

The ApoE gene fact sheet

Genes contain the information to make all the proteins our body needs. Humans have around 25,000 genes, 99.9% of which are exactly the same in all people. There is much interest in the genes that differ between people and the impact that these differences may have on our health and risk of disease. At the University of Reading, we are interested in how these variations affect people's response to foods. For this reason, in some of our studies we ask you to provide a blood sample that we use to determine whether you have variations of a particular gene.

One of the genes we are interested in is the apoE gene, and we will test for variations in this gene in your blood sample. This fact-sheet is designed to explain what apoE does in the body, and what impact variations in the apoE gene may have on your health.

What is ApoE, and what does it do?

ApoE is a protein which is a component of lipoproteins. These are the particles which transport fats such as cholesterol and triglycerides around the body. ApoE has recently been found also to be involved in processes other than fat metabolism, such as regulation of the immune system, and cognitive (thought) processes within the brain.

Does everyone have the same apoE gene?

No, the apoE code may differ from person to person. Three common versions of the gene exist, namely E2, E3 and E4, which result in very small differences in the apoE protein. These differences alter the activity of the protein and the lipoproteins it is associated with.

Everyone inherits two apoE genes, one from each parent. Therefore it is possible for you to have one of the following six combinations or "genotypes", E2/E2 (1%), E2/E3 (11%), E2/E4 (2%), E3/E3 (61%), E3/E4 (23%), E4/E4 (2%), with the figures in brackets indicating approximately what proportion of the UK population have that combination.

How does this affect me as an individual, and what can I do about it?

Our main research interest is into the interaction between diet and apoE genotype, and the way in which different apoE genotypes affect the way in which the body handles different fats, and the impact that this may have on the risk of heart disease in particular. Although the evidence is not fully consistent, it has been estimated that having the E3/E4 or E4/E4 combination is associated with on average a 30-40% increased risk of heart disease relative to the common E3/E3 genotype. At the same time, there is some evidence that having an E2/E2 or E2/E3 genotype may be associated with a lower heart disease risk, especially in women.

There is increasing evidence to indicate that the increased risk of heart disease in individuals who are E4 carriers may be due to an increased susceptibility to the effects of fat and, particularly, saturated fat and cholesterol in the diet, and that these individuals would gain particular benefit from reducing their intake of these fats. The negative impact of the E3/E4 or E4/E4 combination appears to be most evident in smokers, and stopping smoking would particularly benefit individuals with this genotype.

In addition, individuals with the E4 genotype tend to have lower levels of antioxidants in the blood. These can be obtained from the diet, and the recommendation to eat at least five (80g) portions of fruit and vegetables per day is especially important in this group.

Research has also shown that different gene combinations for apoE can influence an individual's predisposition to other conditions including memory loss, dementia and Alzheimer's disease. Again, individuals with the E3/E4 or E4/E4 genotype appear to be particularly at risk. Although estimates vary, having an E3/E4 or E2/E4 combination may increase your risk of Alzheimer's disease 3-5 fold, while an E4/E4 genotype appears to be associated with an increased risk of greater than 5 fold. In addition to increasing risk these genotype combinations also lower the average age of onset of Alzheimer's disease, possibly by as much

as 15-20 years. In contrast, having the E2/E3 or E2/E2 combination may reduce your risk of Alzheimer's disease by up to 50%.

The evidence that lowering the level of cholesterol in the blood will reduce the risk of early-onset Alzheimer's disease is inconclusive but recent evidence suggest that flavonoid-rich plant derived foods such as teas, red wine (in moderation), berries, cocoa and citrus fruit may be effective in reducing age-related loss of memory and cognitive function, and this another of our research interests.

We will tell you the results of your genotype test only if you specifically ask us to do so. In view of the increased risk of heart disease and dementia associated with the E4 genotype, some people might find it distressing if they were to be given this information, and may prefer not to be told their results for this reason. If you were to be told that you have the E4/E4 genotype, we would recommend that you contact your GP to discuss the implications of this. At present there are no treatments available which will completely abolish your risk of developing heart disease or dementia in the long term. However, there is good evidence that dietary modification, stopping smoking and cholesterol-lowering statin drugs will reduce the risk of heart disease, and these measures are particularly important in high-risk individuals. Similar measures may be effective in reducing the risk of developing dementia but the evidence for this is not strong at present. However, this is an active research area, and it is likely that preventative measures will emerge in the near future, and it is clearly important that high-risk individuals take advantage of these.

Keeping physically active and not being overweight are also going to help reduce everyone's risk of heart disease. The British Heart Foundation website, www.bhf.org.uk has lots of tips on how to look after your heart.

Implications for health insurance

The genotyping we do is what is called 'predictive testing' and as such there is no need to disclose the results of these tests, at present or any time in the future, to your insurance company

Why are researchers interested in this gene?

We are interested to further determine whether individuals of different apoE genotype respond differently to dietary change. In the future, rather than providing everyone with general dietary advice, it may be that a more personalised approach is taken, providing tailored advice to suit an individual's genetic make-up.

Sources of further information

It must be emphasised that genotyping is a relatively new area which is still in the research stage, and information in this area far from conclusive. If you would like to read more on this topic, you may find the following web-site of the Human Genetics Commission useful, www.hgc.gov.uk

Your apoE genotype result –

If you have any questions or would like further information please contact your study investigator, or Prof Ian Rowland.

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The COMT Gene Factsheet

Genes contain the information to make all the proteins our body needs. Humans have around 25,000 genes, 99.9% of which are exactly the same in all people. There is much interest in the genes that differ between people and the impact that these differences may have on our health and risk of disease. At the University of Reading, we are interested in how these variations affect people's response to foods. For this reason, in some of our studies we ask you to provide a blood sample that we use to determine whether you have variations of a particular gene.

Your blood sample will be tested for variations in COMT, and this factsheet is designed to explain what COMT does in the body and what impact variations in the COMT gene may have on your health.

What is COMT and what does it do?

The COMT gene provides instructions for making a protein which is involved in a variety of processes in the body, including the metabolism of certain brain chemical messengers, hormones, some medicinal products and food components such as those found in green tea, apples, red wine and chocolate.

Does everyone have the same COMT gene?

The COMT genetic code can differ slightly from person to person. Changes in the COMT gene can alter either the amount of COMT produced, or can change its structure and function. One such change in the genetic code alters a single protein building block (amino acid) in the COMT protein at position 158, which causes the protein to work at a slightly slower rate.

Everybody inherits two COMT genes, one from each parent. Therefore, it is possible for you to have two genes coding for the fast working protein (termed GG), two genes coding for the slow working protein (termed AA) or one of each (termed AG). About 25% will have the GG version, another 25% will have the AA version and the remainder 50% will have a combination (AG). The combination of genes which you have is called your "genotype"

How does this affect me as an individual, and what can I do about it?

Research on the COMT gene is still in the early stages and the effects of the each version have not yet been proven. However, it appears that the AA genotype produces a COMT protein which is of lower activity, so that if you have the AA genotype it means your body inactivates some brain chemical messengers, hormones, medicinal products and food components at a slightly slower rate compared to people who have the high activity GG genotype or the intermediate AG genotype. Therefore, people with the AA version of the COMT gene may retain some medicinal products and food components, and therefore may be exposed to their effects (whether these are positive or negative) for a longer period. Most of the research carried out so far has focused on one particular brain chemical messenger, dopamine. Individuals with the AA genotype may have slightly higher levels of dopamine, and therefore may perform better at some tasks involving the front of the brain, such as working memory (retaining information), and may also be slightly more motivated. There may also be a very small increase in risk for AA individuals in developing obsessive-compulsive or panic disorders, but again these are complex conditions and many other more significant factors which contribute to their development.

People with the GG genotype are thought to have slightly lower levels of dopamine. In a very small number of individuals, this may increase the risk of developing disorders which affect thoughts and emotions, such as eating disorders. However, the increase in risk is very small and many other factors, such as other genes and our lifestyles/experiences, play a much larger part in determining the risk of these complex disorders. This lower level of dopamine may also mean that people with the GG variant have a higher pain threshold, are less anxious and are more resistant to stress than people who are AA.

Individuals with one of each variant (AG) are likely to have an intermediate level of dopamine, and respond in a way that is in between those individuals who are either GG or AA.

The impact on brain function of having a COMT GG is likely to be relatively minor compared to many other factors. For example, abstinence from recreational drugs such as cannabis can decrease your risk of developing disorders which affect emotions and thoughts. A healthy balanced diet, avoiding alcohol, sugar and caffeine in excessive amounts, and increasing intakes of fruits, vegetables, nuts, seeds and oily fish may help to increase brain function. Physical exercise can also help to reduce feelings of anxiety and stress.

Implications for health insurance

The genotyping we do is what is called 'predictive testing' and as such there is no need to disclose the results of these tests, at present or any time in the future, to your insurance company

Why are researchers interested in this gene?

We are interested to further determine whether individuals of different COMT genotype respond differently to changes in their diet. In the future, rather than providing everyone with general dietary advice, it may be that a more personalised approach is taken, providing advice tailored to an individual's genetic make-up

Sources of further information

It must be emphasised that genotyping is a relatively new area which is still in the research stage, with information in this area far from complete. If you would like to read more on this topic, you may find the following web-site of the Human Genetics Commission useful, www.hgc.gov.uk

Your COMT genotype result –

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The eNOS Gene Factsheet

Genes contain the information to make all the proteins our body needs. Humans have around 25,000 genes, 99.9% of which are exactly the same in all people. There is much interest in the genes that differ between people and the impact that these differences may have on our health and risk of disease. At the University of Reading, we are interested in how these variations affect people's response to foods. For this reason, in some of our studies we ask you to provide a blood sample that we use to determine whether you have variations of a particular gene.

Your blood sample will be tested for variations in eNOS, and this factsheet is designed to explain what eNOS does in the body and what impact variations in the eNOS gene may have on your health.

What is eNOS, and what does it do?

The eNOS gene provides instructions for making a protein which produces nitric oxide, a substance which causes the dilation of blood vessels.

Does everyone have the same eNOS gene?

The eNOS genetic code can differ slightly from person to person. The most common change in the genetic code alters a single protein building block (amino acid) in the eNOS protein. Some studies have shown that this variation can change the activity of the protein, causing it to produce less nitric oxide under certain conditions.

Everybody inherits two eNOS genes, one from each parent. Therefore, it is possible for you to have two genes coding for the less active protein (termed AA), two genes coding for the more active protein (termed GG) or one of each (termed AG). About 1 in 10 people will have the AA version, 7 in 10 will have the GG version and 2 in 10 have a combination (AG). The AA version is much less common in Asian populations (1 in 200 people). The combination of genes which you have is called your "genotype"

How does this affect me as an individual, and what can I do about it?

If you have the less active AA genotype, it may mean your body produces less nitric oxide than people with the more active GG genotype. This may mean that the blood vessels of AA individuals may be slightly less flexible. There is evidence that having less flexible arteries may be associated with an increased risk of heart disease. Research on the eNOS gene is still in the very early stages, but some studies suggest that people with the AA eNOS genotype have a 30% increased risk of certain types of heart disease compared to people with the GG genotype. However, many other factors, such as other genes and our lifestyle play a much larger part in determining the risk of heart disease. For example, smoking is associated with a 200-300% increase in the risk of heart disease.

It is thought that individuals with the combination genotype (AG) have a risk of heart disease similar to those with the GG version.

Although the impact of having the AA eNOS genotype on heart health is likely to be relatively minor, individuals with this variation may be advised to pay particular attention to reducing other risk factors. There is some evidence that individuals with the AA genotype are more vulnerable to the negative effects of smoking on heart disease, but also respond more positively to increasing their dietary intake of fish oils. Giving up smoking and regularly eating oily fish or taking fish oil capsules are general recommendations for improved health across the whole population, but it may be that these are even more important if you have the AA genotype. Keeping physically active, eating less saturated fat and salt, increasing your intake of fruit and vegetables and not being overweight are also going to help reduce everyone's risk of heart disease. The British Heart Foundation website, www.bhf.org.uk has lots of tips on how to look after your heart.

Implications for health insurance

The genotyping we do is what is called 'predictive testing' and as such there is no need to disclose the results of these tests, at present or any time in the future, to your insurance company

Why are researchers interested in this gene?

We are interested to further determine if individuals of different eNOS genotype respond differently to dietary change. In the future, rather than providing everyone with general dietary advice, it may be that a more personalised approach is taken, providing advice tailored to an individual's genetic make-up

Sources of further information

It must be emphasised that genotyping is a relatively new area which is still in the research stage, with information in this area far from complete. If you would like to read more on this topic, you may find the following web-site of the Human Genetics Commission useful, www.hgc.gov.uk

Your eNOS genotype result –

If you have any questions or would like further information please contact your study investigator, or Prof Ian Rowland.

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The *FTO* Gene Factsheet

Genes contain the information to make all the proteins our body needs. Humans have around 25,000 genes, 99.9% of which are exactly the same in all people. There is much interest in the genes that differ between people and how they impact our health. At the University of Reading, we are interested in how these variations affect people's response to foods. For this reason, in some of our studies we ask you to provide a blood sample that we use to determine if you have variations of a particular gene.

Your blood sample will be tested for variations in the *fat mass and obesity associated (FTO)* gene, and this factsheet is designed to explain what *FTO* does in the body and what impact variations in the *FTO* gene may have on your health.

What is *FTO*, and what does it do?

The *FTO* gene provides instructions for making the *FTO* protein is involved in the regulation of appetite.

Does everyone have the same *FTO* gene?

The *FTO* genetic code can differ slightly from person to person. Changes in the *FTO* gene can alter its structure and function. One such change in the genetic code (rs9939609), results in an A or T version of the gene. Everybody inherits two *FTO* genes, one from each parent. Therefore, it is possible for you to have two genes coding for the more active variant (termed TT), two genes for the less active variant (termed AA) or one of each (termed AT). The genotype distribution is about 15% for the AA version, 50% for the AT version and 37% for the TT version.

How does this affect me as an individual, and what can I do about it?

If you have the less active AA version of the gene, it may mean that the gene may not process properly the information needed to create a functional *FTO* protein, thus this inefficient protein may lead to excess body weight gain. Research on the *FTO* gene is still in the very early stages, but some studies suggest that people with the AA version of *FTO* weigh 3 kg more and have an increased risk of obesity compared with people with the TT version. Individuals with the combination gene (AT) weigh on average 1.2 kg more compared with people with the TT version.

However, many other factors, such as environmental and socioeconomic conditions and our lifestyle play a much larger part in determining the risk of excess body weight. For example, a high dietary fat intake, energy rich drinks, and a low level of physical activity confer a much higher risk of developing obesity. Keeping physically active, eating less high-energy density food and increasing your intake of fibre, fruit and vegetables are also going to help reduce everyone's risk of excess body weight. The 'change4life' website, www.nhs.uk/Change4Life/Pages/default.aspx has lots of tips on how to look after your weight.

Implications for health insurance

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Why are researchers interested in this gene?

We are interested to further determine if individuals of different *FTO* genotype respond differently to dietary change. In the future, rather than providing everyone with general dietary advice, it may be that a more personalised approach is taken, providing advice to suit an individual's genetic make-up

Sources of further information

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Your *FTO* genotype result –

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The *LEP* and *LEPR* Genes Factsheet

Genes contain the information to make all the proteins our body needs. Humans have around 25,000 genes, 99.9% of which are exactly the same in all people. There is much interest in the genes that differ between people and how they impact our health. At the University of Reading, we are interested in how these variations affect people's response to foods. For this reason, in some of our studies we ask you to provide a blood sample that we use to determine if you have variations of a particular gene.

Your blood sample will be tested for variations in the *leptin* (*LEP*) and the *leptin receptor* (*LEPR*) gene, and this factsheet is designed to explain what *LEP* and *LEPR* do in the body and what impact variations in the *LEP* and *LEPR* gene may have on your health.

What are these genes and what do they do?

The *LEP* gene provides instructions for making a hormone (leptin) which is involved in the regulation of body weight through reducing food intake and stimulating energy expenditure. The effect of *LEP* on metabolism is mediated by a protein called *LEPR*. This leptin receptor is found in high concentrations in certain areas in the brain.

Does everyone have the same *LEP* and *LEPR* gene?

The *LEP* and *LEPR* genetic codes can differ slightly from person to person. Changes in the *LEP* gene can alter the amount of leptin produced. One such change in the genetic code (2548 G/A), results in an A or G version of the gene. Everybody inherits two *LEP* genes, one from each parent. Therefore, it is possible for you to have two genes coding for the higher level of leptin (termed AA), two genes coding for the lower level of leptin (termed GG) or one of each (termed GA). About a quarter of people will have the GG version, another quarter will have the AA version and the remainder will have a combination (GA).

Changes in the *LEPR* gene can alter its function. One such change in the genetic code alters a single protein building block (amino acid) in the *LEPR* protein at position 223. Everybody inherits two *LEPR* genes, one from each parent. Therefore, it is possible for you to have two genes coding for the more active protein (termed RR), two genes coding for the less active protein (termed QQ) or one of each (termed QR). The frequency of the R copy of the gene varies significantly across countries, with about a third of Caucasian population carrying the R copy.

How does this affect me as an individual, and what can I do about it?

Although in animals the *LEP* and *LEPR* gene variants have been shown to play a major role in regulating body weight, in humans the associations has been highly inconsistent. Some studies suggest that people with the GG version of the *LEP* gene have higher BMI and lower leptin concentration in their blood compared with people with either GA or AA version.

If you have the low activity QQ version of the gene it means that these receptors may not work properly and may receive fewer signals from leptin compared with the high activity RR or the intermediate QR version of

the gene. Therefore, people with the RR version of the *LEPR* gene might have lower risk of becoming obese compared with people who carry one copy of Q.

However, the effects of each version of both the *LEP* and *LEPR* remain uncertain. Many other factors, such as environmental and socioeconomic conditions and our lifestyle play a much larger part in determining the risk of excess body weight. For example, a high dietary fat intake, energy rich drinks, and a low level of physical activity confer a much higher risk of developing obesity. Keeping physically active, eating less high-energy density food and increasing your intake of fibre, fruit and vegetables are also going to help reduce everyone's risk of excess body weight. The 'change4life' website, www.nhs.uk/Change4Life/Pages/default.aspx has lots of tips on how to look after your weight.

Implications for health insurance

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Why are researchers interested in this gene?

We are interested to further determine if individuals of different *FTO* genotype respond differently to dietary change. In the future, rather than providing everyone with general dietary advice, it may be that a more personalised approach is taken, providing advice to suit an individual's genetic make-up

Sources of further information

It must be emphasised that genotyping is a relatively new area which is still in the research stage, with information in this area far from complete. If you would like to read more on this topic, you may find the following web-site of the Human Genetics Commission useful, www.hgc.gov.uk

Your *LEP* genotype result –

Your *LEPR* genotype result –

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The *MC4R* Gene Factsheet

Genes contain the information to make all the proteins our body needs. Humans have around 25,000 genes, 99.9% of which are exactly the same in all people. There is much interest in the genes that differ between people and how they impact our health. At the University of Reading, we are interested in how these variations affect people's response to foods. For this reason, in some of our studies we ask you to provide a blood sample that we use to determine if you have variations of a particular gene.

Your blood sample will be tested for variations near the *melanocortin-4 receptor (MC4R)* gene, and this factsheet is designed to explain what *MC4R* do in the body and what impact variations in the codes next to *MC4R* gene may have on your health.

What is *MC4R*, and what does it do?

The *MC4R* gene provides instructions for making the *MC4R*. *MC4R* reduces food intake and stimulate energy expenditure and consequently is important in the regulation of body weight.

Does everyone have the same *MC4R* gene?

The *MC4R* genetic code can differ slightly from person to person. Changes in the *MC4R* gene can alter its function. One such change in the genetic code (rs17782313) next to the *MC4R*, results in a C or T version of the gene. Everybody inherits two *MC4R* genes, one from each parent. Therefore, it is possible for you to have two genes coding for the more active variant (termed TT), two genes for the less active variant (termed CC) or one of each (termed TC). The genotype distribution is about 6% for the CC version, 37% for the TC version and 57% for the TT version

How does this affect me as an individual, and what can I do about it?

If you have the less active CC version of the gene, it may mean that the gene may not process properly the information needed to create a functional protein, thus this inefficient protein may lead to excess body weight gain. Research on the *MC4R* gene is still in the very early stages, but some studies suggest that people with the CC version of the code next to *MC4R* weigh 1.5 kg more and have a higher percentage of body fat and an increased risk of obesity compared with people with the TT version. Individuals with the combination gene (AT) weigh on average 0.7 kg more compared with people with the TT version.

However, many other factors, such as environmental and socioeconomic conditions and our lifestyle play a much larger part in determining the risk of excess body weight. For example, a high dietary fat intake, energy rich drinks, and a low level of physical activity confer a much higher risk of developing obesity. Keeping physically active, eating less high-energy density food and increasing your intake of fibre, fruit and vegetables are also going to help reduce everyone's risk of excess body weight. The 'change4life' website, www.nhs.uk/Change4Life/Pages/default.aspx has lots of tips on how to look after your weight.

Implications for health insurance

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Why are researchers interested in this gene?

We are interested to further determine if individuals of different *FTO* genotype respond differently to dietary change. In the future, rather than providing everyone with general dietary advice, it may be that a more personalised approach is taken, providing advice to suit an individual's genetic make-up

Sources of further information

It must be emphasised that genotyping is a relatively new area which is still in the research stage, with information in this area far from complete. If you would like to read more on this topic, you may find the following web-site of the Human Genetics Commission useful, www.hgc.gov.uk

Your *MC4R* genotype result –

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