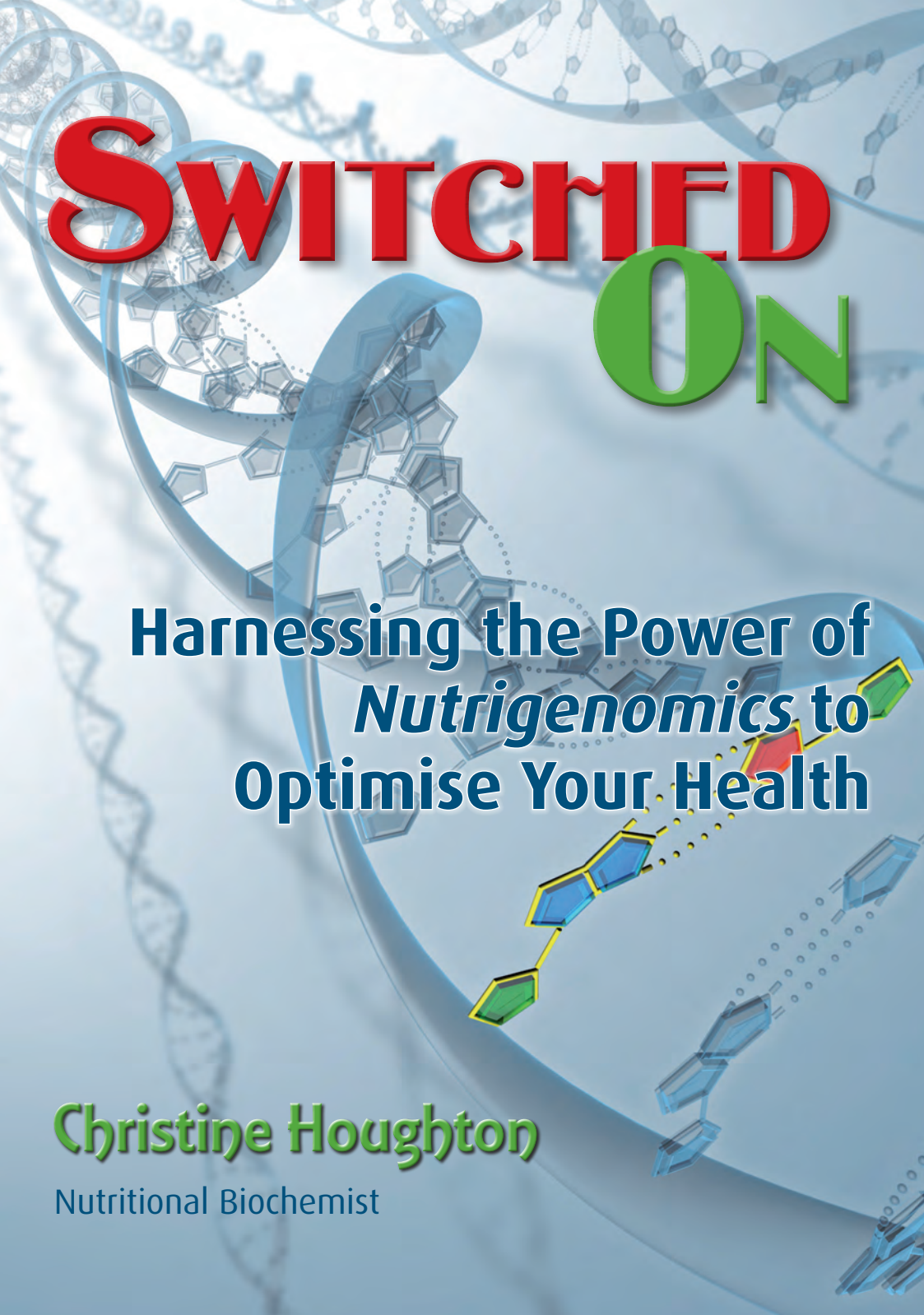
Switched On
Harnessing the Power of *Nutrigenomics* to Optimise Your Health
Christine Houghton
Nutritional Biochemist

‘Switched On’

Harnessing the Power of Nutrigenomics to Optimise *Your* Health

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This book is dedicated to those seekers of truth who wish to regain control of their own health, allowing modern Nutrigenomic Science to complement the time-honoured principles of Nature.

SPECIAL NOTE TO READERS
The information contained within this book is for education and information purposes. It is not intended to provide diagnosis or treatment of any medical condition, nor is it intended to replace the guidance and personalized treatment provided by a health professional. Any application of the information provided in this book is at the readers' discretion and sole responsibility.

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CONTENTS

INTRODUCTION

It's likely you are reading this book because you have a genuine interest in your health and ways of enhancing your wellbeing and preventing disease; so you know that your most valuable asset is good health. Many of us fail to appreciate this fact until we become sick. Modern society encourages us to spend much of our time in search of material wealth, yet this is clearly no substitute for good health.

Do you ever feel as though you have little or no control over your health? Do you feel that you develop sickness without ever knowing why? Do you feel helpless in thinking that you are dependent on pharmaceutical medicines and perhaps surgery to stay reasonably well? Do you feel that you are ageing prematurely? If this is how you feel, rest assured, you're not alone!

This book will help you to regain control of your health by showing you how to use the principles of *Nutrigenomics (pr. Nutri-gen-o-mix)*, a relatively new science which puts the spotlight of health care back on you as an individual and away from helpless dependency on modern medicine. This is not to say that we shouldn't take advantage of the countless marvels modern medicine has to offer. Many of the sophisticated diagnostic and life-saving techniques of modern medicine are nothing short of brilliant!

What's worth considering however, is that the ready availability of pharmaceutical medicines for virtually any symptom you can imagine has discouraged us from looking for our own answers in the way that our ancestors did. Every civilisation has its own healing tradition and

some of the plant foods and medicines used in these traditions have been the basis from which modern pharmaceuticals have been the basis from which modern pharmaceuticals have been developed. Many of these traditional medicines continue to be used today, not only in the countries of their origin but also globally by individuals looking for ways to improve their health or to prevent illness.

The real power of Nutrigenomics lies in the identification and application of powerful food-derived biomolecules capable of 'switching on' certain genes associated with cellular health.

For most of us, every cell of the human body has all the information it needs to remain healthy and this information is coded within the DNA of *every* gene in *every* cell. Once we learn how to 'tap into' this code and better understand how to send it the signals it needs, all sorts of distressing symptoms may disappear. This may be as simple as feeling less tired, experiencing fewer aches and pains, better digestion, a better mood - sometimes just a sense of 'feeling better'.

Although Nutrigenomics may also use plants as sources of medicine, it is not a branch of any traditional medicine we have ever known. Instead, Nutrigenomics is firmly anchored in modern science, yet is simple enough that we can all take advantage of its principles. Although it sits on a foundation of Nutrition Science, the real power of Nutrigenomics lies in the identification and application of powerful food-derived biomolecules capable of *'switching on'* certain genes associated with cellular health.

To learn how this extraordinary new science can give us so much more control over our health and wellbeing, *read on……*

CHAPTER ONE

Has modern Medicine lost its way?

Tools seemingly needed to practice modern medicine have become highly sophisticated but also impossibly expensive. None of them however, has been sufficient to curb the accelerating growth in chronic disease. Populations globally continue to succumb to the '*Diseases of Civilization'*; cancer, heart disease, diabetes, osteoporosis and arthritic conditions to name the most prevalent.

Medicine boasts its ability to transplant organs, reattach severed limbs and replace worn-out joints. Yet, the common ailments which afflict millions the world over continue to defy practitioners of modern Medicine. Whilst pharmaceutical drugs provide relief from the symptoms of many of these day-to-day ailments, they do little if anything to arrest the cause. What's more, most of these medicines produce adverse effects sometimes more distressing to the individual than the symptoms of the original complaint.

Too often we look in the wrong places to find ways to be healthy – pharmaceutical drugs and surgery should be our very *last* option, not our first. Mankind has survived on this planet for millions of years, using only what Nature has provided – so, perhaps we don't need to make day-to-day health care so complicated, nor so impossibly expensive!

The practice of modern Medicine as we know it today is associated with treatments based largely on the prescription of pharmaceutical drugs. When such prescriptions fail, surgery is often the next level of treatment. Such treatments are not without risks.

Barbara Starfield[1], a professor in health policy and management at Johns Hopkins University in Baltimore Maryland, has published frightening statistics on deaths due to medical error in the United States. Her data show that each year there are around 12,000 deaths from unnecessary surgery, 7,000 deaths from medication errors in hospitals, 20,000 deaths from other errors in hospitals, 106,000 deaths from the adverse effects of medications prescribed in error and 80,000 deaths from infections acquired whilst in hospital. This is a total of 225,000 deaths every year which are due to error or to adverse reactions to prescribed medication.

To put this into a different perspective, medical error, she says, constitutes the third leading cause of death in the U.S. after heart disease and cancer. These data are unlikely to be very much different in other developed countries. In Australia where I live, the data are quite similar when one takes into account the population difference between the two countries.

If we were to look at the causes of death 100 years ago[2], we would find that the two leading causes of death were tuberculosis and pneumonia, both infectious diseases. Now that deaths by infections are so much better controlled by improved hygiene and modern medicines, the diseases which plague us today are the chronic *degenerative and inflammatory* diseases.

The degenerative diseases include the *wear and tear* diseases such as break down of the joints and clogging of the blood vessels with fatty plaque. The *inflammatory* diseases include arthritis (pain, redness and swelling) of the joints, asthma (inflammation of the airways) and cardiovascular disease (inflammation of the blood vessels).

Leading the Charge In recent years, the term *Integrative Medicine* has been used to describe those conventionally-trained medical practitioners who integrate aspects of non-pharmaceutical medicine into their mainstream practices.

The U.S. National Institutes of Health (NIH) define Integrative Medicine as *"combining mainstream medical therapies and CAM[i] therapies, for which there is some high-quality scientific evidence of safety and effectiveness."* To the patient, it may appear as if the particular practitioner is trained as both a medical practitioner and a naturopath. To many consumers, this is considered a great advantage, providing what is seen to be the 'best of both worlds'.

Because Integrative Medicine stands outside the criteria for medical registration, an Integrative Medicine practitioner, although satisfying the necessary regulatory criteria to practise mainstream medicine, is not required to meet standards in Integrative Medicine. The internal standards which these practitioners have established to train and credential their members are not acknowledged by governing authorities; nor are they known or understood by consumers. As a result, a consumer has no way of knowing how knowledgeable or competent a particular integrative medical practitioner may be.

Regardless of any such current barriers to practice, those forward-thinking Integrative Medicine practitioners who have stepped outside conventional practice to embrace evidence-based alternatives are in huge demand. I personally know many such clinicians to have *'waiting-list'* practices; surely this illustrates what consumers are really seeking.

Interestingly, medical practitioners in some universities still take the '*Hippocratic Oath'* before they can practise medicine. Hippocrates was a doctor and teacher of medicine some 2,500 years ago and is referred to as the *'Father of modern medicine'*. He is credited with saying, "*Let food be thy medicine and medicine be thy food."*

Although Hippocrates' claim that *food and medicine are interchangeable* seems overly simplistic in the 21st century, there are elements of this philosophy which are still relevant today. This is especially so in the science of Nutrigenomics, as we will see later.

[i] CAM - *Complementary and Alternative Medicine*

CHAPTER TWO

Why do we get sick?

If you've only ever enjoyed good health, you may have never given a thought to the question, "Why do some people get sick and yet others remain healthy?" If you are like most of us, from time to time you will have some experience of sickness but as the years advance, you might notice that your health deteriorates inexplicably. You may become more breathless, you may develop recurrent indigestion, perhaps you feel stiff and sore when getting out of bed in the mornings or you may need frequent naps and so on.

All little things in themselves but nevertheless, they are indicators that things are changing on the inside in ways that limit your experience of life. And then to make things worse, a visit to the GP followed by various tests, shows that those little 'signs' are actually just the tip of the iceberg. The GP may tell you that you have all sorts of things going wrong. High blood pressure, high blood cholesterol and higher-than-normal blood glucose all point to a high risk of your developing diabetes, heart disease or both! Next thing, you are prescribed pharmaceutical drugs to lower the blood pressure, the cholesterol and the glucose, along with a suggestion to eat a low-fat diet and walk more often. How did this suddenly happen, you wonder. "I eat well", you say "and I don't need to do any extra walking – I'm busy all day – I never have a minute to myself."

Mostly, we just accept that this is how things are – that this is the hand of cards we were dealt at birth. You might remember that your parents

or grandparents suffered from some of these same conditions and that you should probably expect to have inherited the same tendencies to disease. To reassure the patient (and perhaps their own ignorance?), it is not uncommon for GPs to 'justify' the presence of a patient's illness by stating that he or she inherited the disease from one or both parents – and yet this is patently untrue because GPs don't typically do genetic tests to determine if diseases run in families.

Although it is now possible to obtain such genetic tests, especially if you are prepared to arrange and pay for them yourself, such tests are still *largely*[ii] the domain of research scientists, not clinicians. It might seem a logical assumption but is laying blame on one's genetic heritage necessarily the correct – or only explanation?

Mostly, we just accept that this is simply how things are – that this is the genetic hand of cards we were dealt at birth.

So if the disease is not inherited, why does the same disease appear to run in families? We've all seen families where the same disease seems to afflict many of its members. But let's stop talking about disease and consider how it may be possible for us to take back control of our own health.

[ii] A technique known as Gene Expression Profiling, still very much in its infancy, investigates a range of genes which act as markers of an individual's likely functional weaknesses. Once these weaknesses have been biochemically identified, the patient may be prescribed a programme to modify the way certain genes are being expressed. The recommendations are based primarily on providing tailored nutritional, exercise and other lifestyle solutions to redress the imbalances created by inefficiently-functioning genes. Gene Expression Profiling, as long as it also makes appropriate recommendations for change, can help put control for health and wellbeing back into the hands of the individual.

CHAPTER THREE

Looking inside our body's cells for answers

Sometimes the concepts we think are the most complicated are really very simple. *'Healthy cells lead to a healthy body'* is a simple message which tells us that if we know how to take care of each of our 50 trillion cells, our health will look after itself! So if we know how to look after *one* cell, we know how to care for them *all*. Probably overly-simplistic but nevertheless, true!

To better understand how we can use Nutrigenomic principles to benefit our own health, let's take a microscopic journey deep inside a typical human cell. Once we know how a cell works, we can more readily appreciate how things can go wrong – but more importantly what we can do to improve cellular function - so that things go right! What benefits one cell can benefit *all* our cells. When all our cells function at their peak, we have reached our highest state of good health. And that should be our goal; to achieve our individual highest possible state of cellular function. The key here is that we don't need to name diagnosed diseases – the principles are the same, regardless.

Now let's explore some of the marvels of a typical human cell. We'll start with the membrane which could be likened to the 'skin' of the cell.

Cell Membrane - the cell's 'skin'. Each cell is surrounded by a protective membrane which preferentially lets in water, oxygen, food and other molecules. Certain molecules simply 'flow' into the cell, whilst others need to be pumped in, using energy the cell has created from food molecules. In the same way, the cell's membrane has a range of complex mechanisms for pumping waste materials out.

Mitochondria - the cell's *'Power Station '* Inside the cell are tiny specialised bodies called mitochondria *(pr. my-toe-kon-dree-a)* which are the 'power stations', producing the energy the cell needs to perform all its functions. If these mitochondria aren't functioning properly, they can't produce sufficient energy.

When your cells are sluggish because of lack of energy production, you will probably feel sluggish too! Sometimes this sluggishness within the cell can be because waste materials aren't being removed efficiently; sometimes, it is because the cell isn't receiving the food molecules it needs. This is one of the areas in which we can exert control; the foods we choose to eat have a direct impact on how our cells produce energy. Certain foods will enable the cell to function at its best while over-processed and refined foods which have lost many of their nutrients will deprive the cell of what it needs and lead to abnormal function. Unprocessed or minimally-processed whole foods are essential for optimal energy production.

Nucleus – the cell's database Just as important as the mitochondria is the cell's nucleus, a large sac which holds our genes. Our genes which are made up of long paired strands of DNA, store our unique *database* of genetic information. This database could be likened to your own personalised *Instruction Manual* – except that it is more the size of an entire library than an ordinary manual!

As well as housing the *database* of information about you, the nucleus is responsible for the cell's reproductive system. Cells are said to replicate by dividing into two new identical cells at intervals. This process is controlled by the DNA.

This is very significant to our health and wellbeing because when healthy cells replicate, two new healthy cells are produced. However, when the DNA has become damaged, the new cells will carry that defect onto the next generation of cells. This sets the scene for ongoing

patterns of disease which can be difficult to reverse; in other words, *chronic disease*.

The DNA has remarkable ability to repair such damage – to a point – but a lifetime of accumulated damage can sometimes overwhelm the cell's natural repair processes. This is where powerful *nutrigenomic* compounds as well as nutrients like folic acid and Vitamin B12 found in certain foods can help the DNA to protect and repair itself.

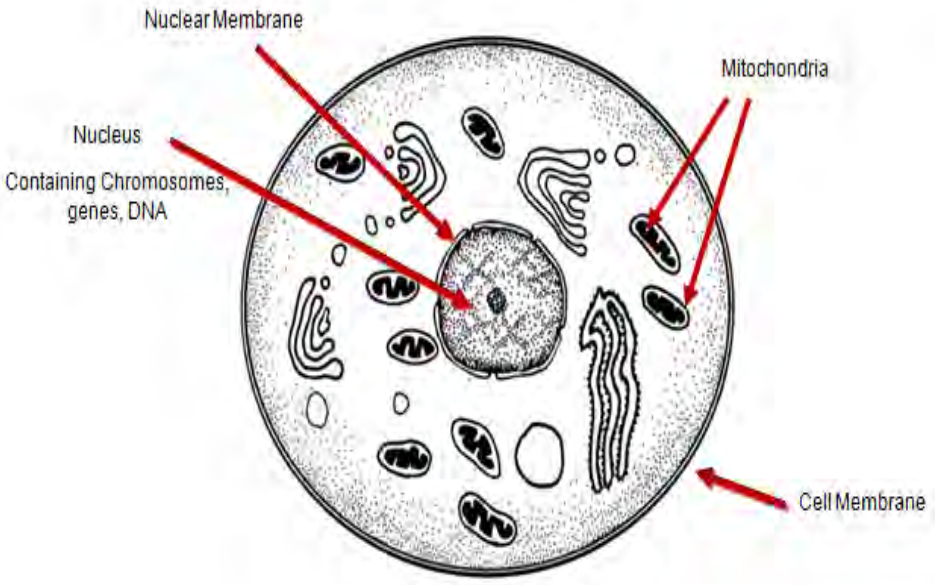


Figure 1 The Human Cell and its Organelles

The Cytoplasm - The cytoplasm is a bit like the 'soup' in which the various cellular structures are suspended. However, this 'soup' is more than just part of the cell's structure; it is a rich source of thousands of essential chemical substances, all playing their own indispensable roles in maintaining normal cell function.

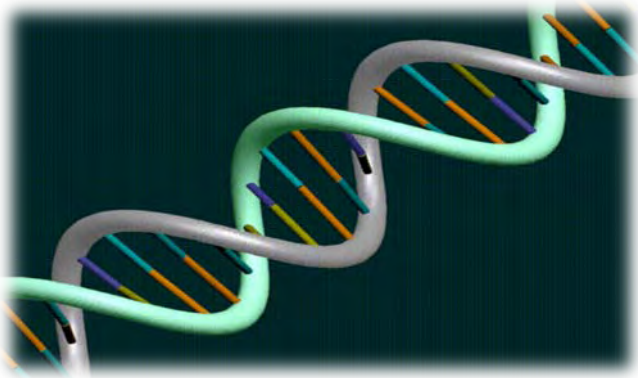
Chapter 4

DNA, Genes and Chromosomes

Now before we explore the really exciting concepts that you can directly relate to your own health, let's zoom into the nucleus and take a closer look at the structures there. Sometimes, the terms *DNA, genes* and *chromosomes* are used interchangeably but they are in fact quite distinct entities. As a scientist, I find the intricacies of human cells absolutely fascinating. If you're not familiar with these concepts, I hope you enjoy this brief glimpse.

The DNA The cell's *database* which contains the code for absolutely everything about you starts with just four molecules, called *base pairs*, abbreviated as A, T, C and G. These base pairs are arranged like the steps in a spiral staircase with the hand-railing coiled in long strands.

This cabled structure is known as DNA and has been described as *'the*



The DNA double helix joined by specific base pairs.

double helix' because of its characteristic helical shape.

Each person's DNA is unique to that individual. One strand of DNA is inherited from the mother and the other from the father. These are the complex molecules which determine everything we inherit – the colour of our eyes, our adult height, whether we can run fast, all of our strengths and weaknesses. In fact, everything we inherit is coded here.

A single chromosome with the DNA double helix visible.

Of course, some of these factors such as eye colour and facial bone structure can't be readily changed because these genes are permanently 'switched off' after birth. But of course these genes can be inherited by the offspring, confirming what we readily observe when we see children who look like their parents.

Scientists are now learning that we *do have control* over many of our very important genes and the way they can be expressed[iii]. Learning how to send the *right* messages to our genes is an important theme of this book. Equally important is the need to ensure that we don't send the *wrong* messages to our genes.

The Chromosomes The 25,000 or so human genes are contained in 23 pairs of non-identical chromosomes. The coiled DNA double helix is clearly seen within the chromosome in the illustration above.

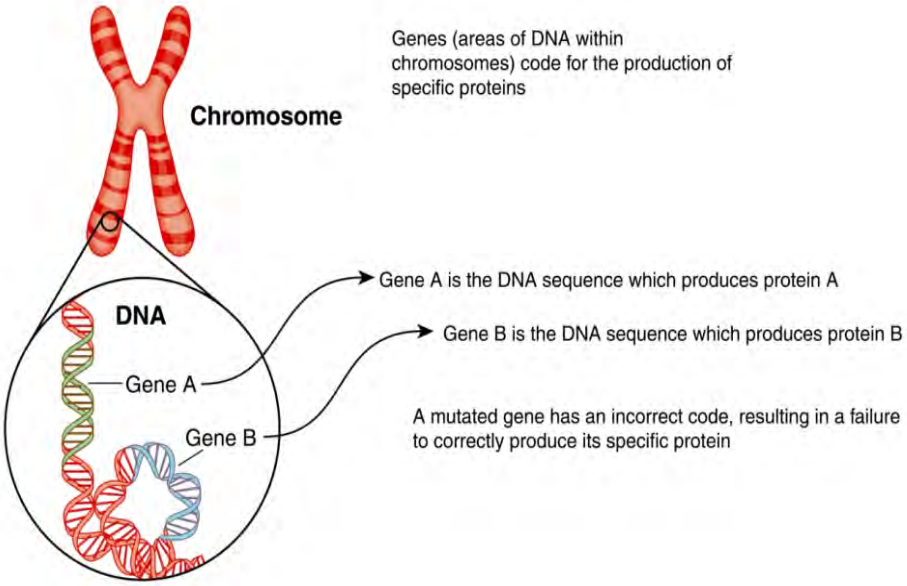
The Genes Even though the double helix is a continuous structure within each chromosome, at various intervals, a section of the DNA code contains a 'stop', signaling the end of the section of code for one gene and the start of the code for another. Each of these separate

[iii] When a gene is '*expressed',* this describes what happens when a gene is 'switched on'. Switching on a gene activates mechanisms which enable a specific protein to be produced. The gene contains the exact code for that protein – a bit like a recipe to tell the cell's 'machinery' the ingredients and the method to make it correctly.

sections is a single gene and each contains the code to tell the cell to make just one specific protein. So when the gene is *'switched on'*, the code can be read and the cell makes a quantity of that particular protein; when the cell registers that it has made enough of the protein, the gene is then switched to the *'off'* position.

The glucose-regulating substance *insulin* is a good example of how this switching works. After a meal, when we have increasing amounts of glucose in the bloodstream, the cells of the pancreas detect this increase and switch the *insulin* gene to the 'ON' position. When the right level of glucose occurs, the *insulin* gene is switched off.

The diagram below shows how chromosomes contain long strands of DNA and how DNA is made up of genes. A gene which has been irreversibly damaged is said to contain a mutation. Mutations are often the fore-runner to the development of serious diseases such as cancer. However, not all mutations are harmful and are often Nature's way of allowing us to adapt over generations to changes in our environment.



CHAPTER 5

Nutrigenomics

– a new paradigm in health care

Scientists who completed the mapping of the human genome in around 2003[iv] identified around 25,000 genes which contain the individual genetic code for each of us. This turned out to be surprisingly few genes, given the apparent sophistication of humans compared to many simpler animal species.

It then became apparent that there was another layer of complexity, the *Epigenome*, which provided a form of modifiable chemical code within the cell's genetic material. *Epigenetics*[v] is a 'sister' discipline to *Nutrigenomics* and later we will explore some of the fascinating aspects of this emerging discipline. Following the completion of the Human Genome Project, research into these relatively new scientific disciplines has become very relevant to human health. *Epigenetic* changes to the DNA are a bit like adding detachable paper clips here and there, making subtle but heritable changes to gene expression.

Quite simply, Nutrigenomics explains how foods (nutrients) interact with our genes (genomics). You can think of *Nutrigenomics* as *'your food talking to your genes'*. Whilst good food and lifestyle choices send 'healthy' messages to your genes, poor choices can damage the DNA in our genes, '*jamming up'* the cell's functions and clogging them with toxic by-products. If this process is ongoing day after day, disease will be the inevitable consequence.

[iv] Known as the Human Genome Project

[v] If you can't wait to learn more about Epigenetics, watch this free video. http://www.pbs.org/wgbh/nova/sciencenow/3411/02.html

From the very first contact a new baby has with its mother's milk or colostrum[vi], signals are being sent to the baby's genome. There can be lifetime consequences to infants (and *their* offspring) who are fed over-processed foods early in life; changes to the child's *epi*genome acquired during its lifetime can be passed down to subsequent generations.

Each of us in our pre-reproductive years has a huge responsibility to take care of the genome our children and grandchildren will inherit. Rather sobering, isn't it, especially when our youthful pre-reproductive years are often spent abusing our bodies in ways that are pushing our cells to their absolute limits?

The burgeoning science of Nutrigenomics in many ways helps us to understand how human health has evolved over millions of years, slowly and constantly adapting to changes in its environment. As environmental factors changed over long periods of time, human cells gradually adapted. Such adaptation literally takes 'thousands and even millions of years' to occur.

Many scientists contend that, as a result of modern technology, Mankind has been exposed to such extraordinary change even in the last few hundred years that it has not been possible for us to adapt fast enough. We have come to the 21st century dressed in Stone Age bodies!

The human genome knew nothing of the refined sugars which have become an integral part of modern dietary intake. In 2008, Americans each consumed on average about 60 kg of sugar[2]. The eight or so generations since we have had ready access to refined sugar has not been sufficient for our cells to have adapted to this. The same can be

[vi] **Colostrum** is a form of milk produced by the mammary glands of mammals in late pregnancy. Most species will generate colostrum within one day of giving birth. Colostrum is rich in antibodies which provide immediate immune protection to the newborn.

said of all of the processed foods which have become a mainstay of many modern diets.

In addition, the bewildering array of modern chemical additives now found in our food supply is unfamiliar to our cells. The cells can become easily overburdened by trying to detoxify the many thousands of foreign chemicals to which our genome is now exposed. Failure to detoxify will result in serious or fatal damage to the cell's delicate mechanisms.

One of the valuable lessons we have learned from Nutrigenomic Science is that there are certain food-derived molecules which can have powerful effects in activating these detoxification processes, allowing us to better prevent these unfamiliar chemicals from harming our cells.

One of the most extraordinary of these nutrigenomic molecules found in food is Sulforaphane *(pr. Sul-4-a-Fane).* Sulforaphane has such remarkable properties that we have devoted a large part of the remainder of this book to it. Sulforaphane and other *nutrigenomic* compounds activate the 'switches' within the cytoplasm of the cell. These switches, as we will see later, are then able to 'switch on' lazy genes or 'switch off' over active genes. As a result of the influence of such nutrigenomic compounds, cells which have lost their ability to properly regulate important functions can again work more efficiently.

Detoxification of unwanted chemical substances is an essential function of all cells[3]. In fact, optimal detoxification is one of the most important ways in which cells can protect themselves against developing cancer. Sulforaphane has been shown to have remarkable potential in this role[4].

Nutrigenomics has opened up a whole new understanding of the role of food in health. Where we once thought that food was just a source of building blocks like proteins, fats and carbohydrates plus essential vitamins and minerals, we now know that food is much more. It provides a huge 'library' of information which is continuously 'talking to our genes'. It has been estimated that foods contain around five to ten thousand different substances[5]. Every one of these which can be

absorbed into our cells has the potential to interact with the function of our cells.

Nutrigenomics has shown us that certain food molecules have very powerful effects, activating switches that can significantly influence the internal health of the cells and their ability to defend and repair themselves. Equally, we know that there are other foods such as the fats found in foods fried at high temperature that send different types of signals to our cells. Signals from such foods can 'switch on' the genes which promote inflammation and destruction within the cells. Similarly, potentially-toxic chemical food additives and agricultural residues found in our food supply are continuously sending messages to our DNA.

There is nothing new about the fact that some foods are 'good for us' and other foods are 'bad for us'. What's new is that a *handful* of particular food molecules have been identified as having exceptional cell-protective properties. When we incorporate these into our daily routine, we can maximize the benefit these remarkable substances can have on our own cells. And if all of your cells are healthy, *YOU* will be healthy!

Nutrigenomics has opened up a whole new way of looking at health. It has given us a much clearer understanding of how we can control the way our own cells work. By selecting the most powerful of the food molecules to be regular 'visitors' to our cells, we can take over a significant level of control of the way our cells function. Food then becomes so much more than a way of satisfying the palate or the appetite, pleasant as that might be. Nor is food just a way of obtaining calories or even vitamins or minerals.

Food is also a signaling system, so that every choice we make sends a message to our cells. Do we choose to send the signals that are destructive to the cell – or those which optimize the cell's function? Can you see that we are on the cusp of a whole new paradigm in health care – one in which you, as the sole owner of *YOUR* body can take back control of your health? To a large extent, it gives you the choice to be well – or to be plagued by illness.

Too often, pharmaceutical drugs are the first approach an individual may select to deal with a health issue or even a diagnosed disease. Just as foods send signals to the cells, so too do pharmaceutical drugs.

Using drugs as a first approach can be much like using a sledge hammer to insert a thumb tack; it results in all sorts of collateral damage. Pharmaceutical medicines are simply not specific enough to make a correction in the cell's function without producing an array of undesirable other effects we call *side effects.* The side effects occur because the drug is just not sophisticated enough to single out the one effect it is designed to produce.

Compare this to being able to select a *nutrigenomic* compound capable of *'switching on'* hundreds of cell-protective genes at the same time; this is surely an opportunity to acknowledge the marvels of Nature! Such nutrigenomic substances are like the conductors of an orchestra, sending continuous subtle signals to the musicians so that the finished performance is perfectly-synchronised. Such is the magnificent and complex function of human cells. We are really only just beginning to comprehend their intricacies.

So, why would you choose a sledge hammer when Nature's approach is so magnificently coordinated, gentler and precisely targeted?

By understanding the real power of *nutrigenomic* substances superimposed on the foundation of a healthy lifestyle, you can literally take back control of your own health. You no longer need to feel a helpless dependence on the sometimes sophisticated (but often clumsy) tools of modern medicine - the pharmaceutical drugs and surgery!

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CHAPTER 6

'Switches' that *talk to* your DNA

Just for a moment, imagine a line of Christmas tree lights with about 200 tiny bulbs attached. The end of the cord is plugged into the power point on the wall. When you throw the switch, all 200 bulbs are illuminated at once.

It might surprise you to know that the cell's internal defence system works in much the same way. There are many different switches within cells but two in particular have profound effects on cellular function.

Meet Nrf2 A small protein known as Nrf2 is the equivalent of the Christmas lights' switch. But instead of lighting up lots of tiny bulbs, Nrf2 in the cell 'switches on' the cell's own defence system[6]! In fact, this switch activates more than 200 or so different genes, all of which code for different aspects of cellular defence.

This is a very clever but logical strategy. How convenient to be able to activate families of related and supportive genes with the one switch! Nrf2 is a relative newcomer to our understanding of how cells protect themselves, having been known only since the mid-1990s.

What's even more exciting than the discovery of Nrf2 itself is the fact that scientists have identified substances which can activate Nrf2. The most powerful known substance capable of activating Nrf2 is *Sulforaphane* which comes from vegetables of the Brassica family (part of the 'cruciferous' vegetable family[vii]).

[vii] Cruciferous vegetables include the Brassica family, cabbage, broccoli, Brussels sprouts, wasabi, watercress and many more but only broccoli is a significant source of Sulforaphane.

Sulforaphane's potential as a therapeutic substance is so highly-regarded that it continues to be the subject of intense research in the hope that a patentable pharmaceutical medicine can be developed by modifying the natural molecule. Interestingly, it has not yet been possible to produce a modified sulforaphane[viii] which is any more powerful in its effect than Sulforaphane itself.

Meet NF-kB *(NF-kappa B)* Just as Nrf2 is a *transcription factor* in the cell's cytoplasm, so too is NF-kB. Where Nrf2's effect is to activate genes of the cell's defence system, NF-kB activates the genes which promote inflammation[7].

We tend to think of inflammation as an undesirable phenomenon – and sometimes it is. You will recognize the effects of inflammation as being the red, hot, swollen appearance of an injured joint or effect of an insect bite. In both cases, *inflammation* is the necessary process the body uses to protect you against further damage. *Inflammation* walls off the location from the rest of the body and stops the damaging stimulus from travelling further into other parts of the body. When you twist your ankle and its swells and feels painful, that inflammatory response forces you to immobilize the joint so that it can repair itself. It is most likely to be NF-kB which initiates this inflammatory process. As the repair processes take over, NF-kB production slows and then stops; usually after a few days, the signs of inflammation have disappeared and early repair allows you to start to walk again, even though it may be a few weeks before full strength has been restored.

That's the 'good' side of inflammation. However, in a person who has chronic arthritis of the joints, the inflammatory process doesn't shut down. Something has kept the NF-kB switch stuck in the *ON* position.

[viii] Known as an 'analogue' when a molecule is similar to the native compound.

The triggers which allow this to happen are not always easily identified. However, it is very clear that certain food molecules such as those found in deep-fried fatty foods don't just *'talk to the NF-kB gene'*, they shout loudly at it, telling it to keep the 'inflammation' genes switched on and churning out large quantities of molecules called *inflammatory cytokines.*

Chronic inflammation (meaning that it continues over a long period) is a situation which underpins many diseases. Here are some examples:

Location of the Inflammation	Name of Condition
Inflammation of the joints	Arthritis
Inflammation of the airways (bronchi)	Asthma
Inflammation of the liver	Hepatitis
Inflammation of skin	Dermatitis
Inflammation of blood vessels	Vasculitis
Inflammation of the fine tubules of the kidney	Glomerulo-nephritis

Table 1 **Inflammatory Diseases by name and tissue source**

Such chronic inflammation causes permanent damage to the associated tissues. These inflammatory conditions are often 'controlled' medically by the use of *anti-inflammatory* drugs. These drugs fall into two main families, the steroids and the NSAIDs (*Non-Steroidal Anti-Inflammatory Drugs*). Although both groups provide quite powerful reduction in the signs and symptoms of inflammation, they are responsible for a range of side effects which restricts their long-term use. As with pharmaceuticals in general, these are just not sufficiently specific to target inflammation without producing *collateral damage* elsewhere. (Remember the analogy of the sledge hammer and the thumb tack).

One of the NSAIDs marketed as a 'breakthrough medicine' in inflammation control, *rofecoxib* and marketed as Vioxx, was withdrawn from sale in 2004 when it appeared to double the risk of heart attack in its users. Merck, the manufacturer settled a U.S. class action for $4.85 billion in 2007[ix]. Steroids similarly have long been known to produce a range of adverse effects when used for long periods. So, although pharmaceuticals such as these are a valuable part of crisis management, they are not really suitable for longer-term use.

So, what should one do when inflammation in one form or another seriously compromises day-to-day activities and enjoyment of life? Now, we've already seen that inflammation occurs in response to some type of *irritant* to the cells. This irritant has the ability to activate NF-kB in the cytoplasm. Once activated, NF-kB moves out of the cytoplasm and into the nucleus. Here, it lines itself up alongside the genes which code for the production of the *inflammatory cytokines.* Next thing, the cell starts churning out these cytokines which activate the inflammatory process. Very soon, the characteristic swelling, redness, heat, pain and consequent immobility seriously compromise quality of life.

If an individual is predisposed genetically to asthma (inherited usually from the father's side), the inflammation appears as swelling of the bronchial tubes, affecting breathing. In those individuals predisposed to skin problems, the skin may begin to redden, itch and weep.

Clearly we need to know what the triggers are and how to limit their ability to keep NF-kB 'switched on' when it appears to be unnecessary.

The good news is that we have answers to both of these problems. We do know to a large extent what the factors are that trigger the inflammatory process. And now Nutrigenomics has taught us that there

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ix http://www.theaustralian.com.au/business/in-depth/judge-rules-vioxx-doubled-heart-attack-risk/story-fn36luj2-1225837530031

are certain plant molecules[x] which can inhibit or 'switch off' NF-kB[8]. Knowing how to regulate the process in both ways helps us to take control of diseases we may have thought we were 'stuck with'.

Having the ability to *'switch off'* NF-kB to reduce the tendency for inflammation and *'switch on'* Nrf2 to help cells to protect themselves provides us with a powerful weapon against disease, whatever that disease may be named.

As is becoming apparent, the ability to regulate cellular function is independent of the name of the disease. As we saw earlier, the diseases listed as being inflammatory in nature all appear to be unrelated. Typically, we consider diseases like asthma and arthritis to be completely unrelated but when we see them instead as different manifestations of uncontrolled inflammation in the cells, we see that there is a common link.

What this means is that when we look at health and sickness through the eyes of Cellular Medicine, we don't need to know the medical name of the condition. What we do need to know is the *abnormal process* which is leading to this condition. Inflammation is one of the most common processes underlying common diseases. All chronic diseases appear to have an *inflammation* component.

The next question we need to ask is, "what are the triggers which lead to the inflammatory process initiated by NF-kB?" And probably more importantly, "what is the safest most effective way to *switch off* excessive production of NF-kB?"

And as you guessed, *Nutrigenomics* can provide the answers!

[x] To save you having to wait for the answer in Chapter 9, *Sulforaphane* has been shown to be a powerful inhibitor of NF-kB.

CHAPTER SEVEN

Free Radicals & Antioxidants

Any stroll through a supermarket will highlight many products with the term *'Antioxidant'* prominently displayed on the label. Food marketers have been quick to pick up on consumer perception that 'antioxidants' are a desirable attribute of foods. This is a rather simplistic and incomplete view as we will soon see.

Free Radicals To understand the nature of an antioxidant, it is first necessary to describe a *free radical*[xi]. Without involving ourselves in too much chemistry, we can say that *free radicals* are molecules or atoms which have become unbalanced. To regain their balance, they attack other molecules, removing one of their electrons, thereby making the second molecule unbalanced. This process repeated over and over sets up a chain reaction. Whenever a molecule becomes an *unbalanced* free radical, it damages the part of the cell with which it is in contact. Naturally, cells try to avoid having uncontrolled free radical activity and this is where antioxidants can play a role.

Antioxidants Quite simply, antioxidants *'neutralise'* unbalanced free radicals, stopping the continuation of the chain reaction. We say that antioxidants *'quench'* free radicals. In that sense, antioxidants are essential tools for preventing uncontrolled cellular damage. *Appropriate* antioxidant reserves are one of the cornerstones of cellular defence, one of the themes of this book.

[xi] More correctly described as *Reactive Oxygen or Reactive Nitrogen Species* (ROS or RNS) but for familiarity, we will continue to use the term, *free radical.*

Many myths surround the concept of antioxidants and we can't explore all the issues here. However, it is important to know that the most powerful antioxidants are produced by the cells themselves. These cellular antioxidants are literally *millions of times more powerful* in their effect than those derived from foods or supplements. Vitamins C, E and beta-carotene, even at high doses have only a fraction of the antioxidant potential of the cell's own antioxidants.

The way a Vitamin C molecule quenches a free radical is like this; one Vitamin C molecule quenches one free radical. In the process, the Vitamin C molecule becomes *oxidized* and can no longer function.

Free Radical	+	Vitamin C molecule	⟶	**Inactivated** radical	+	**Oxidised** Vitamin C

Many of the foods being promoted as antioxidant-rich sources include pomegranate juice, grape juice, green tea and berries, especially blueberries. These foods contain a wide array of beneficial bioactive compounds but nevertheless as antioxidants, they also simply quench free radicals *one-for-one* as does Vitamin C.

Oxidative Stress When the extent of free radical activity in a cell is greater than the available antioxidants can handle, the cell's reserves become so overwhelmed that we say the cell is subjected to *'Oxidative Stress'.*

When a cell is affected by oxidative stress, the resultant damage is likely to affect every part of it. This can include all of the cell's critical functions; the energy-generating mitochondria, the protective membranes, key enzymes, the DNA within the genes, and more.

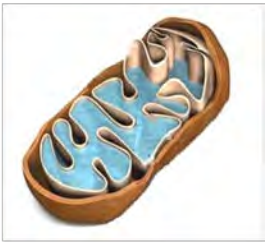


Figure 2 Typical Mitochondrion - 'Powerhouse' of the Cell

Mitochondria and Fatigue Loss of normal function of the mitochondria is likely to promote fatigue in the individual so affected. Not only do the mitochondria provide the energy that makes us feel bright and alert but this same energy is required to drive every important function of the cell. If mitochondrial function is compromised, *EVERY OTHER FUNCTION OF THE CELL IS COMPROMISED!*

Not all free radical activity is harmful but if it overwhelms the cell's internal reserves and produces *oxidative stress*, widespread cell destruction will be the inevitable consequence. *Oxidative Stress* is known to underpin many diseases, including the major chronic diseases, heart disease, diabetes, asthma, cancer and arthritis.

The cell's own antioxidants which appear to have the most profound effects on cell function are the following:

- **Antioxidant Enzymes**
  - Superoxide dismutase (SOD)
  - Glutathione Peroxidase (GPx)
  - Catalase (Cat)
- **Glutathione**
- **Others**, some of which are enzymes and some which are not.

What is special about an Antioxidant Enzyme? An enzyme is a protein molecule that promotes a chemical process but doesn't get used up itself in the process. We say it is acts as a *catalyst.* Most of the chemical reactions which occur in cells require enzymes. So, when an *Antioxidant Enzyme* encounters a free radical, it quenches (neutralizes) that free radical and then goes on to quench another and another and another.

The Antioxidant Enzymes literally quench *millions of free radicals per minute* in this way and continue to do so over 3-4 days until the enzyme is broken down in the cell and replaced.

Primary Antioxidants The pyramid diagram in Figure 3 illustrates that the greatest protection to the cell is offered by the three Antioxidant Enzymes, with Superoxide dismutase (or SOD) at the apex; these are known as the *Primary Antioxidants*. As we saw earlier, the reason these enzymes are so powerful is that they can ***quench millions of free radicals per minute.***

Secondary Antioxidants The secondary Antioxidants support the Primary Antioxidants but are so much more limited in their activity because one of these antioxidant molecules can quench only one free radical! Even taking megadoses[xii] of Vitamin C (as many people do) is a bit like tossing a glass of orange juice into the Pacific Ocean – the effect is minimal in comparison with that of the Antioxidant Enzymes.

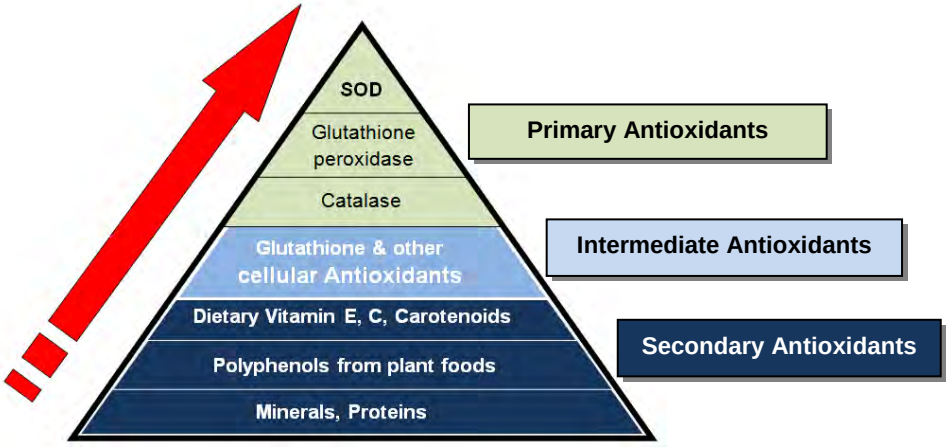


Figure 3 Increasingly Protective Effect with progress up the Pyramid

[xii] The Recommended Daily Intake of Vitamin C is around 30-60 mg; this has been determined as the quantity needed to prevent scurvy. Many people take as much as 12,000 mg daily in the hope that this will confer greater antioxidant protection. However, there is no consistent clinical evidence to support this approach. As little as 500mg daily will saturate the cells and the remainder is excreted, unused. Learn more here: http://www.jacn.org/cgi/reprint/22/1/18

Intermediate Antioxidants The intermediate category is made up of antioxidant compounds which are made by the cells themselves. However, because they are not 'catalytic' in action like the Primary Antioxidants, they still directly quench just one free radical per antioxidant molecule. Nevertheless, they are produced in such significant quantities by healthy cells that they contribute to the essential mechanisms the cell uses as part of its own defences. One of the most important of these essential compounds is Glutathione (*pr. Gloot-a-thigh-oan*). We will discuss its significance in more detail later.

Incidental Antioxidants The Pyramid diagram may give the impression that the secondary antioxidants are of little importance beside the Primary and Intermediate Antioxidants. However, all these substances have other very important roles to play in human cells. Vitamin C for example, is essential for normal function of skin, bones and teeth among other key functions but its antioxidant activity is not its strong point.

What this means is that all or most of the Secondary Antioxidants are largely *incidental antioxidants* but their primary function is something else. So when the supermarket shelves are displaying products claiming to contain antioxidants, these foods may have beneficial effects on human health – but they are unlikely to be particularly effective as antioxidants. Such foods include green tea, berries, goji berries, grape juice, extra virgin olive oil, turmeric and so on.

ORAC Value You might have noticed food products which claim to have a high ORAC[xiii] value. This is a measurement which some food marketers like to use on their products as a way of inflating their apparent value in human health. The test is done in a laboratory with food samples in test tubes. What happens in the lab cannot be directly translated to what happens when the food is consumed. The inference

[xiii] ORAC stands for Oxygen Radial Absorption Capacity and is a *test tube* measurement or determining a foods' ability to quench free radicals.

is that the higher the ORAC value, the stronger the antioxidant potential of the food. This is not necessarily true for several reasons explained below.

Bioavailability[xiv] Many of the foods which rate high on the ORAC scale contain big bulky molecules called *polyphenols.* These molecules are so bulky that they don't easily slip through the cell's membranes; as a result, very few of the polyphenol molecules can enter the cell. The bioavailability of the polyphenols can be as low as 1%[9]. Very large amounts need to be consumed for the substances to reach the cells in any quantity.

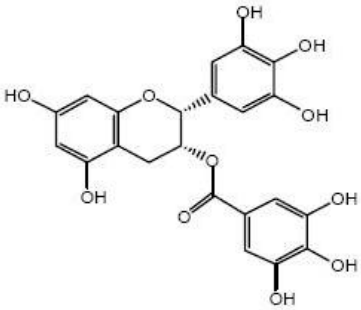


Figure 4 A 'bulky' Polyphenol molecule from green tea – known as EGCG. This bulk means that polyphenols are not readily absorbed through the cell's membrane. EGCG refers to Epigallo- Catechin Gallate.

As a consequence, these molecules contribute very little to the antioxidant capacity *within the cell or the bloodstream*. Where these polyphenol molecules do exert their antioxidant effect is in the digestive tract. Here the polyphenols are in *direct contact with the free radicals in the food itself*. Barbecued meats, processed meats and deep-fried foods of all kinds contain large amounts of free radicals and are known to contribute to various forms of cancer[10] and other diseases.

Because the bioavailability of the polyphenols is so low, it is not known whether the often extraordinary reported *test tube* effects actually occur

[xiv] Bioavailability is used to describe the percentage of a supplement taken by mouth which appears in the bloodstream, assuming that 100% of an intravenous dose of the same substance appears in the bloodstream.

in human cells! In the test tube, many of the polyphenols appear to have nutrigenomic effects but how significant is that effect in our cells if we can't absorb very much of them?

The French Paradox The French are known to enjoy relatively low levels of cardiovascular disease in spite of the fact that they don't consume a low-fat diet, as is usually recommended. Because it has been suggested that the polyphenol-rich red wine they consume with their main meals is what offsets their dietary fat, the term, *French Paradox* has been coined. *(Cheese, pate and butter are high fat foods.)*

Whether the red wine is the reason has not been proven beyond doubt but other scientists have suggested that consuming various polyphenols with meals, especially with foods likely to contain cancer-forming substances, can be protective. An Israeli research group[11] has shown that the polyphenols in one glass of red (but not white) wine is sufficient to completely quench the free radicals in an average meat kebab.

Do you need to consume red wine to achieve this benefit? Now, I accept that you might *like* to consume red wine with every meal and if so, the evidence is that in moderation this is beneficial. However, this may not suit everyone including children and those whose health is already compromised. There are many other polyphenol-rich choices and many of these are the same rich colour as red grapes. Foods such as hibiscus and beetroot, as well as most berries contain compounds similar to those in red wine. Significant health benefits have been attributed to these foods and continue to undergo investigation.

Green Tea and the health of Asians Some Asian populations but especially the Japanese have been able to achieve similar protection against cardiovascular disease by consuming polyphenol-rich green tea in significant quantities *with meals*[12]. And this is the key: *With Meals*. What the evidence seems to show overall is that the polyphenols act as antioxidants *in the digestive tract* and *not in the cells* - because too little actually gets into the cells to have an antioxidant effect. So, the

message is that to get the most out of a polyphenol-containing food – or supplement – have it with the meal most likely to be a significant source of free radicals. That includes but is not limited to bacon, ham and other smoked foods, blackened foods of any kind such as barbecued or roasted foods, fried foods and even toasted bread.

So, whether you choose red wine, green tea, pomegranate juice, extra virgin olive oil, beetroot or any of the berries as good sources of polyphenols, ideally consume them *with* a main meal.

Be wary of the Resveratrol hype! We can't leave this section without a word of caution. The polyphenol, *resveratrol* has been identified as a compound found in red wine and some claim that this is the reason for the 'French Paradox'. Resveratrol has more recently been shown in yeast and animal studies to promote longevity. It appears to do this *nutrigenomically*, activating a gene known as Sirt-1.

Even though there is absolutely *NO EVIDENCE* for any such effect in humans, supplement marketers have exploited the animal research to make resveratrol readily available as capsules or tablets. What the marketers omit to tell you, however is that[13]:

- The animals in the study (mice) consumed the human equivalent in resveratrol of about 1000 bottles red wine per day!
- 1000 bottles of red wine is about 75 capsules, each containing 100mg resveratrol. That would represent 7,500 mg daily.
- The only research in this field has been done on yeast and mice where huge experimental doses were used.
- The longevity effect *only occurred when the animals were* ***started on resveratrol at birth***; no change at middle age.
- Resveratrol as a polyphenol has low bioavailability[14].

There needs to be a little bit of scientist in each of us! Even if you are not trained as a scientist, always check that research used to

support a product is conducted in humans at *practical* daily doses and not in animals using impossibly-large doses or worse still, in test tubes!

That is not to say that animal and *test tube* research is not valuable; it is an integral part of the progression towards our understanding of how a compound *might* behave in human systems. It just isn't enough on its own for us to draw useful conclusions about its potential value to us.

A quick word on Lipoic Acid and Coenzyme Q10 Two other important substances made in human cells exhibit antioxidant activity; these are *Lipoic Acid* and Coenzyme Q10. These substances have been reasonably well researched in humans and are also available as supplements. Although both substances are promoted for their antioxidant activity, this is not their main function in the cell.

However, both substances as supplements have limited bioavailability; a standard oral dose of Coenzyme Q10 has a bioavailability[15] of only 2-4%, necessitating large doses to achieve a clinical response. The bioavailability[16] of Lipoic Acid is better at around 30% but is still rather limited.

What is the ideal Antioxidant? If we are to take advantage of the power of the Primary Antioxidants, the ideal supplement would have the nutrigenomic capacity to '*switch on* 'the genes which code for the Antioxidant enzymes as well as the other key cellular antioxidants, typified by Glutathione.

Do such nutrigenomic compounds exist and are they bioavailable? Before we go into detail, let's round out this chapter with a brief overview of the role of Glutathione, arguably the most important[17] of the non-enzyme antioxidant compounds produced within your cells.

Glutathione – essential for normal cellular function Glutathione is a rather remarkable and multi-functional small antioxidant molecule

which is present abundantly in healthy cells but is easily depleted. It is essential in the process of detoxifying harmful substances.

As you might therefore expect, excessive consumption of alcohol readily depletes glutathione reserves; cigarette smokers and those exposed to other forms of air pollution tend to have low glutathione reserves. This occurs because glutathione is consumed by the cells in trying to protect themselves against the harmful effects of the toxins associated with these two recreational drugs. Even the common analgesic, paracetamol (aka. *acetaminophen*), if taken to excess, will deplete glutathione reserves.

Individuals with oxidative stress-related diseases such as chronic asthma[18], heart disease[19] and diabetes[20] have also been shown to have abnormal cellular glutathione status. Typically such individuals also show dysfunctional Antioxidant Enzyme activity in the three Primary Antioxidant Enzymes, especially Superoxide Dismutase (SOD).

Can Glutathione be taken by mouth? Again the supplement marketers have exploited the extensive body of science which describes the importance of glutathione in human cells; glutathione supplements in various forms are available for purchase. However, the problem with such supplements is that they are readily digested by the secretions of the stomach[21]. Glutathione is made up of just three amino acids[xv] linked by 2 chemical bonds. These bonds are exactly what the protein-digesting secretions of the human digestive system are designed to break! ***There is absolutely no value whatsoever in taking pre-formed Glutathione supplements*** because they simply get broken down into their constituents; no glutathione remains to be absorbed into the cells.

[xv] Amino acids are the 'building blocks' used to make proteins, assembled like a coiled string of beads. When a protein is digested, the amino acids are the product.

What about taking the *precursor* amino acids? One of the three amino acids which make up Glutathione is said to be *rate-limiting.* This means that if it *(cysteine)* is in short supply, it reduces the overall production of glutathione in the cells. Attempts to supply extra cysteine haven't worked either as this amino acid is not bioavailable in this form. Another form of the amino acid, *N-Acetylcysteine* (NAC) has been found to act as a suitable precursor and can therefore be used to get more of the rate-limiting amino acid into the cell.

N-Acetylcysteine however is not universally permitted for use as a supplement, even though it is used intravenously for drug overdose in hospital emergency departments. In Australia where I live, the regulatory authority considers that there is insufficient evidence for its safety in humans to allow it to be used in an over-the-counter oral supplement.

Important as the role of Glutathione is in the cell, even enhancement to Glutathione reserves is only a small part of what is required to enhance cellular defences.

Another limitation of N-Acetylcysteine, even in those jurisdictions where it is permitted is the fact that Glutathione is a member of a large 'Supporting Cast' within the cell. Important as it is, it *is not the leading actor*. In addition to its own role as a non-enzyme antioxidant, Glutathione is an essential *partner* to the Primary Antioxidant Enzymes and in particular to *Glutathione peroxidase*. As we will see in the next chapter, it is also an essential *partner* to the Detoxification Enzymes which are a key element in cellular defence.

What this means is that even enhancement to Glutathione reserves is only a small part of what is required to enhance cellular defences. It is the nutrigenomic compounds which can *'switch on'* the 200 or so genes related to cellular defence that make the real difference. Remember the

Christmas tree lights analogy? One switch lights up 200 light bulbs all at once, simultaneously mobilizing many cellular defences.

Why the antioxidant vitamins can do more harm than good. In some scientific circles, there has been, for some time, an uneasy and growing undercurrent of concern surrounding the use of the antioxidant vitamins, C, E and Beta-carotene. Theoretically, they should be capable of quenching free radicals in cells. However, the evidence is conflicting, so that in some studies they have *no beneficial effect* and in other studies, they have been found to be harmful[22]!

A large 1996 study[23] gave beta-carotene supplements to smokers to see if the development of lung cancer could be prevented; both smoking and cancer are associated with oxidative stress. The study had to be stopped early because the smokers on beta-carotene were developing lung cancer *faster* than the group on the inactive placebo.

We now understand why these and other adverse effects might be occurring. *'Swamping'* the cells with excess antioxidant vitamins actually *'switches OFF'* Nrf2, hijacking the cell's major defences[24]. Now, doesn't this *upset the apple cart* for the proponents of vitamin megadoses? Vitamins are absolutely essential to human health and do contribute to the redox status of human cells – but they are ***NOT*** the cell's major means of managing redox balance. It is wise to steer clear of megadoses.

There is nothing natural about taking excessively large doses of vitamins such as Vitamin C. Such therapy is akin to using vitamins as pharmaceutical drugs. Human cells are not adapted to the presence of these vitamins in excess of what can be manageably eaten in food.

More importantly, Vitamin C is synthetically manufactured in a laboratory and it might surprise you to know, no Vitamin C supplement has ***ever*** been anywhere near an orange ……. or any other fruit or vegetable!

CHAPTER EIGHT

Detoxification & Cellular Defence

Imagine your car's performance if you never bothered to take it to the mechanic to be serviced. Failure to change the oil, grease various essential components and keep the running parts clean and tuned would result in sluggish performance – or worse! The cells of your body are no different. They need to be kept clean and have waste products removed regularly if they are to function at their peak year after year.

Most of us pay more attention to looking after our cars than we do our own bodies!

Unlike your car, your body doesn't need a mechanic to keep it in good running order; that's because you have chosen the highly-sophisticated *self-cleaning, self-tuning* model! The only thing you have to do is to regularly feed it what it needs most, move it appropriately and avoid over-stressing it. Depending on your individual DNA 'blueprint', you may or may not need to focus more conscientiously on certain aspects of its function.

Now wouldn't you agree that many of us pay more attention to looking after our cars than we do our bodies – until something goes horribly wrong? And then, there's a quick trip to the GP hoping that he can get rid of whatever sign or symptom sent you there. And as we saw in Chapter 1, what's going wrong *at the cellular level* isn't usually permanently corrected by mainstream medicine's pharmaceuticals.

Now, you're driving down the freeway in your under-serviced car and a red warning light on your dashboard flashes on. The red light is there for a reason – and in this case, probably to tell you the oil needs

attention. But you're far too busy to bother with the detective work, so you decide to pull over to the side of the road so that you can disconnect the bulb which has been annoyingly red for the past 10 kilometres. Great – fixed the problem – no more annoying red light.

Now, isn't this a parallel situation to the use of a pharmaceutical drug when it is prescribed to get rid of a symptom? Does an anti-inflammatory fix the underlying cause of an inflamed joint, does an anti-histamine fix the underlying cause of the allergy and does an anti-hypertensive address the fundamental cause of the high blood pressure? Of course not; these prescriptions are just disconnecting the annoying red light bulbs, while the underlying cause continues to tick away silently in the background – for now! Eventually, your cells will be unable to cope and you find your health *suddenly* disappearing when a serious disease has been diagnosed. Of course, none of this happened suddenly at all. We just chose to ignore the clues that may have been present for months, years or even decades!

Knowing how your cells defend themselves gives you the control to optimise their function and enhance your overall health and wellbeing. Understanding the cell's built-in *'spring-cleaning'* system is an excellent starting point. Whether you call it 'spring-cleaning' or 'detoxification' doesn't matter; the process is the same.

Do you remember that in Chapter 6 we looked at a molecular 'switch' in the cytoplasm known as Nrf2? Nrf2 once activated, is able to move off into the nucleus to line itself up against the major genes which govern the cell's own defence system. When it is activated, it switches on all 200 or so genes at the same time. This defence system includes the genes of the cell's Detoxification system.

To simplify our understanding of the way cells protect themselves, we will consider a three-legged stool to explain the process. Of course such a stool needs to have all three legs strong to remain steady.

Before we get into the *nuts and bolts* of how cells detoxify waste materials, we should look at WHY a cell needs a Detoxification system.

What does the cell need to protect itself against? A live cell is continuously generating wastes products from its many activities. These waste substances may be toxic chemicals, but they may also just represent 'clutter'. In any case, they need to be removed so that the cell's 'machinery' can continue to work efficiently.

As we know, one of the greatest threats to a cell's function is *oxidative stress.* This can occur when free radical activity exceeds the cell's antioxidant reserves. As we saw, free radicals can be present in food, especially in fried, overcooked and processed meats. Free radicals can also be generated by exposure to ionizing radiation to which the body may be exposed. By far the greatest source of free radicals to which we are exposed is that produced by the cells themselves!

How Superoxide Free Radical is formed Our cells require energy to function and a steady supply of this energy is produced in the cell's powerhouses – the mitochondria. In simplified fashion, the mitochondria 'burn' the glucose from our food in the oxygen we breathe.

However, in the process, about 2-4% of the oxygen doesn't get used to produce energy. Instead, it is converted to a free radical known as Superoxide. This might seem like a defect in the cell's function – but in fact it is an essential part of the cell's signaling system.

Superoxide dismutase (SOD) to the rescue Healthy cells are equipped to deal with the Superoxide free radical by generating the Primary Antioxidant Enzyme, **Superoxide dismutase** (or SOD). SOD's job is to quench the excessive Superoxide free radical before it can set up chain reactions of free radical damage which can bounce their way through the cells, wreaking havoc as they go. When free radical activity overwhelms the cell's ability to deal with it, *Oxidative Stress* prevails.

There is now substantial evidence about many chronic diseases to show that the primary event which leads to all other effects is a state of oxidative stress. This has been researched extensively in relation to Type2 diabetes[25], cerebro[26]- and cardiovascular disease and asthma,[27] to name a few.

What is very clear from all these studies is that the closer we can get to dealing with the *CAUSE* of a condition, the better our chance of preventing it from getting out of control. Scientists use the term, *upstream factors* to refer to the earliest events in a disease. Knowing that free radicals set up chain reactions which magnify their effect as they go, it makes sense to try to get as far *upstream* as possible to stop widespread cellular damage.

When we use pharmaceuticals to deal with the symptoms of disease, we are only dealing with the 'downstream' effects. Working as far 'upstream' as possible gets us closest to the CAUSE of a disease.

It should be clear then that when pharmaceuticals deal with the symptoms of a disease, they are typically dealing with the *downstream* effects. This is why it is so important that the cell keeps control of excessive free radical activity. As we age or are unwell, our cells become less efficient at producing these Antioxidant Enzymes as required. In Chapter 10, we will look at nutrigenomic mechanisms we can use to enhance our ability to produce Superoxide dismutase at more youthful levels even as we age.

How Diabetics are at increased Risk There is one more important point to make about Superoxide free radical. Most of the free radicals generated in the human cell are the result of burning glucose in oxygen to make energy! Types 2 Diabetes is a disease which is sweeping the

globe and as more of us become more overweight and unfit, we are more prone to develop it. Why? Because diabetics accumulate higher levels of glucose in some of their cells, the amount of glucose available to the mitochondria is higher. As a result, the 2-4% of oxygen which is normally converted to superoxide free radical is much greater in a diabetic than it is in a healthier person. Diabetics therefore produce substantially more Superoxide than their cells can handle. Not only is a diabetic prone to the complications of diabetes itself but to all the diseases which are associated with oxidative stress in general.

As we will see in the following chapters, there are valuable *nutrigenomic* strategies we can use to support the improved lifestyle practices which are essential for optimum function.

So, in summary, a cell primarily needs to protect itself from:

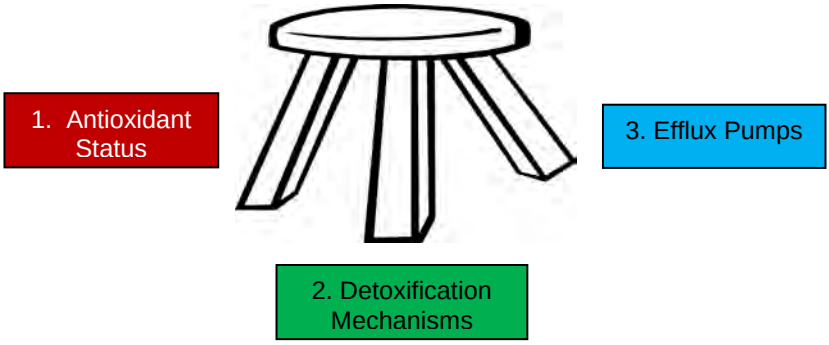
- ionizing radiation
- chemical additives in processed foods
- heavy metals which enter the plant through the soil
- agricultural chemical residues which remain on the food
- inhaled environmental pollutants
- free radicals in inappropriately-cooked or processed food
- free radicals generated within the cell itself
- other metabolic breakdown products produced within the cell

Back to the Three-legged Stool Luckily, as owners of our own bodies we are not required to know and understand all the intricate processes a cell uses to do its own *'spring-cleaning'.* With a bit of basic care from us, the cell knows *exactly* what it needs to do!

The Three legs of the Detoxification Stool

The 3 legs of the stool carry equal weight in ensuring that your cells are continuously being cleaned. Briefly, here they are:

1. **Antioxidant Status**, including Glutathione – to *'neutralise'* cellular toxins or quench excessive free radicals.
2. **Detoxification mechanisms** – to break toxins down to harmless substances.
3. **Efflux pumps** – to pump toxic wastes out of the cell by activating 'shuttles' in the cell's membranes.



The good thing for us is that ***Nrf2 activates all three aspects*** of the Detoxification process. All we need to know is what are the most effective *nutrigenomic* compounds we can consume to switch on Nrf2 and production of the Primary Antioxidant Enzymes?

Figure 5
Fresh Spinach

Here's how the Detoxification process works. Let's zero in on the actual process a cell uses in breaking down a toxin. Let's imagine that you have eaten some fresh spinach leaves that were grown on a farm. The spinach had been sprayed with pesticides so that the green spinach leaves arrived at the market in perfect condition. However, some of those chemicals weren't removed when you washed the vegetable before cooking it at home. After you've consumed the vegetable and it has been digested and the components absorbed into

your bloodstream on the way to your cells, your cells recognize the presence of the toxic pesticide residue; they then 'crank up' their detoxification machinery to break it down and get rid of it. Here's what they do.

Phase 1. The toxin is attacked by enzymes which belong to a group known as the Cytochrome P450 family (CYP450). CYP450 pulls the molecule to bits but can' totally inactivate it. However, it does what it can before passing it onto Phase 2, producing an intermediate compound and often large amounts of superoxide as well.

Phase 2. Phase 2 uses several Detoxification Enzymes which are known as *Phase 2 Detox Enzymes.* There are 3 main enzymes for detoxification (all with complicated chemical names). Two of these are important in our discussion, ***Glutathione-S-transferase*** (GST for short) and ***Quinone reductase***[xvi] (we'll call it QR to make things easy).

Let's say that the pesticide from our spinach required the GST enzyme for its second stage of detoxification. The intermediate compound is then presented to the GST enzyme, using Glutathione as part of the process. After a few slick little chemical manoeuvres, what started out as a toxin capable of poisoning the cell is now released as a harmless water-soluble substance which can be excreted.

Now there's just one potential problem here. When Phase 1 produced the partly degraded intermediate compound, sometimes that compound is more toxic than the pesticide that came from our spinach. Here's where a good reserve of antioxidants is absolutely essential. The available antioxidants, (especially Glutathione and SOD) are called upon to prevent a chain reaction of free radical activity from occurring.

If the antioxidant reserves are inadequate, this intermediate compound can severely damage the cell, including damage to the cell's DNA. This

[xvi] **Quinone reductase** is also described as **NAD(P)H:Quinone Oxidoreductase**

is one of the situations which sets the scene for the development of cancer cells, so it is critical that these Phase 1 intermediates are not being produced at a rate too great for Phase 2 or the associated antioxidants in the cell to accommodate.

Superoxide dismutase and Glutathione in key roles Amongst the most important cellular antioxidants acting here are Glutathione, Superoxide dismutase and the other Primary Antioxidant enzymes. These are then supported by antioxidants from the food itself such as vitamin C, beta-carotene and other plant biomolecules.

Although the liver is the organ specialised to detoxify wastes, the process occurs in every single cell of the body, albeit to a lesser extent.

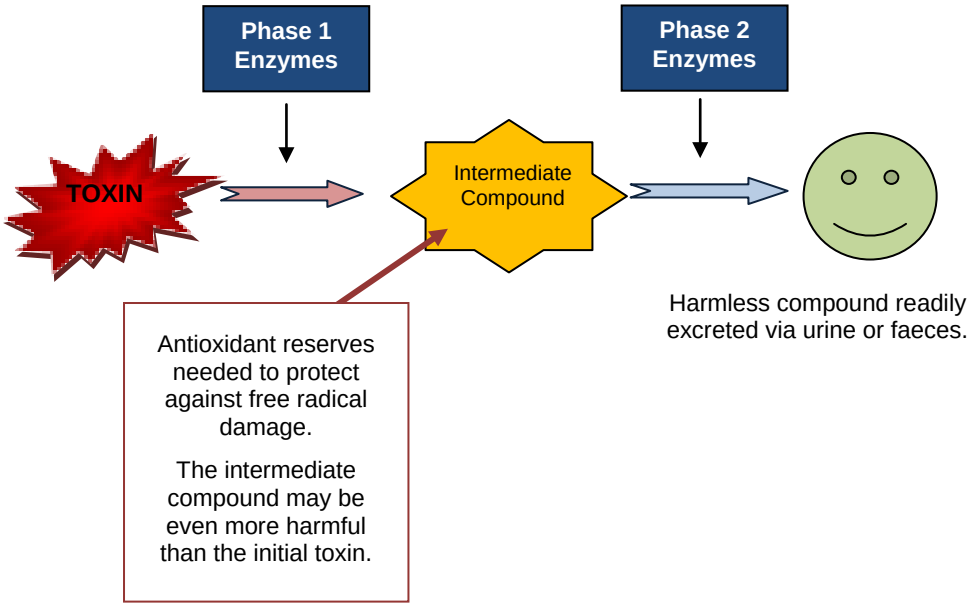


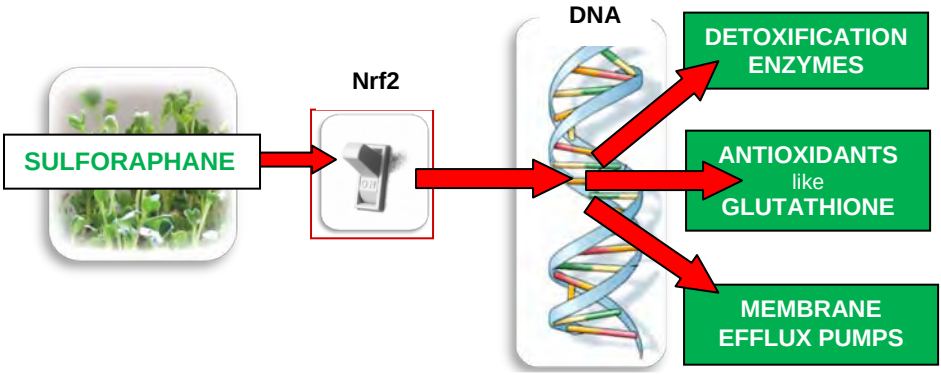
Figure 6 The Detoxification Process

CHAPTER 9

Sulforaphane

One of the most extraordinary findings of our times is a small, sulphur-containing molecule, *Sulforaphane*, derived mainly from Cruciferous vegetables such as Broccoli. Although the plant doesn't actually *contain* any sulforaphane itself, it does contain 2 essential compounds (one of which is an enzyme) needed to produce sulforaphane under the right conditions.

What makes Sulforaphane so extraordinary is its ability to activate the cellular *'switch'* Nrf2, which controls the 200 or so genes[28] related to the cell's defence system. In fact, Sulforaphane is considered to be the most powerful of the naturally-occurring substances capable of doing this[29]. Better still, its high bioavailability [30]of around 80% makes it a very practical supplement to the well-balanced daily diet. As we have seen, much of the cell's ability to defend itself is due to its ability to activate three key processes as shown.



How Sulforaphane 'talks to' your DNA, activating Cellular Defences

With these protective genes able to *'switch on'*, the cells operate more efficiently, energy is produced more readily, immune and inflammatory[31] pathways are well-regulated and the cell's 'spring-cleaning' processes remove waste materials before they have a chance to damage delicate cellular structures, including the DNA. When *all 50 trillion of your cells* are working just as Nature intended, your entire body can operate at its peak. As we said at the outset, when your cells are healthy*, YOU* are healthy!

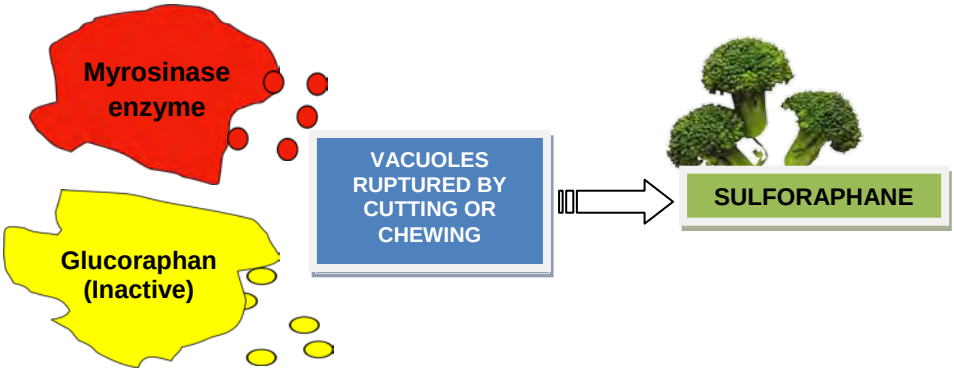
Status of Current Sulforaphane Research Much of the research conducted on Sulforaphane in the last decade has focused on its potential to prevent diseases for which mainstream medicine has few solutions; cancer[32], heart disease[33], degenerative brain disorders[34] and gastric ulcers[35] as the most notable. Not all this research has yet undergone clinical trials in humans but the number of research groups around the world investigating different aspects of this remarkable nutrigenomic compound, continues to grow.

This more recent research has also helped to explain why cruciferous vegetables[36], more than other vegetable families, have been associated with prevention against disease in general, but especially against cancer.

Diabetes and Sulforaphane My own clinical research in Brisbane, Australia is focused on the possible role of Sulforaphane in preventing the life-threatening complications of Type 2 diabetes. There is already substantial evidence that the primary *upstream* event which leads to all other complications of diabetes is oxidative stress[37]. It appears that the process is initiated by the Superoxide free radical and as we will see in the next chapter, a melon-derived nutrigenomic compound is capable of *switching on* the genes which code for the three Antioxidant Enzymes, led by Superoxide dismutase (SOD).

Where is Sulforaphane found? It has been long known that broccoli doesn't actually contain any Sulforaphane at all. Instead, the plant contains an inactive precursor compound known as *Glucoraphanin*

in a sac within the plant cell and an enzyme, *myrosinase* in a separate sac. Cutting or chewing the plant breaks the small sacs and a chemical reaction follows which stimulates the myrosinase enzyme to convert the precursor compound, Glucoraphanin to Sulforaphane.



Formation of Sulforaphane from Inactive Glucoraphanin

Cooking destroys the activity Sulforaphane is not very stable once it is formed, so needs to be consumed fairly soon. The other issue to consider is that because the enzyme *myrosinase* is heat-sensitive, cooking destroys it.

Consuming cooked broccoli vegetable provides the precursor but without the active myrosinase enzyme present as well, little or no Sulforaphane can be produced. Raw broccoli is not commonly consumed, so few of us really obtain maximal benefit from eating it. There is some research to show that the intestinal bacteria which are a normal part of the human intestine are capable of converting glucoraphanin to active sulforaphane; however, it turns out that these bacterial microflora are likely to convert as little as zero to 8% of the glucoraphanin[38].

Vegetable vs Sprout A research group in the U.S. in the 1990s discovered that the precursor

substance, Glucoraphanin is found most abundantly in the tiny *sprouted seed* of the broccoli plant; in fact the sprouted seed contains 20-50 times more of this compound than the mature vegetable. This finding makes it possible to obtain significant amounts of bioactive sulforaphane from only small quantities of plant material.

As the science on this remarkable compound continues to unfold, it has become imperative that it be conveniently available as a functional food or nutraceutical supplement.

It is possible for you to grow your own sprouts from broccoli seeds but such a process requires the time and a level of dedication few could muster. Oddly enough, the fresh sprouts contain an inhibitor[39] which partially *hijacks* the conversion from glucoraphanin to sulforaphane, producing an inactive sulforaphane *nitrile.*

Broccoli Sprout Powder for convenience The logical option is to produce powdered broccoli sprout. However, this is not as easy in practice as it might seem because it is necessary to carefully dry the delicate sprouts while still retaining the myrosinase enzyme activity.

Although industry is very experienced at producing many dried vegetable powders using the usual drying techniques, specialised technology is required to produce a broccoli sprout powder which can be standardized for an optimal Sulforaphane Yield. **CAUTION:** Be very cautious about products which are brown and are simply made from *unsprouted* seeds; broccoli seeds contain a toxin, *erucic acid* which is toxic to the heart but fortunately disappears during sprouting.

Sulforaphane Yield vs Sulforaphane Potential Because the specialised technique required to produce a broccoli sprout powder with a consistently high Sulforaphane Yield is not widely-known, some of the products which have appeared on the market are of poor quality. When tested in the lab, many have been shown to have little or no myrosinase enzyme activity. However, the label can be confusing because these products may claim a high Glucoraphanin level. Others may also claim a numerical value for their 'Sulforaphane Potential'. The 'Potential' as it

turns out, is simply a calculated value based on a theoretical 100% conversion to sulforaphane ***if*** the product contained the enzyme.

Some products blatantly (or in ignorance) claim that their powder contains a defined amount of sulforaphane. As is already clear, the product *CANNOT* contain sulforaphane itself. The ideal product contains a high level of glucoraphanin along with active enzyme which should have been retained through careful processing. Once the powder is consumed, moisture activates the process of converting the glucoraphanin to bioactive sulforaphane.

You can see how confusing it can be for the consumer to evaluate the worth of a particular product. However, once you do find a product which satisfies the criteria for bioactivity, it's surely worth making it an integral part of your day-to-day routine.

Healthier Ageing I've never been comfortable with the term, '*Anti-Ageing'* because surely there is no such thing! However, I do like the concept of *healthier* ageing because it is something over which we do have some control. Unfortunately as we age, the cellular defence mechanisms become less efficient, making us more prone to illness. Even the *Master Switch* Nrf2 gets a bit 'rusty' and doesn't respond to the signals as efficiently as it did when we were younger[40].

Immune Responses A fascinating 2008 study[41] on aged animals showed that Sulforaphane restored Nrf2 function to the levels of much younger animals. Abnormalities in the immune system commonly accompany old age and this study showed that using Sulforaphane increased Glutathione levels in these animals. Moreover, their immune function returned to normal and signs of skin allergy normalised. This has rather exciting possibilities for future research but whether the same response will occur in humans is yet to be seen.

CHAPTER 10

Superoxide dismutase

At various intervals throughout earlier chapters, the Primary Antioxidant Enzyme, Superoxide dismutase (SOD) has been mentioned. Let's enlarge on its importance in the function of the cell.

The main task of SOD is to quench excessive Superoxide free radical as it is produced in the cell. Do you remember that 2-4% of the oxygen used in 'burning' glucose into energy in the mitochondria is converted to the superoxide free radical? Although we tend to think of the superoxide radical as being harmful, there are several situations where it is essential to the function of healthy cells. Where superoxide is harmful is when it is being produced at a rate that overwhelms the SOD which is designed to keep it in check.

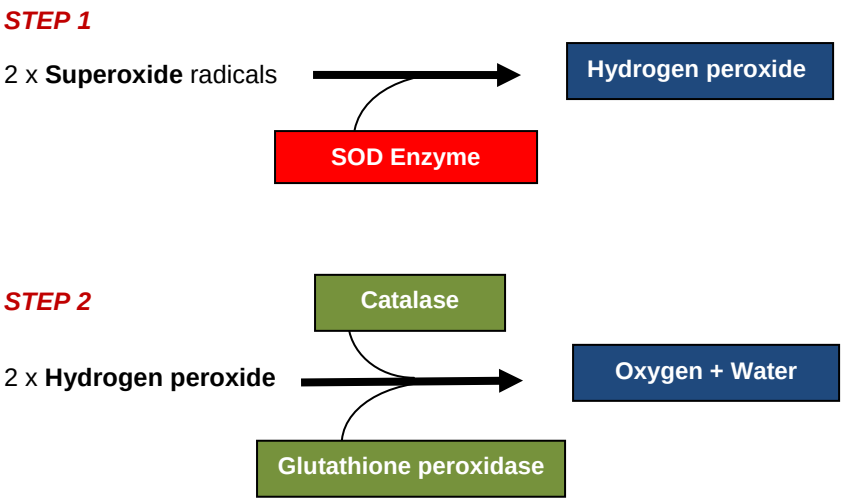
By a nasty twist of Nature, as we age, our cells tend to produce more of the Superoxide free radical while our overall antioxidant reserves progressively decline[42]. As a result, we are more likely to be in a state of Oxidative Stress as we age. This fact has significant implications for our state of health as the years advance.

Can we enhance levels of SOD? When the SOD enzyme was discovered in the late 1960s, it generated a great deal of excitement in the research world when the significance of this discovery was realized. Because of its relationship to the ageing process and the diseases associated with ageing, it wasn't long before it was considered to have 'anti-ageing' possibilities.

The earliest research used a bovine source of SOD (marketed as Orgotein) as a treatment for a range of diseases; osteoarthritis,

rheumatoid arthritis, other inflammatory joint diseases as well as reduction in the side effects of radiotherapy to name the most common. It was acknowledged as having *'potent anti-inflammatory activity with very low toxicity'*[43]. Orgotein, however never realized its full potential because BSE or 'mad cow disease' cast suspicion over any products of bovine origin and it was soon withdrawn from sale. In spite of the very promising clinical responses, injectable SOD was not without its downside; the drug was both expensive and inconvenient, requiring daily shots. Its other serious limitation was that it provided SOD but not its companion Antioxidant Enzyme, Glutathione peroxidase. Let's see why that matters.

How SOD works If the sight of the equations below makes you shudder, ***all you need to know is that toxic superoxide is converted to nothing more than oxygen and water by the antioxidant enzymes acting sequentially.*** It is also worth being aware that SOD on its own only does half the job because the Hydrogen peroxide it produces is also classified as a Reactive Oxygen Species (free radical). That's why a nutrigenomic stimulus to all three Antioxidant Enzymes is a more appropriate strategy than the bovine SOD used in the Orgotein therapy.



The major pathway used by the Primary Antioxidants in quenching Superoxide

SOD, the 'Lion Tamer' An easy way to consider the role of SOD in the cell is to see it as a Lion Tamer and Superoxide the lion. As the lion tamer is in the circus ring cracking his whip, the lion behaves himself but as soon as the tamer loses control, the lion jumps the boundary and is out into the assembled crowd, wreaking havoc as he goes.

Such is the damage wrought by superoxide if it overwhelms SOD. As we age, we lose the ability to produce SOD as efficiently – a bit like having a very old lion tamer trying to keep control of a young willful lion.

Nutrigenomic activation of SOD So when bovine SOD was made unavailable by the 'mad cow' disease scare, it forced researchers to find another way to take advantage of this essential enzyme. A group of French scientists developed a melon-based SOD[44] using a patented process which allowed the enzyme to pass through the human digestive tract without being broken down[xvii].

Once this form of SOD reaches the intestine, it exerts a *nutrigenomic* effect, 'switching on' the genes which code for the Antioxidant Enzymes. Better still, it *'switches on'* all three Antioxidant Enzymes and not just SOD. Quite serendipitously, this *nutrigenomic* response to the melon-derived SOD was superior to that shown by the bovine injectable!

Clinical Trials demonstrating the value of *nutrigenomic* SOD There are two clinical trials which illustrate the enormous potential of this approach. In the first[45], healthy male scuba divers were exposed to 100% oxygen at 2 ½ times atmospheric pressure for one hour. Such exposure is known to produce significant DNA damage, a real risk for deep sea divers. One half of the men had been pre-dosed with the

[xvii] Because food-derived SOD enzyme is a protein, it gets digested with other proteins in food. The patented process protected the enzyme from digestion.

melon-based SOD for two weeks, while the other group took an inactive identical-looking placebo capsule.

When the DNA damage was analysed along with other markers of oxidative stress, the group who took the supplement showed no damage at all. By comparison, tests on the placebo group showed the predictable DNA and other signs of oxidative damage. These findings were published in a respected peer-reviewed scientific journal in 2004.

Why not just use Vitamin C and E to protect the cells? In an earlier chapter, we looked at the way in which dietary antioxidants (*the secondary antioxidants)* quench free radical on a one-to-one basis and not catalytically like nutrigenomically-induced SOD and its partners which literally quench millions of free radicals per minute. The following study illustrates the significance of this.

This 2006 study[46], not related in any way to the first, also used healthy men and exposed them in two groups to oxygen at 2 ½ times atmospheric pressure. The study group here took 500mg slow-release Vitamin C and 272 IU of Vitamin E for a month prior to exposure. The placebo group took inactive capsules.

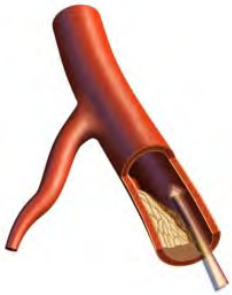
The results of this study were remarkably different from the first; the *Vitamin C and E offered absolutely no prevention* against the oxidative damage caused by the hyperbaric oxygen. This study was also published in a respected, peer-reviewed journal. It's hard to argue with the evidence!

Cardiovascular Protection using melon-based SOD A similarly noteworthy three-year study[47] which was published in 2007 again illustrated the clinical significance of *nutrigenomic* SOD. This time the study used individuals with pre-diabetic signs who had not been diagnosed with either frank diabetes or cardiovascular disease. Such

individuals will typically progress to significant levels of disease and could expect to be prescribed a range of pharmaceuticals designed to lower blood glucose, blood pressure and total cholesterol levels. All the participants in this study followed the *Lyon Heart Diet*[xviii] and half took the melon-based SOD while the remainder took an identical placebo.

The study measured the usual markers of oxidative stress but they also used *carotid artery thickening*, a clinical measurement considered to be a gold standard[48] in assessing clinical change in a patient with heart disease.

To cut a long story short, after two years, the group taking the SOD supplement showed *regression* of carotid thickening, whereas the placebo group continued to worsen. This is a remarkable result for a non-pharmaceutical compound. Mainstream medicine typically uses the *statin* drugs to address abnormalities such as these in blood vessels and consider a *slowing* of arterial thickening to be a positive result.



A two-year study[49] similar in design to the one just described but which used a 40mg dose of a statin drug showed a *slowing* of arterial thickening but not *regression.* Typical of pharmaceuticals, statins are not sufficiently specific in their action to avoid adversely affecting other functions in the cell. The way statins affect cholesterol production in the cell is to block a key enzyme needed to produce cholesterol. However, this same enzyme is needed by the cell to produce its own Coenzyme Q10, an essential part of normal function of the mitochondria.

Antioxidant Vitamins in Cardiovascular Disease Regardless of the theory, several large-scale trials involving many thousands of

[xviii] The Lyon Heart Diet aims to replicate the well-known cardiovascular benefits of the Mediterranean Diet.

subjects have failed to show any benefit in prevention of cardiovascular disease by non-nutrigenomic antioxidant vitamins. Perhaps surprisingly, some studies showed that higher-dose vitamin E (more than 400 IU per day) might even be harmful.

SOD and Glutathione As you may have noticed, some of the biochemistry here is rather complex! One of the aspects which can get a bit confusing is in trying to work out how Glutathione and SOD fit together. They are both very important 'players' in the cell's antioxidant system. They are both absolutely essential but have slightly different roles.

Think of Glutathione as the 'antioxidant' soup of the cell, quenching free radicals as they float about. SOD, on the other hand, exists in three separate forms, one in the mitochondria keeping a close watch on the amount of superoxide being produced; the second SOD exists in the cytoplasm of the cell and the third form operating outside the cell.

Glutathione is produced in relatively large quantities but quenches free radicals *one-for-one*. However, it gets involved in a broad range of activities. SOD is more selective and has the sole job of dealing with superoxide. Remember SOD as the lion tamer who can't take his eye off that wayward lion!

But one more thing to note! SOD also needs Glutathione to perform its job properly. Quenching superoxide is a two-step process and the second stage involves the Antioxidant Enzyme, *Glutathione peroxidase*. This enzyme needs Glutathione before it can undergo the chemical reaction.

So the nutrigenomic message here is that if we can 'switch on' SOD production with the melon-based compound and 'switch on' Glutathione with Sulforaphane, we have the ideal combination!

SOD and protection from the sun In France where melon-derived SOD was developed, dermatologists have been researching its effect on protection of the skin against sun exposure. Sun exposure is a form of radiation and as we saw in Chapter 7, radiation generates free

radicals. Not only is excessive sun exposure responsible for sun burn but over time, it alters the texture and resilience of the skin.

The formation of compounds known as ***A**dvanced **G**lycation **E**nd products,* conveniently called AGEs is a characteristic of ageing skin[50]. AGEs develop when sugar molecules such as glucose attach themselves to proteins, therefore reducing the normal function of the proteins. AGEs are responsible for cross-linking the protein chains in the major proteins of the skin, *collagen* and *elastin.* Clearly, approaches to limit the formation of AGEs in skin are a key to healthy ageing.

The melon-based SOD has been investigated[51] for its effect in recovery from sunburn across a range of skin types. When pre-dosed for two weeks before exposure to UV radiation, the treated groups showed significantly faster recovery than the untreated. It was also noted that in the fairer more sensitive skin types, up to nine times more UV exposure was tolerated in the treated group. Research in this area continues.

Superoxide and the Skin Ageing Process The Superoxide radical is produced at various locations in the cell but one of the most abundant sources is from an enzyme family known as NAD(P)H Oxidase; usually abbreviated to NOX. Interestingly, some of the members of the NOX family are only produced as we age, appearing at around age 30 and peaking at about 55 in women and 65 in men.

Because the levels of NOX are directly correlated with skin damage regardless of exposure to the sun, it is generally considered that it is the excessive superoxide radical which could be responsible. SOD, as we

have seen, has been shown to reduce levels of this skin-damaging superoxide, so nutrigenomic inducers of SOD such as the melon-derived form become the logical choice for helping to protect the skin against premature ageing.

Other Theories Some researchers have hypothesized that blocking NOX activity in the skin might be a way of reducing the skin ageing process. Attempts to find compounds which do this are under investigation. Some of the substances[52], [53] found to block the NOX enzyme are the statins, salicin, apocynin, Coenzyme Q10, green tea and an extract from the daffodil bulb. As we saw in Chapter 7, both Coenzyme Q10 and the green tea polyphenols have very poor bioavailability, so may not be ideal for this purpose. Whether this approach is effective remains to be seen and at this stage of the research, it is probably too early to know.

Of more concern is whether it is a good strategy to block a naturally-occurring enzyme. We have no way of knowing at this stage whether this approach is safe because there is insufficient evidence. As we saw earlier, the *statin* drugs used to block the cholesterol-producing enzymes are not without side effects because this enzyme is associated with other desirable functions within the cell.

Furthermore, is this approach trying in some way to reinvent a much older wheel when *nutrigenomics* already allows us to work *with Nature* to restore the cell's Antioxidant Enzymes to levels more closely associated with younger cells? Blocking an enzyme may have effects we can't yet predict and why artificially block an enzyme which produces superoxide when SOD is Nature's built-in mechanism for handling excessive free radical production? Better still, published peer-reviewed research confirms the clinical value of one approach but not of the other!

CHAPTER 11

Putting it all together

If you're now better acquainted with your cells and their pivotal role in your own health, I've achieved my goal in writing this book. I suggested at the outset that I would provide you with tools to help you to take back control of your health and minimise *over*-dependence on mainstream medicine.

Our journey together in exploring the emerging science of Nutrigenomics has taken us to places where few others have ventured. This is because much of the best scientific research findings remain on dusty library shelves, never to be translated into the type of simple and practical guidelines a consumer can use in day-to-day health care. Although its focus is on Nutrigenomics, this book has gathered data from a broad base, some of which is the intermingling of my own clinical experience gained over 30 or so years in clinical practice.

From that experience, I *KNOW* that sick people can become well by embracing the principles of Nutritional Medicine; I know too that for the day-to-day ailments that fill the seats in most medical waiting rooms, the pharmaceutical drugs and surgery of mainstream medicine are best left as the *weapons of last resort*.

Unfortunately, the *average* GP will tell you he or she is too busy to investigate a patient's diet and lifestyle in a standard five or ten minute consultation – and he is right! If he were a little more honest with you (and himself), he would say he is just not trained in this area – and if he really wanted to confront the *absolute* truth, he would say that he doesn't believe anything outside what his training provided. And by

'training', I refer as well to the ongoing reinforcement of these principles via the regular visits from the pharmaceutical industry's sales force.

So, how does an ordinary family get a more balanced view on practical health care, the sort of information that can help to prevent the *diseases of civilization* to which so many of us succumb? With global budgets collapsing under the financial weight of health (or disease) expenditure, why aren't we taught how to *really* prevent illness?

To some extent, this is due to the politics of health care (*read dollars!!*). However, it is also due to the huge philosophical divide which separates the practice of mainstream medicine and the preventive strategies proposed by this book with its suggestion that better-informed individuals have more choices for their health care.

We have focused on Sulforaphane and SOD as our main avenues for enhancing cellular defence because there is considerable research to support their use and also because they can be readily incorporated into an individual's daily routine in manageable doses. Because Sulforaphane can be obtained through carefully-manufactured high-yielding broccoli sprout powder, it is possible to consume it regularly. Sulforaphane exhibits broad-spectrum activity that we have only just touched on in this book. In addition to its role in 'switching on' the cell defence genes, its actions include many other protective roles.

With its safety[54] in humans confirmed, Sulforaphane stands *head and shoulders* above the many popular but poorly-bioavailable supplements that marketers have exploited on the basis of *test tube* and not human clinical trials. As the science of Sulforaphane continues to unfold, it is likely that we will continue to reaffirm its valuable role in human health and disease prevention[55].

Accelerating research in this field is showing that nutrigenomic properties are emerging for other nutrients and food-derived compounds. Sulforaphane has been shown to protect against DNA

damage but the essential nutrients including folic acid, vitamin B12 and others have also been shown to protect against DNA damage[56]. Where we once thought B12 and folic acid were primarily associated with the development of normal red blood cells, we now know that they play other important roles within the cell. Decades ago, *Recommended Dietary Allowances* for these nutrients were set to ensure that we didn't become deficient in these nutrients because deficiency is known to lead to a type of anaemia affecting the red blood cells.

More recent research has shown that these recommended daily intake levels may be too low[57]; in fact, they may be so low that they continue to allow DNA damage to occur even when the anaemia is prevented.

It turns out that a particular gene, the MTHFR gene can be mutated and if an individual carries two copies of the mutated form, the effect of such damage is more severe than if only one copy carried the mutation. It now appears that these people require higher levels of the appropriate nutrients than if the gene were normal.

Fortunately, testing for the MTHFR gene is becoming increasingly common. Variants of the normal gene are associated with such seemingly-unrelated disorders as cardiovascular disease and birth defects. But it is the more recent research which is showing us the importance of this same gene in protecting us against DNA damage.

And to think that that every mouthful of food we consume contains compounds which engage in complex and intricate *'conversations'* with our genes, setting up elaborate signaling systems throughout the cell.

Ultimately, the extent to which we allow *health-promoting* or *disease-promoting* foods to talk to our genes is our individual choice! The more we learn about Nutrigenomics, the more we regain control over our own health – and that of the generations which follow us.

A sobering responsibility, isn't it?

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What if you could...

- Maintain excellent health, day after day, even as you get older?
- Take back control of your health and avoid the common 'diseases of civilisation'?
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This book shows you how

It's no secret that governments across the globe are struggling under the enormous and growing financial burden of managing their health systems.

Increasingly complicated technologies are employed to treat the common complaints which fill hospital and doctors' waiting rooms daily. Chronic diseases account for an alarming 70% of all deaths in the U.S., with one in every two Americans living with a chronic illness. The statistics are similar globally.

More alarming is the fact that health authorities acknowledge that these chronic diseases are largely preventable. Where I live, Australia, the following 5 chronic disease categories account for an astronomical 2/3 of government spending: Asthma, Cancer, Heart/Stroke/Cardiovascular Disease, Osteoarthritis/Osteoporosis.

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About the Author

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With over 30 years' experience as a private-practice Clinician in Nutritional Medicine, Christine is now a Research Biochemist investigating Bioactive plant compounds with significant Clinical Potential. Her particular interest is focused on Nutrigenomics, a strategy for identifying natural compounds capable of upregulating the genes that cells use to prevent disease-promoting processes. The Nutrigenomics concept elevates the importance of what we eat to a higher level and heralds a new paradigm in health care.

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