

## HOW FOOD CAN CAUSE CHRONIC DISEASES

# Fat to blame for diseases

**Cardiovascular diseases, asthma, diabetes and even cancer may well have one thing in common: a chronic inflammatory reaction in the body that begins in fat tissue. New insights from Wageningen food scientists suggest that nutrition plays a big role in this.**

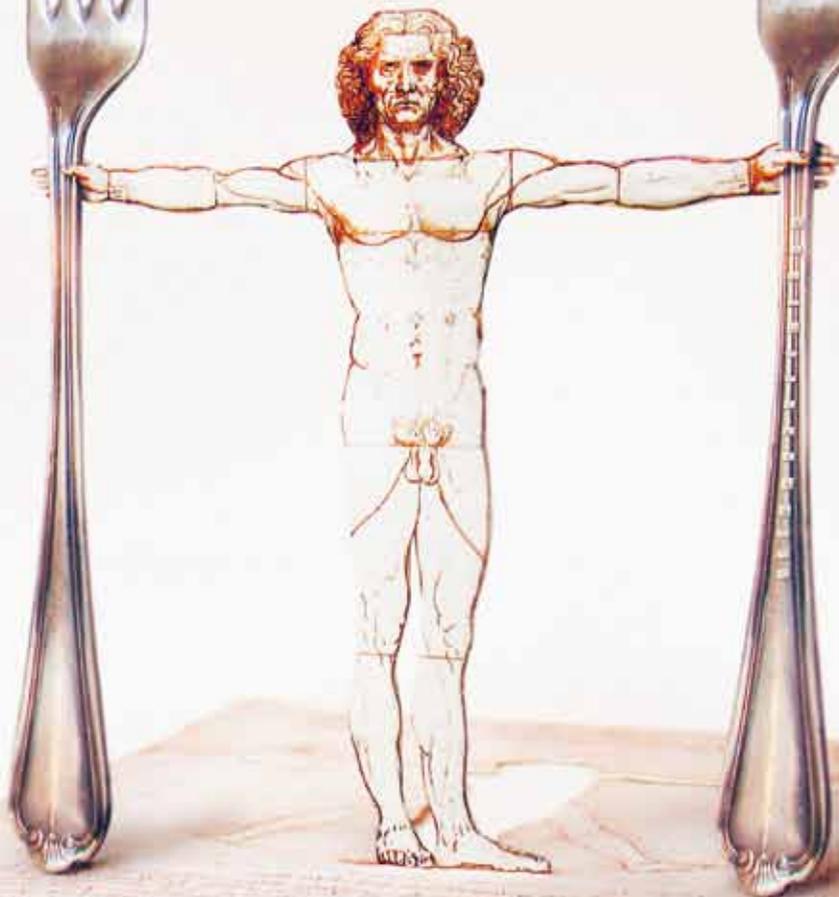
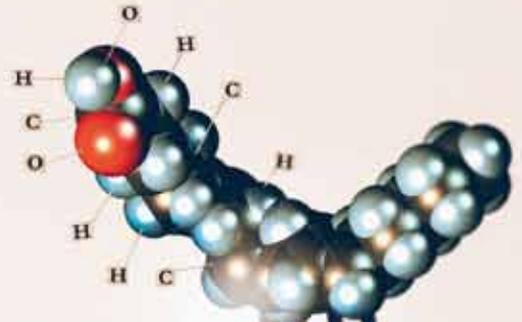
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**B**ad eating habits can lead to overweight and the excess fat can become chronically inflamed and lead to cardiovascular diseases, asthma, diabetes and cancer. By eating healthily and, most importantly, avoiding becoming overweight, you help prevent inflammation from getting established in your body. So it appears that there is a strong relationship between several chronic diseases and nutrition. Michael Müller, Professor of Nutrition, Metabolism and Genomics is researching food-related molecular processes, paying special attention to fat metabolism. He is also researching how you can increase the body's resistance to disease through healthy eating and lifestyle. Müller believes that food has a big influence on the development of chronic inflammation, because certain nutrients activate a range of genes. His research group showed this using nutrigenomics techniques, with which you research which genes are switched on and off by which nutrients, and which metabolic process is then started off. For example, Susan van Dijk, a research scientist in Müller's group,

investigated the gene expression in the fat of overweight test subjects who alternated between a diet rich in saturated fats and one rich in unsaturated fats. 'Saturated fats appeared to stimulate inflammation processes while unsaturated fats did not. If anything, in fact, they stimulated anti-inflammatory processes', explains Müller. 'So diet influences which genes are activated and which genes are not.' According to Müller, modern nutrigenomics techniques enable you to see from the activities of various genes who is healthy and who is not, before any disease symptoms appear. Such techniques are also interesting for the food industry, as they make it possible to demonstrate the functionality of new food ingredients.

### MOLECULES OF PLEASURE

Professor of Food and Pharmacology Renger Witkamp also found a clear relationship between food and inflammatory processes in the body, albeit via a totally different mechanism. Witkamp researches the relationship between food and medicines, but is also >



interested in the problem of too much and too fatty food. In this way he hopes to tackle many of the diseases of prosperity at their source, in the Western diet which is too one-sided and too fatty. But it seems that the urge to eat more and increasingly unhealthy food is tremendous. 'Eating is a primal urge', Witkamp claims. 'The body stimulates and rewards eating by making what we call the 'molecules of pleasure'. The body's own drugs, the endocannabinoids, play a central role in this. One of the things the body uses to produce these substances is the fats in food. These fats attach themselves to the same receptors as cannabis and give the satisfied feeling we experience after a good meal.

Witkamp says that these endocannabinoids also play a central role in controlling inflammation, and therefore probably also have an indirect role in controlling chronic diseases. 'Chronic diseases such as asthma or psoriasis, and even arteriosclerosis, all have an inflammation component that causes or aggravates the disease', explains Witkamp. 'It looks as though some endocannabinoids play an important role in combating chronic inflammation.' It is mainly the type of food that determines which kinds of cannabinoid the body

## 'Overweight is a constantly recurring factor in many types of cancer, cardiovascular diseases and diabetes'

creates. 'For example, the cannabinoids that the body makes from fish oil have a strong anti-inflammatory effect.' Or more broadly: the range of fatty acids in our diet determines the type of biologically active molecules that are made, which either stimulate or limit chronic inflammation. In other words, by choosing the right food – that will manufacture anti-inflammatory cannabinoids, for example – you can to some extent put the brakes on chronic inflammation and perhaps even limit the impact of certain diseases. So it seems that there are several different mechanisms by which healthy eating limits chronic inflammation in fats and organs, and that if you prevent such inflammation you might well be able to fend off a whole range of chronic diseases.

### CHRONIC INFLAMMATION AND FAT

If you eat too much, the body stores the extra energy as fat in organs and fat tissue. In itself, fat tissue is a perfectly good storage place for excess fat, but organs are not – it makes them extra vulnerable to inflammation. Visceral fat around the organs is highly sensitive and prone to inflammation, generating numerous toxic byproducts as a result.

In a liver that is too fatty there are specialized liver cells, the Kupffer cells, which are responsible for these local fat inflammations. And they can cause a lot of damage: liver cells die out and connective tissue is formed. The liver becomes cirrhotic. But the inflammation can also spread: inflammatory factors leak into the blood and can cause secondary damage to other organs. When people are overweight, fatty tissue can easily become inflamed because fat cells get too big and eventually die. At this point the body employs macrophages to clean up the dead cells. And so local inflammation can spread, become chronic and potentially form the basis of chronic diseases.

### FISH WITH SPINACH

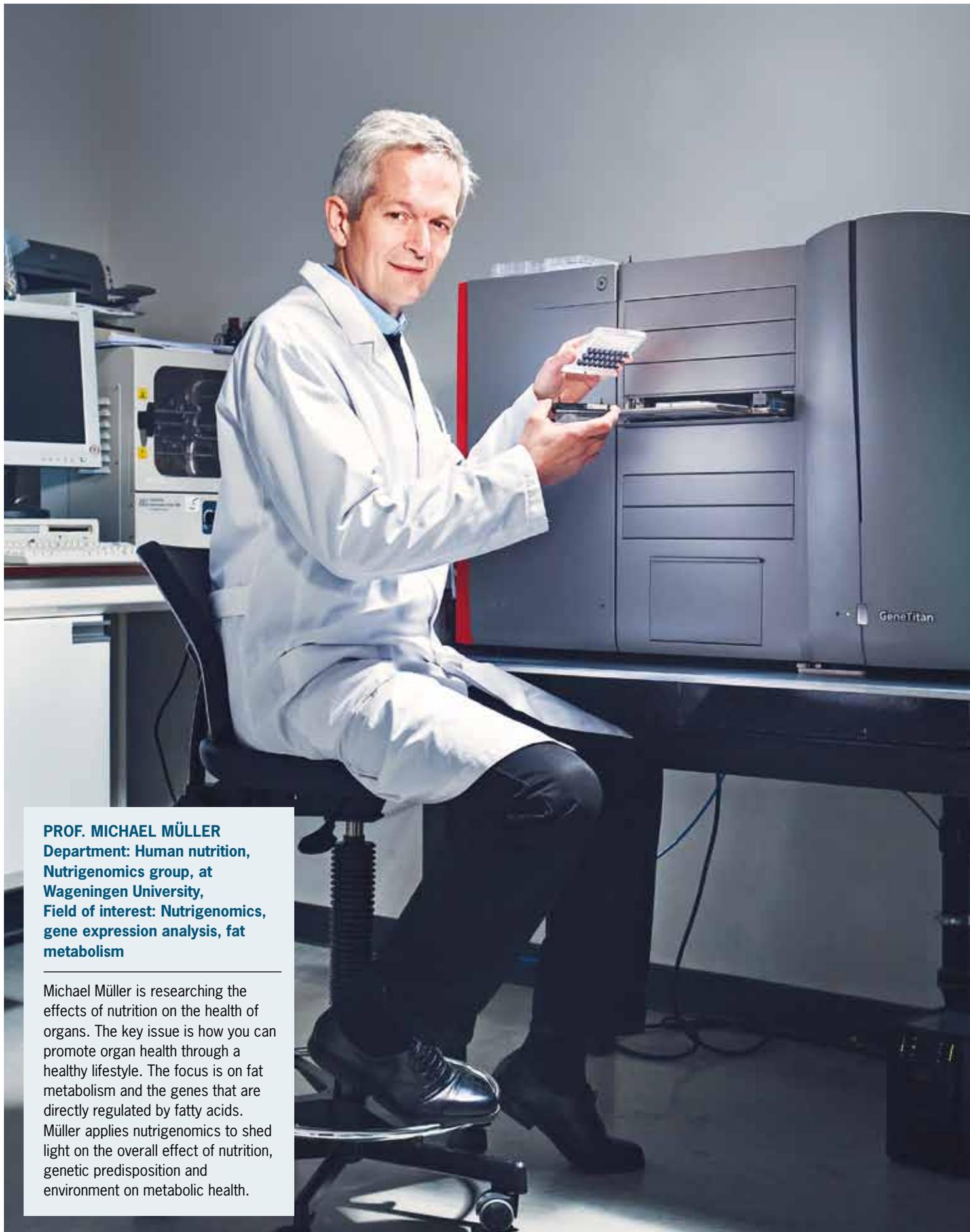
Ellen Kampman, Personal Professor of Nutrition and Cancer, does a lot of research into the relationship between eating habits and the prevention of tumours. She stresses the importance of adequate exercise and preventing overweight in maintaining health.

Kampman's hunch is that inflammation could play a role in cancer too, only it is not yet clear exactly how this process works. It is clear, she says, that a varied diet is important in keeping the risk of cancer to a minimum. 'Healthy eating is part of a package deal, in which exercise also plays an essential role', Kampman explains. 'It is estimated that we can prevent thirty to forty percent of all cases of cancer through good nutrition, more exercise, and avoiding overweight.' But overweight is the Achilles heel of Westerners. Twenty five years ago over a third of Dutch adults were overweight; now it is almost half, and this undoubtedly has >



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Ellen Kampman wants to gain a fuller understanding of the influence of overweight and fat distribution on bowel and breast cancer. She is studying the underlying metabolic processes – such as inflammatory reactions – involved in cancer of the colon, as well as the effect of overweight on breast cancer and its treatment. She will do her research in close collaboration with the Gelderse Vallei hospital.



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Michael Müller is researching the effects of nutrition on the health of organs. The key issue is how you can promote organ health through a healthy lifestyle. The focus is on fat metabolism and the genes that are directly regulated by fatty acids. Müller applies nutrigenomics to shed light on the overall effect of nutrition, genetic predisposition and environment on metabolic health.

implications for the prevention of numerous diseases of prosperity. 'In the Netherlands we eat too few low-calorie plant-based foods', claims Kampman. 'Only five percent of the Dutch population manages the recommended 200g vegetables and two pieces of fruit per day.' The impact of those extra kilos is considerable: 'Overweight is risk factor number one for many chronic diseases of prosperity. It is a recurring factor in many forms of cancer, cardiovascular diseases and diabetes.'

There is a lot to be gained from good nutrition.

'We know for sure that many fruits and vegetables can help prevent certain cancers, for example tumours in the head and throat area, and lung and stomach cancers', says Kampman. But she stresses that it is difficult to pinpoint specific foodstuffs as 'bad': 'It's all extremely subtle and complex. What matters is how often you eat something and to what extent you've been chronically exposed to certain substances.' In cases of acute exposure, such as a one-off burnt steak or dish of fish combined with spinach, the body is able to mop up any damage. But if you ate these things day in day out over a longer period, the body would not be able to keep up.

## METABOLIC FITNESS

Although the Wageningen food scientists believe that chronic inflammation may be a central factor in causing chronic diseases, there are other issues involved in staying healthy. 'The message is not simple. There's no magic pill that will keep us healthy and it is clear that to keep healthy, people have to go back to what they eat', Müller explains. He underlines that his food research doesn't focus on illness but on health: how do you stay healthy as long as possible, how can you improve your health, and what role can nutrition play in this? 'Our research gives people a toolbox for healthy eating, as it were.' Just like Kampman, Müller declares that there is no such thing as bad food as long as you eat a varied diet. If you do, the occasional fatty snack from the snack bar won't do any harm. In the light of this, Müller thinks it's important to realize that there's more to health than not being ill. Health is all about the body's ability to adapt and be resilient. 'Just as you can improve your fitness through regular

## 'Preventing inflammation may ward off a wide range of chronic diseases'

exercise, you can also improve your metabolic fitness by eating a varied and healthy diet', he explains. 'A varied diet puts various systems in your body on alert and places the body under mild stress.' The body then goes into action to adapt itself to the situation and so you create extra capacity and resistance. With more resistance the body can cope with a lot more, and a little of a toxic substance or a fatty snack from time to time is not a disaster. Infections can be fought off better as well. With a monotonous diet you get rusty, as it were: all the systems that you don't use become less active, or they may even become completely non-functional. It's clear that there is a 'use-it-or-lose-it' principle at work. That rustiness sets in at the gene level: unused genes lose the capacity to adapt, causing the cell to lose part of its functionality. Müller: 'This process looks a lot like ageing: so unhealthy eating does make people age faster.' >

## THE ROLE OF THE INTESTINES

The surface of the intestine is roughly the size of two football fields, and the body is exposed to outside influences all along it. It is not for nothing that fifty percent of the immune system is active here. Because Western food has been too completely optimized, many nutrients are extracted in the first part of the intestines. By eating enough nutrients and fibres, you get the whole of the intestines working and the system is challenged in various ways. The intestines help the rest of the body with digestion, doing some of the preliminary work involved in burning fat, for example. Besides burning fat, the intestinal epithelium wraps up fats in things called chylomicrons. These are like fat balls wrapped up in protein, and they make it easier to transport the fats to the organs via the lymphatic system. The more fat cells are broken down by the intestinal cells themselves and not sent to the organs in the form of chylomicrons, the less fat organs such as the liver have to break down. The liver can then save its energy for other metabolic tasks.

Unsaturated fats are an important key to your metabolic fitness level, as these fats are potentially dangerous. Oxidation in the body creates all sorts of harmful by-products which the body needs to get rid of as quickly as possible. It does this efficiently by binding unsaturated fats to specific receptors, and these in turn stimulate genes which increase the cell's capacity to burn fat so that it gets rid of fat quickly. A nice side-effect is that this extra capacity is also used to burn other fats faster, a clear sign that the body is in good shape. The reverse is true too: a body that is not in good shape has too little capacity to burn fat. A systematic increase in fat and fat transporters – or lipoproteins – in the blood is the first warning sign of an impending problem. If the process continues unchecked there is a danger of metabolic syndrome developing. This is a complex of metabolic conditions, of which the main symptoms are high blood pressure, diabetes and raised cholesterol levels.

### **BROCCOLI**

Along with unsaturated fats, broccoli is an example of a food item that sharpens up the body's systems. Like most plant-based foods, broccoli contains many biologically active substances which are not toxic in low concentrations but which nevertheless cause a sort of stress in cells. This causes the body to bring more detoxifying enzymes into play to break down the potentially dangerous substances. As a result, the cells

### **CANCER AND ALCOHOL**

Our food contains few carcinogenic substances, but there are exceptions. Some foodstuffs (red meat, alcohol, and combinations of leafy vegetables and fish) are known to raise the risks of certain forms of cancer if large amounts are consumed over a long period of time. Heavy drinkers need to watch out.

'The main carcinogen in our food is alcohol', says Kampman. 'Quite a lot of people expose themselves daily, and that means chronically, to this toxic carcinogenic substance. I find the drinking habits of Dutch adolescents particularly worrying.' Young people are being lured en masse into drinking more and more hip alcoholic drinks. The possibly big health impact of this chronic heavy drinking, which the body's repair system cannot keep up with, will only become clear later.

## **'A varied diet puts the body under slight stress and keeps various systems on top form'**

are better armed against other dangerous toxins that may occur in high concentrations in foodstuffs, such as aflatoxins in grain and peanut products. Untrained cells cannot get rid of these sorts of toxic substances fast enough. This can lead to cell damage and can form the basis for a tumour. In short, what doesn't kill you makes you stronger. The problem with Western diet is that there are too few foods in it – for instance, vegetables and oily fish – that challenge the body, so that adaptation mechanisms go unused and diseases get more of a chance. If you want to keep your body healthy, you must expose it continuously to challenging foods.

### **BALANCE IN THE BODY**

Müller wants to test the body's resilience in relation to healthy nutrition in somewhat overweight men who appear to be healthy. He will do this in collaboration with the Gelderse Vallei Hospital and the entire Human nutrition department. The idea is to test resistance before and after a period of healthy eating by submitting the body to mild stress and examining its recovery using all the methods offered by modern nutrition science, such as nutrigenomics and MRI techniques. 'One of the things we want to look at is how quickly a big intake of fat can be burned up and therefore how well regulated the balance in the body is. Like this you can see at a very early stage, before there are any clinical symptoms, how healthy someone is and whether there is a risk of any chronic diseases.' Müller hopes to make clear that it really does help to eat healthily, and he hopes to get people to make lifestyle changes that will bring them better health. Müller: 'There's a lot to be gained because you really can hold off chronic diseases by using good nutrition to improve your metabolic fitness.' ■



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Renger Witkamp's research includes work on imitating the effect of endocannabinoids, which give us a pleasant feeling after we have eaten a lot. One of his ideas is to find methods of slowing down the breakdown of the 'molecules of pleasure'; another is to artificially stimulate their formation. Then you would get a satiated feeling even without a copious dinner.