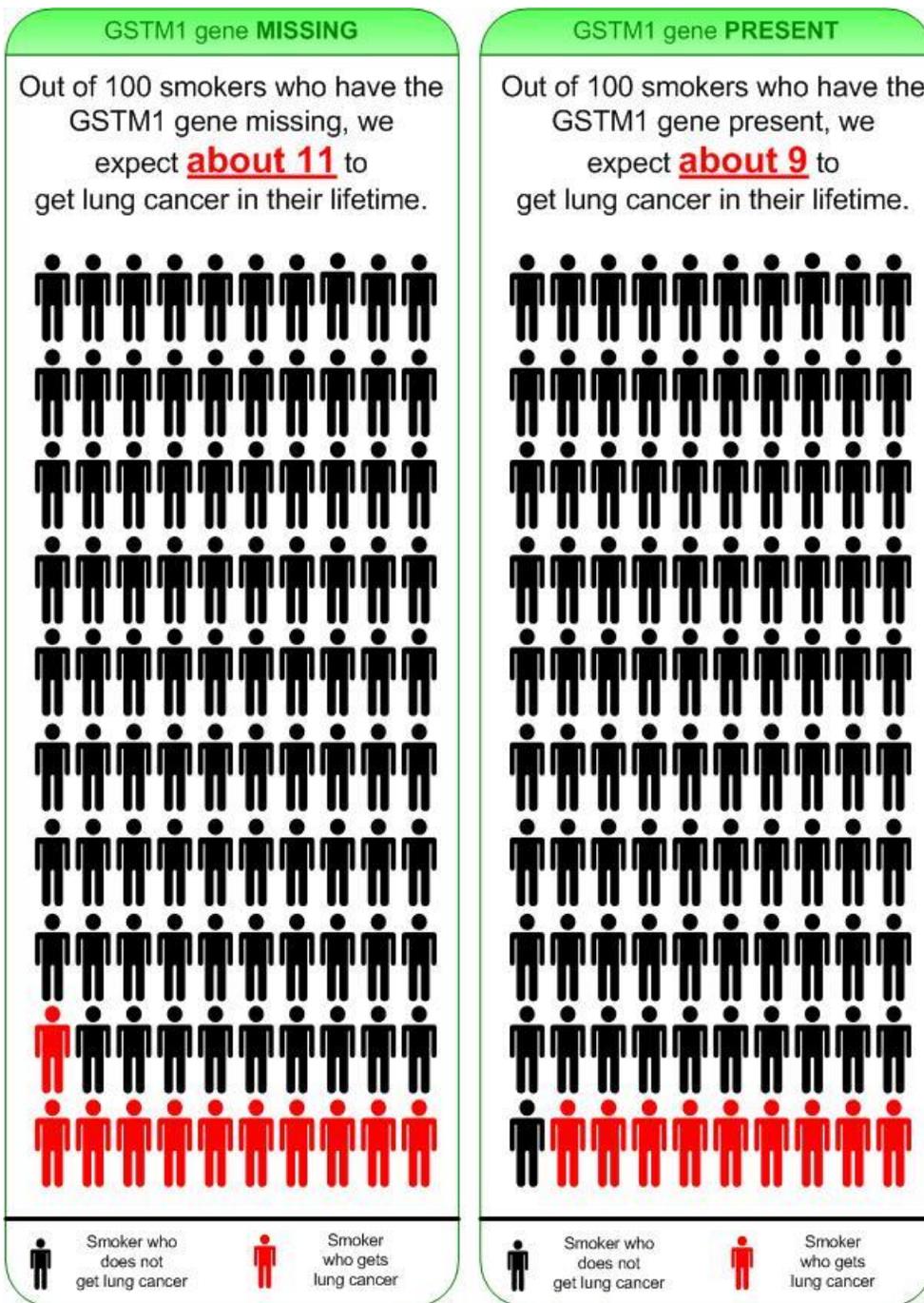
## What do 'GSTM1 gene missing' and 'GSTM1 gene present' test results mean?

If you are a smoker and are missing the *GSTM1* gene you have a higher risk of getting lung cancer than a smoker who has the *GSTM1* gene present, because your body is not producing the GSTM1 enzyme. If you are missing the *GSTM1* gene, then your risk of developing lung cancer is about 20% higher than if you have the *GSTM1* gene present.

If you have the *GSTM1* gene present you have a lower risk of getting lung cancer than a smoker who is missing the *GSTM1* gene, because your body is producing the GSTM1 enzyme. If you have the *GSTM1* gene present, then your risk of developing lung cancer is about 20% lower than a smoker who is missing the *GSTM1* gene. In sum, it's good to have the *GSTM1* gene; it's bad to be missing the *GSTM1* gene.

What this translates to in terms of the number of smokers expected to get lung cancer based on having the *GSTM1* gene present or missing is provided on the next page.

# What do 'GSTM1 gene missing' and 'GSTM1 gene present' test results mean?



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## Accuracy of the *GSTM1* genetic test

The *GSTM1* genetic test tells people whether or not they have the *GSTM1* gene (and therefore the *GSTM1* enzyme) with almost 100% accuracy.

This will tell you whether your risk of developing lung cancer in the future is increased or decreased based on this gene alone.

Remember, *GSTM1* is only one of a number of different genes that are all involved in making the enzymes which clean up the toxins in cigarette smoke, and we do not know how many of these other genes you do or do not have. Your future risk of getting lung cancer may be higher or lower depending on these other genes.

## Possible benefits and risks of *GSTM1* genetic testing

### **Benefits of taking the test:**

- The result provides some information about one way in which your body may handle the chemicals in cigarette smoke that cause lung cancer.
- The result could increase your motivation to avoid smoking and in so doing, lower your risk of developing lung cancer.
- The test is simple and painless.
- Your participation in this research study could help provide useful information to help us develop improved ways of helping people to quit smoking and therefore prevent disease in the future.

### **Risks and limitations of taking the test:**

- The result may cause you to worry or feel upset.
- The result can only tell you whether your chance of getting lung cancer is higher or lower than average, but cannot tell you whether you will get lung cancer with any certainty.
- The result will not tell you about your genetic risk for other smoking-related diseases (such as heart disease, emphysema, and other cancers).
- Although it is illegal, there is a small chance of employers or insurance companies using genetic test results to discriminate against people who have taken genetic tests. However, the study staff will take all the necessary measures to maintain confidentiality of your private information obtained during the study.

## Participant rights and shared decision making

Whether you decide to take this genetic test or not is completely up to you. Testing is voluntary, and only done with your written consent.

The results are confidential, and it is up to you to decide whether and to whom you wish to disclose your result.

We will not share the result of your test with any individuals or organizations outside of the research team, and all information is coded and made anonymous so that your identity cannot be known by anyone outside the research setting. Your result will not be told to anyone else.

Please discuss any questions or concerns you may have with the health educator present.

You can talk to your partner, friends, or doctor about your *GSTM1* genetic test result if you want.

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## Additional support and information

Visit [www.quitnet.com](http://www.quitnet.com) for tips and advice about how to make a quit plan, or to get connected with other smokers who are trying to quit.

Call **1-877-4UU-QUIT** or **1-800-4CANCER** for more information about quitting and cancer.

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## Sources of information

- The section, “What are genes?”, is adapted from the US National Institutes of Health website, <http://history.nih.gov/exhibits/genetics/kidsf.htm> [accessed 3 June 2008].
- “What are genetic tests and what are they used for?” is adapted from The Royal Society’s webpage, <http://www.royalsoc.ac.uk/page.asp?id=1264> [Accessed 3 June 2008].
- Additional information about genetic testing was drawn from the ‘What is a genetic test?’ leaflet on the website, <http://www.eurogentest.org/web/info/public/about/public.xhtml> (Eurogentest is an EU-funded Network of Excellence which, through a series of initiatives, encourages the harmonization of standards and practice in all aspects of genetic testing, throughout the EU and beyond) [accessed 3 June 2008].
- The information in this leaflet on lung cancer risk and smoking was drawn in part from the <http://understandingrisk.cancer.gov> website (National Cancer Institute, US National Institutes of Health website) [Accessed 3 June 2008].
- Information about the *GSTM1* gene and lung cancer risk is taken in part from the following peer-reviewed journal article: Benhamou et al (2002) Meta- and pooled analyses of the effects of glutathione S-transferase M1 polymorphisms and smoking on lung cancer risk. *Carcinogenesis*, 23(8):1343-50.