Aligning nutrigenomics and ELSA

Towards a politics of classification

Expectations and laboratory practices in nutrigenomics often vary significantly, especially when considering the challenge of personalising nutrition. This paper analyses both expectations and laboratory practices, and their relationship. It argues that both are relevant for the advancement of nutrigenomic practice, however, that the differences between them need to be taken into account. Ethical, legal and social aspects (ELSA) research of nutrigenomics has focussed primarily on the expectations uttered by nutrigenomicists for various reasons, thus constructing an ethical agenda that does not fully correspond to nutrigenomic practice. This paper argues for a new ethical agenda that takes into account both expectations and laboratory practice, thus (re-)aligning ELSA with nutrigenomic practice.

1. Introduction

Recent research in life sciences has shifted away from a reductionist focus on single, genes, proteins or metabolites. The emergence of high-throughput biology, combined with the development of computational tools for analysis, has presented an opportunity for life scientists to simultaneously measure and consider tens of thousands of variables (e.g. Fox Keller 2005). This approach has been coined the ‘omics’ approach (Weinstein 1998). Albeit of slightly different ages, proteomics (the ‘omics approach’ directed at proteins), transcriptomics (directed at mRNA transcripts) and metabolomics (directed at metabolites), as well as the object directed integrated versions such as pharmacogenomics (drug-centred) and nutrigenomics (nutrition-centred) are still in their infancy. This is something we need to keep in mind when reviewing expectations and practices of the field and their relation. Here, I do not intend to give an extensive historical overview of the emergence and advancement of nutrigenomics. Instead, in this paper, I will discuss the co-evolution of nutrigenomics and
research into ethical, legal and social aspects of nutrigenomics as two distinct but very interrelated practices.

The longer term ‘nutritional genomics’ had been around for quite some time when at the turn of the century several scientists coined the shorter ‘nutrigenomics’ (see e.g. Fogg-Johnson and Meroli 2000). Some discussion exists about whether nutritional genomics is the genomics of the eaten while nutrigenomics is the genomics of the eater. In this paper I will limit myself to the genomics of the eater part. The even shorter term ‘nutrinomics’ never really became an accepted term (Arab 2004). I do refer to it because it is an attempt to rename what is now still called nutrigenomics as a reaction to the incorporation of other classes of molecules next to the gene. When I, and many others, refer to nutrigenomics, we do not strictly refer to the genome-nutrient interaction but also to nutrient-transcriptome, nutrient-proteome, nutrient-metabolome, nutrient-epigenome interaction and a number of other nutrient–‘ome’ interactions that I have not mentioned, do not know of, or that might not even exist yet.

Personalised nutrition is one of the subsets of problems nutrigenomics addresses. Whereas nutrigenomics targets gene-nutrient interaction (or ‘ome’-nutrient interaction), personalised nutrition focuses on the differences in genes, related to nutrient intake. In this paper, I would like to address the promises and expectations of personalised nutrition, the (laboratory) practice of nutrigenomics and the ethical, legal and social aspects of nutrigenomics research\(^1\). I will focus on the theme of personalised nutrition to demonstrate how these three areas relate, what the differences between them mean and how we can deal with them.

2. Promises and expectations

One of the most clear and presumably more radical expectations of personalised nutrition has been voiced by German and Watzke, when they state that ‘it is not a question as to whether personalized foods will become a part of the food marketplace, but simply when they will become the rule rather than the exception’ (German and Watzke 2004).

\(^1\) For a general introduction and comments upon research into the ethical, legal and social aspects of genomics, see Radstake and Penders (2007).
German and Watzke use the term ‘personalised’, but the same idea of nutrition specific to individual needs is also called ‘individualised’, or ‘tailored’, two terms Hoolihan and Harlander (Hoolihan and Harlander 2004) use, distinguishing between all single individuals:

This growing body of nutrition science research, combined with the rapidly accelerating genomics movement has shown undeniably that everyone is a unique individual with specific needs. We have thus entered the stage of individualized, or tailored, nutrition […]. We are developing the capacity to make dietary recommendations aimed at optimizing health and reducing risks of the diseases to which one is genetically predisposed, based upon knowledge of one’s nutritional status, lifestyle, disease risk and genetic make-up. […] We are at a point in the history of nutritional sciences where we have expended our knowledge of nutrition and are ready to utilize what we know for the better health and well-being of not just the population as a whole but every single individual (Hoolihan and Harlander 2004) (my emphasis).

However, people do not only write down their expectations, they express them in interviews and at conferences. In an interview, the project leader of a Dutch nutrigenomics research project assured me that:

I still am convinced that we will, in the end reach a personalised dietary advice, based upon nutrigenomics. Because I remain to be convinced that the effects of nutrition are immensely different between people and that can only be, based upon differences in genes and constitutions […]. It might be very complicated, but in the end one must be able to find the right combinations that can predict why one’s cholesterol rises and the other’s doesn’t. And […] with the calculation power and the immense acceleration at which several things are being analysed […] that sort of information becomes available faster […].

I think that nutrigenomics will, and this obviously is oversimplified, that in your food disc […] radials² will shift a bit like this and mine will shift a bit like that [arm

² In the Netherlands, the nutritional education model is not a pyramid, but a compartmentalised disc (the schijf van vijf) indicating overall the same recommended daily intakes as other models such as the US MyPyramid. The ‘schijf van vijf’ (disc of five) was recently updated and reintroduced November 16, 2004. It was first designed in 1953 and in 1981 it was redesigned into the ‘maaltijdenschijf’ (the ‘dinner disc’ or ‘disc of four’), grouping meats and dairy into one compartment. In 1991 it was remodelled again, into the ‘Voedingswijzer’ (the food guide). In 2004 the ‘drink’ compartment was added to make it a ‘disc of five’ again. A disc-like model is also used in
gestures]. So certain compartments will grow bigger and other smaller, depending on what nutrigenomics will tell you³.

*Interview M001, 20050316.*

In their expectations, these senior scientists are presenting a certain image of what ‘personalised nutrition’ is going to be like. They voice the conviction that ‘personalised nutrition’ is, indeed, the future. This future nutrition is going to be tailored to the unique needs of every individual, whether based upon ‘difference in genes and constitutions’ as the Dutch project leader stated above, or ‘based upon nutritional status, lifestyle, disease-risk and genetic-make up’ as Hoolihan and Harlander state. At the centre of these claims lies the shift from a ‘one size fits all’ approach towards the focus on individual genetic differences:

The previous ‘one-size-fits-all’ approach to diet and dietary recommendations of the distant past is limiting and may even be erroneous [...]. This new paradigm and way of viewing foods and their components will ultimately shift broad population-based nutrient recommendations to ones more tailored to the individual. (Hoolihan 2003).

The scientific and popular press have not ignored such promises and expectations. They have used catchy phases such as ‘Eat right for your genotype’ or ‘the DNA diet’ (or the Dutch ‘elke eten de juiste hap’⁴ (van Ommen 2001) to explain the tailoring of nutrition to individual needs (Grierson 2003a; 2003b). In such newspaper articles, mini scenarios are used to illustrate and to monitor this trend away from ‘one size fits all’. I intentionally say ‘away from one size fits all’ and not ‘towards something’, because it is not entirely clear towards what this trend is leading us. In these mini scenarios we read about someone pricking their finger, sending the blood to a lab and receiving an email indicating the recommended diet for the next month, which ‘doesn’t look too bad: lots of salmon, spinach, selenium supplements and bread with olive oil’ (Grierson 2003b).

³ Excerpts from interviews, notes and lectures have – where relevant – all been translated from Dutch and German into English by the author. Part of the empirical material has been used in a previous publication (Penders et al. 2007).

⁴ English: ‘Every eater the right bite’.
Expectations are – by their very nature – about the future and have the luxury of being able to abstract from certain practical requirements that actually doing the experiments in a laboratory may introduce. Many of these can be reasoned away by assuming technological advancements, or are simply ignored. Even though expectations and promises serve their purpose – many do so very well – finding out what science is actually about, requires more than just listening to its promises. Let us turn to the laboratories where nutrigenomics is performed, the conferences where nutrigenomics is discussed and the journals where findings are reported: let us turn to the sites where nutrigenomic science is performed and personalised nutrition is (becoming) a practice.

I have travelled to and through these sites, spending several months in Dutch genomics, proteomics, microbiology and bioinformatics laboratories, attending dozens of meetings, half a dozen conferences and have interviewed nearly thirty laboratory researchers during the last two years. These scientists cannot avoid practical problems by assuming that they will be solved. They have to solve them themselves.

3. Nutrigenomic practice

The practice of nutrigenomics is an interdisciplinary one. At one of the conferences I went to last year, one of the speakers said to the audience: ‘Look to your left and to your right. Chances are high that your neighbour is from an entirely different discipline than you are’. Even though colleagues tend to sit together – her overall message was true. Out of all of these disciplines, one in particular is very much involved in diet-genotype interaction, the base of personalised nutrition: epidemiology.

Epidemiologists are correlating several parameters – such as genotypic variation and dietary intake - measured in large cohorts of patients or volunteers. Even though historically a very fruitful line of investigation, there are upper limits to the number of variables, as Ben van Ommen argues:

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5 Observation Sian Astley, 20050913.
The current way people work, from epidemiology, the manner at which cohorts are screened do not allow us to reveal complicated relations for more than a few genes at a time, or for more than a few genetic differences at a time.

*Interview Ben van Ommen, 20060125.*

Ben van Ommen is the grant holder for NuGO, the European Nutrigenomics Consortium: one of the largest programs in the European 6th Framework program. He is part of international nutrigenomic practice and through NuGO aware of the issues addressed and the limitations encountered in the various disciplines in the consortium, epidemiology amongst them.

In order to ever reach the unique diet for every individual, it is imperative to incorporate gigantic numbers of variables. At a previous occasion Van Ommen gave a quantitative example, illustrating where he thinks practical limits will be encountered:

Imagine a cohort of 10,000 people. If polymorphism A exists in 2% of all people, and B in 20% and C in 3% of all people, you will end up with 1 person in your population who has all three. That is not enough. Even if you screen the whole world you will not find enough people and you will not find out, and that with only a few genes.

*Observation Ben van Ommen, 20050330.*

The task of ‘doing the maths’ with respect to these correlations, that comes with these large studies, lies upon the shoulders of bioinformaticians. In their work, they too cannot abstract from the practicalities that come which their type of work. One of the genomics computational experts tells us that ‘the number of combinations and permutations of genes and environmental factors are so huge that one will never be able to evaluate all such interactions’.

Van Ommen restricts himself to gene-gene interactions and identifies that set of variables to be too large. Parnell includes environmental factors – amongst them, diet – thus increasing the number of possible combinations even more. Both Van Ommen and Parnell identify obstacles on the path towards unique nutrition for individual genotypes: practical obstacles such as the huge numbers of volunteers needed and the huge number of variables to be considered. They do not contest the notion that all people are different, but what they are

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6 Observation Larry Parnell, 20050910.
telling us is that they think finding out how all of that is relevant in terms of nutritional requirements, is subject to practical limitations.

Van Ommen takes up this point to show that this way of approaching the diet-genotype interaction is not only impractical, but also that there is no reason for unique diets tailored to single genotypes:

If you reason the other way around, there are a number of pathological deviations known from differences in genotype. There are lethal mutations and there are a number of mutations that make people truly obese, pathologically obese. But there are only six of them. If you go to the more subtle deviations … at a certain moment the relevance of the difference between the trees in the forest disappears. The art is not to wander to deep into the forest but still notice the use of your work. […] It matters that one is capable of separating sense from nonsense and useful from the useless and find out for which nutritional parameter it is useful to keep looking for differences.

*Interview Ben van Ommen, 20060115.*

Van Ommen argues, that with health in mind as the sole driver for the tailoring of nutrition to individuals, there is no reason to regard everyone individual as unique because the major differences on a genotypic level are irrelevant.

Van Ommen identifies practical (or logistical), as well as theoretical reasons for personalised nutrition not being directed at the individual, but at groups. The personalised diet is not about tailoring to the individual:

We do not tailor every article of clothing to the individual, we live comfortably with the fact that clothing sizes exist. This is the way in which I see genotyping. In the end we will be able to match a clothing size 42 to a genotype size 42. That means that we do not have to go down to the individual level, but we can also stay on the level of clothing size cohorts.

*Interview N002, 20051211.*

The personalised diet is about groups, about assigning certain diets to certain groups or subpopulations. As Jim Kaput, one of the leading US nutrigenomicists, stated at the Personalised Nutrition Conference 2005: ‘the better word for personalised nutrition would be
group nutrition. Let's be practical about that. [That is] the way to better health' [7]. His position both as a senior scientist and the Chief Scientific Officer of the biotech firm Nutraceuticals enables him to consider both scientific and commercial limitations to individualisation.

Scientist N002 compares these groups to clothing size cohorts and because the word ‘tailoring’ is prominent in the nutrigenomic vocabulary, the clothing metaphor is used a lot. Scientist I007 takes it up as well. He is an R&D scientist working a large dairy company in the Netherlands. To him these groups have to be large groups:

> What we actually do with products, is that we make confection products, like in the clothing industry. One has no tailors anymore, just plain confection clothing. That means one uses several sizes, for its own size, a group has to be big enough. We are talking about larger groups here, to which […] one can sell a large quantity of products.

*Interview I007, 20051221.*

He uses an economic argument to restrict the personalised diet to groups, large groups. Where scientist N002 explicitly mentions the genotype as the entity to tailor to, I007 tailors to the individual, not exclusively mentioning the genotype. As I mentioned in the beginning of this paper, there is more to nutrigenomics than genes and genotypes. A large part of nutrigenomics is neither about genes nor about gene expression at all:

> The fields of clinical chemistry and clinical biochemistry are very well developed. They can tell you precisely what optimal cholesterol values are, without measuring the expression of 300 genes involved in cholesterol expression. So I think one has to be pragmatic here too and that is why I’d like to loose the term genomics, as being linked strictly to genes or gene expressions, let alone the difference in genes.

*Interview Ben van Ommen, 20050125.*

That is why people such as Ben van Ommen and Michael Müller, presumably the two main Dutch nutrigenomic ‘champions’ increasingly refer to their field as ‘molecular nutrition studies’ or ‘biomics in nutrition research’.

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The genotype does not 1:1 reflect the phenotype. Earlier, Parnell included environmental factors as relevant modifiers as well and Bruce German has summarised the relationship of genotype and environment in what he calls ‘the equation of life’ (German and Watzke 2004):

\[
\text{Phenotype} = \text{Genotype} + \text{Environment} + \int_{\text{birth}}^{\text{now}} \text{Genotype} \times \text{Environment}
\]

Summarised, it states that genotype is relevant, but at every moment in life the environment one has been exposed to up to that moment is equally important. The same formula can be found in which environment is substituted by lifestyle.

What does all of this show us? Nutrigenomics in practice is increasingly less and less about genes and more and more about other molecules, and so is personalised nutrition. These other molecules are measured in high-throughput systems as well and they provide nutrigenomicists with lots of information about both genotype and environment, but in an integrated way. In their quest for the healthy phenotype, understanding the relationship between nutrition and the genotype enables intervention. At the centre of nutrigenomic enquiries is not the eaters’ genome, but the foodstuff. With the human genotype only subject to limited relevant variation, as Van Ommen told us earlier, reaching the healthy phenotype is all about environment, about lifestyle.

A recent review paper, co-authored by 88 nutrigenomic professionals, lists several examples of non-nutrient environmental factors or lifestyle related factors that might be of importance: sleep time, altitude, non-prescription drugs, water intake related to other beverages, physical activity, stress, allergens and pollutants, circadian rhythm and seasons changes as well as energy balance (Kaput, Ordovas et al., 2005) and scientist W001 expresses himself quite clearly when saying that he is convinced ‘that when one eats varied and with moderation and exercises a bit, that – with the exception of a few unfortunate people – one does not need any nutrigenomics to stay healthy’.

I suggest rephrasing ‘Genes load the gun, environment pulls the trigger’ - a statement accredited to many people in genomics - into ‘Genes load the gun, but lifestyle pulls the

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8 These 88 professionals include mainly academic scientists and R&D scientists, but also ethicists and social scientists that address nutrigenomics in their research.
9 Observation scientist W001, 20051005.
trigger’. What we can learn from watching Crime Scene Investigation is that (nutrigenomic) research may look for the bullets mobilising every piece of technology in their labs, but only to find the triggerman. The acronym NuGO, originally meaning ‘European Nutrigenomics Organisation’ is also said to mean: Never Use Genomics Only’ (Müller 2005).

4. ELSA in nutrigenomics

Social scientists, ethicists, philosophers and lawyers have been interested in nutrigenomics almost from the very beginning. Nutrition science is an interesting subject, where description and prescription are very close. And genomics technologies introduce their own set of interesting problems and issues. In their report on the subject, the Utrecht Ethics Institute explains why it is relevant for ELSA researchers, to look into nutrigenomics early on:

> It is not too early to review and discuss the ethical consequences of the development towards tailor-made diets, even though currently no such diets are available. Ethical questions are not questions that are only related to the application of certain knowledge or technology but are often already implicitly present in the research stage […]. Even though we are not yet confronted with tailor-made dietary advice offered in the medical sphere, it is possible to imagine topics that are likely to become morally relevant when food is tailored to an individual person’s genetic makeup (Ethics Institute 2005).

Many ethical, legal and social aspects have been identified related to nutrigenomics, to name but a few: the shift from curing to preventing to enhancement (Korthals 2002b), the creation of new risks and uncertainties, issues surrounding the screening and sampling of every individual (Korthals 2002b), the loss of the meal as a moment for sharing and gathering (Korthals 2002a; Swiersta et al. 2002), the relation of identity to nutrition (Meijboom et al. 2003), the abundance and availability of genetic information (Korthals 2002b; Chadwick 2004) and the conflict between whether it is legitimate to consider health as the main, or even sole, value relevant to food choice (Korthals 2002b; Lemke 2002; Chadwick 2004; Görman 2006). Certainly not all, but many of these issues are related to the presumed individualising effects of genomics (Korthals 2002b; Swiersta et al. 2002; Chadwick 2004).
As Michiel Korthals notes in his book: ‘Individualising effects of genomics are being identified by nutrition scientists and nutrition journalists […]’ (Korthals 2002b). He continues by telling us that:

This individualised approach means that individuals are to be screened and sampled, that their information needs to be stored and that individualised prescriptions need to be given. Of course this can mean an enhanced control; furthermore it burdens the individual with new responsibilities with respect to their kin, their partners and networks (Korthals 2002b).

In his work he draws from the expectations expressed by scientists and press and in fact he uses the exact same mini-scenario I have listed in the first section of this paper both in his 2002 book and again 2006 in a short paper (Korthals 2002b; 2006).

I have chosen the example of personalised nutrition exactly because many of the ethical, legal and social aspects of nutrigenomics are connected to a fear or worry that nutrigenomics will somehow hyper-individualise society, or at least add some scientific momentum to the ongoing trend when ‘[c]ommon meals threaten to disappear, simply because my DNA profile prescribes a different menu from yours’ (Swiersta et al. 2002).

This individualising effect of genomics and nutrigenomics has an empirical foundation. The material used by the ELSA researchers to draft their first normative agendas with respect to personalised nutrition, is derived from the context of expectations and promises, simply because in the beginning, the personalised diet existed only in those terms. However, nutrigenomics has moved on from existing only in the realm of expectations into actual scientific practice, and research into the ethical, legal and social aspects of nutrigenomics should stay in touch with these developments. This implies that ELSA research has to acknowledge the way genomics technology is actually used and the effects it has on the relation between nutrition and genes and the notion of personalised nutrition. The normative agenda set up by the ELSA researchers, empirically rooted in the expectations uttered by nutrigenomic professionals, is in need of some revision. Rooting ELSA in nutrigenomic practice means making two significant shifts: first, shifting the focus from genes to almost all other molecules and acknowledging that these other molecules reflect not only genetics but lifestyle as well. Second, a shift from the issue of individualisation to the issue of making groups.
5. Towards a politics of classification

While many of the issues brought forth by ELSA researchers are still very relevant, rooting the normative agenda in nutrigenomic practice implies that new issues have to be discussed. The loss of the meal as a moment for sharing is indeed under pressure from existing trends towards individualisation of lifestyle – but not as the result of a nutrigenomics prescribed individual diet:

If one would issue a [population-wide] advice with respect to healthy nutrition, only very few people would get uncomfortable from that. So, again, it is merely a fine-tuning for segments of the population. I do not think food industry wants to produce ten million different confections, but I do think it is good that everyone of those ten million people thinks about – and has the means available to find out – what is healthy for him or her. For a professional athlete, something else is healthy than for a baby… that type of personalisation has existed for a long time. That it gets more firmly rooted in science, fine… that more target nutrition arises, that is merely logical.

*Interview Ben van Ommen, 20050125.*

Genomic information might not be relevant in all cases and despite talk about the 1000$ genome, experts consider screening the whole population irrelevant:

I actually am convinced that it is not necessary to sequence each an everyone’s genome to find out that this person has a nutritional problem. [...] Let’s phrase it this way: nutrigenomics is not needed for such applied questions; I am convinced about that. I have expressed that in Mallorca [Personalised Nutrition Conference, BP], when I said that the solutions to the large nutritional diseases, from adipositas, diabetes type II and cardiovascular disease, do not need nutrigenomics. They need political steering.

*Interview N002, 20051112.*

Furthermore, as Ben van Ommen explained earlier, looking into other molecules and variables may be much more enlightening. He used the well-known example of cholesterol, but others
exist as well, varying from blood pressure to blood free fatty acid levels. Although the threat
of hyper-individualisation appears not to be that great as was thought by ELSA researchers in
the beginning, issues of personal responsibility remain relevant. When lifestyle becomes the
focus of nutrigenomic research, pressure towards healthy living may grow and the question
whether health is the only value worth pursuing though food remains unchanged.

The Food Ethics Council conceptualises personalisation as a ‘political project’ in
which both food industry and government are actively involved (Food Ethics Council 2005,
p.5-6). In the part of their report that addresses nutrigenomics, the quoted scientific and ELSA
research is, however, also largely based upon expectations (p.24-30). I argue that nutrigenomic
ELSA research needs to shift their agenda away from the politics of personalisation and look
into the politics of classification that the practice of personalised nutrition generates. New
questions arise from such a politics with respect to nutrition and society. I would like to end by
suggesting a few of these questions. Nutrigenomic practice is creating group related nutrition.
Who is going to be in a group at all? No classification is perfect and every classification has
some sort of ‘left-over’ category. What advice do people in that group get? Which groups are
going to get their own advice and based upon which criteria? And do the categories created by
science match the categories created by industry through the products and options they
supply? What if not?

Who will pay for issuing an advice when it is not individual? What are the
consequences of being in a certain category? And how do you get into a different one? Is there
a reason to try? Is there going to be pressure towards being in a certain category? By health
insurance companies, by the government or from ones own drive towards health? Does every
category get the same health insurance, or any insurance at all? Is there a top category? Who
says so? Can it be full? What if I choose unhealthy living? Who gets to know that?
Furthermore, in the light of increasing international alliances (Kaput, Ordovas et al., 2005),
will the classifications be global, national or local? What consequences does this have for
worldwide public health?

The normative agenda initially drafted by ELSA research identified several relevant
issues based upon expectations by nutrigenomics professionals. Many of them remain relevant
when based upon practice; however, many also require a shift of focus, from genes to lifestyle
and from individuals to groups. ELSA researchers should keep in mind that ‘science is a
moving target and those that study that target simply have to move along’, as Helga Nowotny recently reminded us (Nowotny 2006).

Acknowledgements

We would like to acknowledge support from the Societal Component of Genomics Research Program (MCG) of the Netherlands Organisation for Scientific Research (NWO) to BP (Project no. 050-32-011; ‘Nutrigenomics and society in the making’) and thank R. Vos, K. Horstman and E. Aarden for reading and commenting draft versions. I thank the nutrigenomic professionals for allowing entrance to their field and additional cooperation through interviews. Finally I thank the reviewers for critical reading and constructive comments.

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© Graduate Journal of Social Science - 2007 - Vol. 4 Special Issue 1

Graduate Journal of Social Science, 2007 vol. 4 special issue 1: 4-10.

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