

# Nutrigenomics

## How Food Influences Genes

By Michael Donaldson, PhD

What took over 10 years and \$3 billion can now be done in 24 hours for a mere \$1,500.<sup>1</sup> That's the incredible story of genome research.

After 10 years and \$3 billion of data processing, the human genome was completely sequenced in 2001. Ten years later, technology allows massive amounts of parallel processing that enables high throughput sequencing in 24 hours for only \$1,500.

To put this into perspective, if this was a \$300,000 house in 1990, you could buy a similar but better quality house in 2011 for \$0.10; and instead of taking a year to build it, it would be done in about 2 hours.

However despite much fanfare and promise of new medicine in 2001 and after 10 subsequent years of research, we really understand very little of what these 3 billion base pairs in our DNA mean.

However, since then techniques have improved with massive amounts of parallel processing enabling high throughput sequencing.

### THE CIRCULAR FLOW OF INFORMATION IN SYSTEMS

Genetic information is like any other intelligent, robust information system. It involves input and feedback with a whole network of sensors and signaling molecules so that the best possible outcome can be achieved.

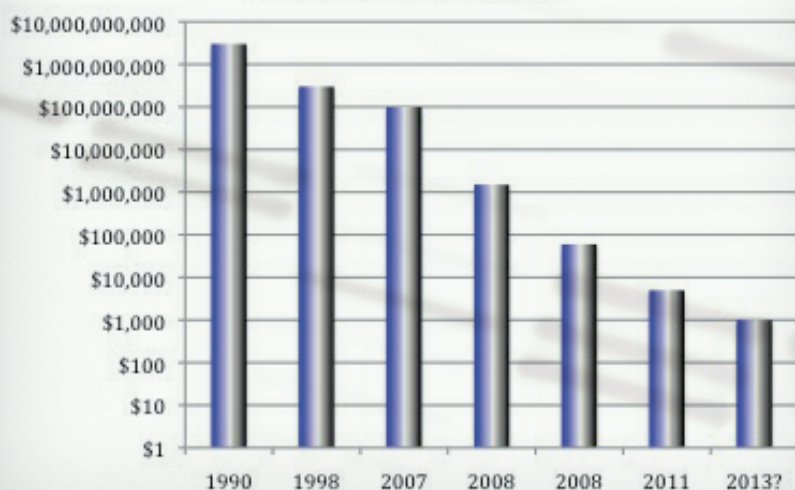
Here's how it works. The human body relays information from DNA to RNA to protein. DNA contains genetic material and RNA translates the genetic material into protein structures. To put it simply, RNA carries out the instructions of DNA.

This information flow was always thought to be a one-way simple process — one piece of DNA became one piece of RNA, which made one protein. That is what we have all been taught in high school and college biology.

However, we are now discovering that this flow of information is circular and dynamic, not linear and static. The expressed genetic code is more like water than ice—it takes the shape of the container that it is in.

In other words, the environment around an

**Dramatic Decrease in Cost of Genomic Analysis**



## *Nutrigenomics — How Food Influences Genes - continued*

organism (or put into an organism through food and chemicals) has a tremendous impact on which genes get expressed and how much.

Before the human genome project was completed it was thought that most of our DNA (about 99%) was, without purpose. Scientists actually referred to it as “junk” DNA.

This is because only 1% of our DNA actually has the code to make proteins. Scientists thought that this was the only purpose of DNA—to make proteins. (Remember that we were all taught the linear flow of information of DNA to RNA to protein.)

A huge collaborative effort called the Encyclopedia of DNA Elements (ENCODE) was begun in an attempt to understand how our DNA functions and ultimately brought to light some of these limitations in our understanding of how genomes work. Their results are quite startling.

In a pilot study of the human genome, they sought to identify all of the non-junk parts of DNA in a small fraction (1%) of the human genome.<sup>3</sup> This 4-year study included 35 different research groups representing 80 different organizations around the world.

ENCODE researchers found that the majority of DNA in the human genome is transcribed into functional RNA molecules. They didn't find any junk! All of the DNA was being used. This was a radical finding.

Another earth-shattering finding was that the RNA transcripts from the DNA actually overlap each other. It was previously thought that one section of DNA would yield one RNA molecule, not various parts of several RNA molecules.

### **WHAT GENOMIC SCIENCE REVEALS**

At Hallelujah Acres we have come to experience that dietary and lifestyle changes overcome almost all of the genetic weaknesses we have inherited.

So, will ENCODE's finding enable scientists to identify a “gene” for a particular disease, give you a replacement gene, and “cure” your ailments? No, because diseases are not caused by single gene defects. A network doesn't collapse because one node is non-functional, nor is our genome so fragile that a single gene defect causes most diseases.

On the contrary, genomic analysis will finally show that our destiny is not in our genes, but in the control of which genes are expressed and in what order.

This will bring the focus back to diet, lifestyle factors, and beliefs. In fact, there is new evidence that related gene expression to diet.

But before we get into the evidence, you'll need to understand some terminology.

Remember that DNA is transcribed into RNA and then translated into protein. The DNA can be transcribed many times into RNA or only a few times.

When we say a gene is “up-regulated” we mean that the DNA of the gene is transcribed more times than in the comparison case. (Like a father repeating his instructions over and over to his children so that they remember them.)

When we say a gene is “down-regulated” we mean that fewer copies are made compared to the comparison case. In these experiments scientists are measuring the relative number of RNA copies that exist in a cell.

Now on to the evidence.

Lycopene is the red pigment in tomatoes. When breast cancer cells and normal breast cells were treated with lycopene there were marked changes in their genetic expression.

One study found that lycopene modulated the expression of 726 genes in breast cancer cells compared to the normal breast cell-line.<sup>4</sup> One nutrient changed the expression of 726 different genes!

Gone is the idea of “one nutrient, one effect” inherited from the pharmaceutical mindset.

In another study lead by Dr. Dean Ornish, MD, 30 men with early stage prostate cancer made comprehensive lifestyle changes (whole foods, low-fat vegan diet, daily exercise, stress management, group support, nutritional supplements with extra plant protein, vitamins E and C, selenium, and fish oil) for 3 months.

Biopsies of normal prostate tissue before and after the intervention showed gene expression was up-regulated in 48 genes and down-regulated in 453 others due to the intervention<sup>5</sup> — and this was in normal tissue, not in the prostate tumor itself, due to sampling issues. I suspect the changes were even more dramatic in the tumor stem cells.

As you might suspect, just as good dietary choices can have positive effects, poor dietary changes can have negative effects.

For example, being obese causes a host of genetic expression changes. Rats fed a normal diet were compared to rats that got obese eating a high-fat diet. When the expression pattern of 4,500 genes in the rats' fat tissue were compared in the two groups, about 15 percent (over 650 genes) of the genes had changed expression, either higher or lower.<sup>6</sup> Genes, like leptin, for fatty acid metabolism were up-regulated while genes for redox and stress response were down-regulated in the obese rats.

In a Norwegian study, a control diet (their usual diet), a diet with 3 kiwi fruits added per day, and a diet higher in fruits and vegetables (more berries, berry juice, cruciferous vegetables, nuts, and seeds replaced other foods) were compared for 8 weeks. Ten people from each group (all smokers) submitted blood samples for genetic analysis.

Compared to the control diet, the antioxidant rich diet increased the expression of genes involved in cellular defense (DNA repair, hypoxia, apoptosis, stress, stress and response, and oxidative stress).<sup>7</sup> Overall about 800 more genes in the total diet and 400 more genes in the kiwi diet were significantly changed compared to the control diet.

*Nutrigenomics — How Food Influences Genes - continued*

---

In an animal model of esophageal cancer researchers identified 2,261 genes that were dysregulated when the rats were treated with a carcinogen. Feeding the rats a compound from cruciferous vegetables before and during the carcinogen dosing normalized 1,323 of these genes.

Using the same protocol, but using freeze-dried black raspberry powder instead of the vegetable compound, resulted in 462 of the genes being normalized.<sup>8</sup>

Not only were genetics normalized, but the appearance of esophageal tissue under the microscope was indistinguishable between the untreated (negative) control group and rats treated with the black raspberry powder or the vegetable compound. So, the results that we can visually see can also be found rooted in the expressed genetic code.

Clearly, diet and lifestyle make a big difference in the whole network of genetic expression.

On the flipside, unfavorable genetic expression changes also happen with pharmaceutical drugs. These synthetic compounds are toxic, loose cannons. Instead of normalizing cellular biology, the drugs cover up one problem while causing 10 other problems.

The benefit to using this new genomic science is to show that the control of genomic expression still lies in our hands—mostly when holding our forks and spoons. It would be fascinating to see the myriad of positive changes that happen in the expression of people's DNA when they adopt The Hallelujah Diet. ☺

---

**References:**

1. Anon. What is the Cost of Human Genome Sequencing?
2. Wadman M. James Watson's genome sequenced at high speed. *Nature*. 2008;452:788.
3. ENCODE Project Consortium. Identification and analysis of functional elements in 1% of the human genome by the ENCODE pilot project. *Nature*. 2007;447(7146):799-816.
4. Chalabi N, Satih S, Delort L, Bignon Y-J, Bernard-Gallon DJ. Expression profiling by whole-genome microarray hybridization reveals differential gene expression in breast cancer cell lines after lycopene exposure. *Biochim. Biophys. Acta*. 2007;1769(2):124-130.
5. Ornish D, Magbanua MJM, Weidner G, et al. Changes in prostate gene expression in men undergoing an intensive nutrition and lifestyle intervention. *Proceedings of the National Academy of Sciences*. 2008;105(24):8369-8374.
6. Lopez IP, Marti A, Milagro FI, et al. DNA Microarray Analysis of Genes Differentially Expressed in Diet-Induced (Cafeteria) Obese Rats. *Obesity*. 2003;11(2):188-194.
7. Bøhn SK, Myhrstad MC, Thoresen M, et al. Blood cell gene expression associated with cellular stress defense is modulated by antioxidant-rich food in a randomised controlled clinical trial of male smokers. *BMC Med*. 2010;8:54.
8. Stoner GD, Dombkowski AA, Reen RK, et al. Carcinogen-Altered Genes in Rat Esophagus Positively Modulated to Normal Levels of Expression by Both Black Raspberries and Phenylethyl Isothiocyanate. *Cancer Research*. 2008;68(15):6460-6467.