Nutrigenomics – so much confusion...

Dr Ben Lynch, ND, founder of www.MTHFR.Net, and Anne Pemberton, RGN, DipION, head our April 11 CAM Conference on Nutrigenomics. The onset of affordable genetic testing marketed direct to consumers has created a minefield for clients and practitioners alike. Here Anne summarises many months of research and practical experience applying the new science of nutrigenomics, as a primer for the conference.

I felt inspired to write this partly as an aide memoire for my students. There is so much confusion and angst around the whole issue of genetic testing. I was on the periphery for so long, but once I started to learn and understand the "methylation gene" MTHFR and all its counterparts, I was soon hooked.

Even before I ran my own tests I could see that both my parents and grandmother were homozygous for MTHFR. My children are on the spectrum of autism. Thanks to much nutritional therapy and various other therapies, my children are both contributing to society with a good work ethic and their own circles of friends. But have I done enough for them? The intrigue still grabs me. I'm the one in the family who had to undertake the 23andMe genetic testing to see whether potential cancers or dementia were my likely fate. Like many of you, I am my own scientific experiment, too.

I thankfully got into 23andMe just before the FDA quite rightly stopped them educating the world. The results from these tests can be devastating when there is a lack of understanding on the purchaser's part. I fully endorse the fact that these tests should only be in the hands of experienced practitioners. To this end I will try to make some pieces fit.

What to do with the data

Before the introduction of the 23andMe test, and well before it came to the UK, I had run the Laboratoire Reunis detoxification profile. Since the FDA stopped us learning our fate from a computer, several websites have sprung up that offer interpretation of the 23andMe raw data, which you or your clients can download from the 23andMe website or upload to other websites very easily. I work with the most popular and run my raw data through them all, comparing each one with the Lab. Reunis test.

I've tabulated the results and my impressions here. The first table is a cost/value analysis; the second table looks at some key genes and how the different sources report them. This is only my personal view, from my practical experience. I would have liked to compare to the Genova/Metametrix analysis too, but the cost soon begins to outweigh the benefits. I have not chosen Laboratoire Reunis test as a comparison for any other reason than easy access to the test, as it was available in the York clinic.

Cost Analysis:

LABORATORY OR COMPANY	COST	INTERPRETATION PROS AND CONS
Laboratoire Reunis: (https://www.labo.lu/en/home.html)	£592 for methylation, varies according to range of SNiPs.	Excellent report with good explanations of SNiPs and food relationships. BasicGen is a good starter if practitioners are unsure which test range is appropriate, Tech support mediocre from Regenerus. Seem very quick to send practitioner information, but lacking in ability to answer queries. Training very poor; focused on the sales and treating the SNiPs. May need more than one test to complete the full picture.
Genovations: Genova (https://www.gdx.net)	£200-£520 add ons such as APO-E for £100	Good reports overall. Price dependent on test focus, with EstroGenomics being the more comprehensive and therefore more expensive. The need to undertake more than one test can really make this cost-prohibitive. Buccal swabs, so no need for blood draw. Western medicine approach to testing in both Lab Reunis and Genova.
23andMe: (www.23andMe.co.uk)	£150	SNiPs identified by rs ID numbers, so need cross-referencing. There are genetic databases to do this easily, but it's time consuming. Better to run this through other software. Not understandable to the general public.
MTHFR: (www.mthfrsupport.com)	£15	Takes 23ndMe raw data. Nice-looking report. Easy to navigate. Really extensive number of SNiPs identified and reported; rs ID and variation code reported. Personal results colour-coded as Lab Reunis. All relevant genes reported. No indication of impact of variation or food/supplements, but this is available on the gene database which can be added in the notes column on the report. Measures 290 alleles; 100 were important to me – ie homozygous or heterozygous. It groups the alleles into sections – detox, tongue tie/cleft palate, allergy/mould, IgG, clotting factors, methylation, coeliac disease/gluten intolerance, thyroid, eye health, mitochondrial function, other immune factors, sulfotransferase. This report could be handed to clients once the practitioner has added relevant comments.
NutraHacker: (www.nutrahacker.com)	£16	Takes 23andMe raw data. Explanatory front page 58 SNiPs assessed, but it only reports the ones you need to be aware of – 19 in my case. Reports rs ID, alleles, gene function, consequences, supplements to encourage and those to avoid. In my case it congratulated me on my fast phase 1. Not very thoughtful, considering many SNiPs in the methylation and sulphation pathways. Report not user-friendly; it appears as if the information is from a database and the irrelevant SNiPs are blanked out so you might get two SNiPs per A4 sheet. If you pay the £16 you do get a password to access your own nutrient data, but some of this is incorrect.
Genetic Genie: (http://geneticgenie.org)	Donation	Takes 23andMe raw data. Nice colour-coded report with gene and variation, rs ID, alleles and results. Reports only the alleles important to you – 26 in my case.
Livewello: (https://livewello.com)	£12.50	Takes 23andMe raw data. Colour-coded report similar to MTHFR and Genetic Genie. Reports gene, rs ID, minor allele, genotype and phenotype. Separated into sections containing SNiPs for the following groups: allergy, clotting factors, detox, gluten intolerance, IgA, IgE, IgG, methylation, mitochondrial function, other immune factors, sulfotransferase, thyroid, tongue tie. There is no information on eye health or a comments box (MTHFR).

ALLELE*	COMPANY AND ALLELES IDENTIFIED	NUMBER OF ALLELES MEASURED	CONSISTENCY IN RS ID WITH OTHERS	INTER-COMPANY RESULTS CONSISTENCY	COMMENTS
CYP (Cytochrome P450 enzymes important in detoxification pathways)	Lab. Reunis	3 (1A2*f, 1A2*c, 1B1*3)	No	No	Inconsistency in rs ids * means non-accredited parameter (NAP).
	MTHFR (23andMe data)	1	No	No	
	NutraHacker (23andMe data)	2 (2C9; 2D6)	No	Yes and No	Congratulated me on being a super-fast metaboliser. Not good to fast metabolise xenobiotics and drugs if my phase two is poor.
	Genetic Genie (23andMe data)	0	NA	NA	
	Livewello (23andMe data)	21 (1A1, 1A2, 1B1, 2A6*2, 2C19, 2C9, 2Cp*2, 2D6, 2E1, 3A4) many rsID's for same gene.	Yes with MTHFR	Yes, although many genes not Id'd on other results	
	Genovations	7 (1A1*, 1B1*, 2A6, 2C9, 2C19, 2D6, 3A4)	NA	NA	
GSTM1 (Glutathione S-transferase)	Lab Reunis	1	No	No	NAP. No rs ids
	MTHFR	7	No	No	
	NutraHacker	0			
	Genetic Genie	0			
	Livewello	6	Yes with MTHFR (12562055 missing)	Yes with MTHFR. Unsure with NutraHackers	Unable to assess consistency for this as it isn't a problem SNiP for me.
	Genovations	1	NA	NA	
GSTP1 (Glutathione S-transferase)	Lab Reunis	1 (1105V)	Yes with MTHFR	All 3	Different rs id Nutrahackers
	MTHFR	2 (1105; A114V)	Yes with L-R	All 3	
	NutraHacker	1 (1695)	No	All 3	
	Genetic Genie	0			
	Livewello	2 (1105, A114V)	Yes (MTHFR)	All 3	
	Genovations	2 (GSTP1 at 2 locations)	NA	NA	
GSTT1 (Glutathione S-transferase)	Lab Reunis	1	NA	NA	Unimportant -/- non-accredited parameter
	MTHFR	0			
	NutraHacker	0			
	Genetic Genie	0			
	Livewello	0	NA	No	
	Genovations	0	NA	NA	
MTHFR (Methylenetetrahydrofolate reductase, the key to methylation)	Lab Reunis	2 (1298; 677)	NA	All 4 (1298)	
	MTHFR	14 (1298; P39P; 1572; 677; 1793; other unnamed)	All 4(1298) 3 (677)	All 4 (1298)	
	NutraHacker	1 (1298)	Yes	All 4 (1298)	
	Genetic Genie	3 (p39p; 1298; 677)	Yes	All 4 (1298)	
	Livewello	11 (P39P, 1298, 1572, 677, 1793, others unnamed)	Yes with MTHFR	All 4 (1298, P39P)	
	Genovations	0	NA	NA	
MTR (5-methyltetrahydrofolate-homocysteine methyltransferase, the final step in methionine synthesis)	Lab Reunis	1 (2756)	Yes	3 (2756)	Non-accredited parameter. -/-
	MTHFR	1 (2756)	Yes	3 (2756)	
	NutraHacker	0	NA	NA	
	Genetic Genie	1 (2756)	Yes	1 (2756)	Unable to assess N-H: no result for me
	Livewello	1 (2756)	Yes (MTHFR, N-H, GG	All 4	
	Genovations	0	NA	NA	
MTRR (5-methyltetrahydrofolate-homocysteine methyltransferase reductase, important for amino acid processing)	Lab Reunis	1 (66)	NA	Yes	Non-accredited parameter
	MTHFR	10 (66, 595, 350, 415, 664, others unnamed)	Yes	Yes (66 & 664)	
	NutraHacker	1 (66)	Yes	Yes	
	Genetic Genie	5 (66, 595, 350, 415, 664)	Yes	Yes (66 & 664)	
	Livewello	5 (66, 595, 350, 415, 664)	Yes (66 + 595, 350, 415, 664)	Yes	
	Genovations	0			
COMT (catechol-O-methyltransferase, controls levels of hormones and neurotransmitters)	Lab Reunis	NA	NA	NA	
	MTHFR	4 (61-P199, 62)	Yes (Livewello)	Yes	
	NutraHacker				
	Genetic Genie	3 (158, 62, 199)	Yes (199 & 62)	Yes	
	Livewello	4 (61-P199, 62)	Yes (MTHFR)	Yes	
	Genovations	1 (158)	NA	NA	
MAO A (monoamine oxidase A, involved with dopamine, norepinephrine, and serotonin)	Lab Reunis	NA	NA	NA	
	MTHFR	1 (6263)	Yes	Yes	
	NutraHacker	1 (6263)	Yes	Yes	
	Genetic Genie	1 (297)			
	Livewello	1 (6323)	Yes	Yes	

Overall conclusions

I like the report from MTHFR Support for its thorough coverage of 200 SNiPs. Some will argue that many are not yet accredited, but the ones from the current UK-based tests are mostly marked as non-accredited parameters. Laboratoire Reunis clearly state the ones they consider to be non-accredited. Interestingly, genomic educator Dr Michael Culp, ND, has stated that preventative genomic profiles should be:

Relevant
Prevalent
Modifiable
Measurable.

They should also be grouped in condition-related profiles. The MTHFR report seems to comply with this. I found no SNiPs that were not on the database.

The MTHFR report also measures tongue tie/cleft palate, allergy/mould, IgG, IgA, clotting factors. The methylation panel additionally includes ACE (ace inhibitors), ADD1 (related to hypertension), ACAT (related to deficiency in acetyl co A), AGT (hypertension), DAO (3 – associated with kidney disease, hyperoxaluria), DHFR

ALLELE*	COMPANY AND ALLELES IDENTIFIED	NUMBER OF ALLELES MEASURED	CONSISTENCY IN RS ID WITH OTHERS	INTER-COMPANY RESULTS CONSISTENCY	COMMENTS
CBS (cystathionine-beta-synthase, involved with the B6 and homocysteine pathway)	Lab Reunis	NA	NA	NA	
	MTHFR	5 (13637, 360, 19150, 699, 212)	Yes (360 & 699)	Yes	4 x +/-
	NutraHacker	2 (360, 699)	Yes	Yes	
	Genetic Genie	3 (699, 360, 212)	Yes (360 & 699)	Yes	2 x +/-
	Livewello	5 (13637, 360, 19150,699, 212)	Yes	Yes	
	Genovations	0	NA	NA	
BHMT (betaine-homocysteine S-methyltransferase, involved in homocysteine and methionine)	Lab Reunis	NA	NA	NA	
	MTHFR	6 (02, 04, 08, 239)	Yes	Yes	
	NutraHacker	3 (02, 04,08)	Yes	Yes	
	Genetic Genie	3 (02,04,08)	Yes	Yes	
	Livewello	4 (239,02, 04, 08)	Yes	Yes	
	Genovations	0	NA	NA	
AHCY (adenosylhomocysteinase, important in methylation reactions)	Lab Reunis	NA	NA	NA	
	MTHFR	3 (01, 02, 19)	Yes	Yes	
	NutraHacker	0			All 3 above -/- so unimportant
	Genetic Genie				
	Livewello	3 (01, 02, 19)	Yes	Yes	
	Genovations	0	NA	NA	
SHMT1 (serine hydroxymethyltransferase 1, important for synthesis or methionine and purines)	Lab Reunis	NA	NA		
	MTHFR	2 (1420 & unnamed)	Yes	Yes	+/-
	NutraHacker	0	NA	NA	
	Genetic Genie	1 (1420)	Yes	Yes	+/-
	Livewello	1 (1420)	Yes	Yes	
	Genovations	0	NA	NA	
SHMT2 (serine hydroxymethyltransferase 2, a mitochondrial gene that codes for an active B6-dependent enzyme for glycine synthesis)	Lab Reunis	NA	NA	NA	
	MTHFR	2 unnamed			-/-
	NutraHacker	0	NA	NA	Unimportant?
	Genetic Genie	0	NA	NA	
	Livewello	0	NA	NA	
	Genovations	0	NA	NA	
NAT2 (N-acetyltransferase 2, a SNiP here decides whether you are a fast, medium or slow acetylator)	Lab Reunis	NA	NA	NA	
	MTHFR	6 (560, 803, 190, 590, 857, 341)	Yes	Yes	+/- on 2
	NutraHacker	1 (341)	Yes	Yes	+/-
	Genetic Genie	NA	NA	NA	
	Livewello	5 (unnamed)	4/6	Yes	
	Genovations	6 (64, 187, 114, 197, 286, / 268)	NA	NA	64-286 slow metabolisers. 268 fast metabolisers
SOD2 (superoxide dismutase 2, encodes for the most important mitochondrial antioxidant)	Lab Reunis	NA	NA	NA	
	MTHFR	3 (16 & 2 unnamed)	Yes	Yes	2855262 Id'd as SOD2
	NutraHacker	1 (16)	Yes	Yes	
	Genetic Genie	NA	NA	NA	
	Livewello	2 (unnamed)	some	Yes	2855262 id'd as SOD3
	Genovations	3 (93, 4 – SOD1) (16 – SOD2)	NA	NA	
DAO (D-amino-acid oxidase, important for detoxification)	Lab Reunis	NA	NA	NA	
	MTHFR	3 (unnamed)	Yes	Yes (Livewello)	
	NutraHacker	0	NA	NA	
	Genetic Genie	0	NA	NA	
	Livewello	3 (unnamed)	Yes (MTHFR)	Yes (MTHFR)	
	Genovations	0	NA	NA	

* Descriptions sourced from www.genecards.org and http://ghr.nlm.nih.gov.

(linked to megaloblastic anaemia and kidney failure), FOLR (4, folate receptors), FUT2 (3), G6PD (2, provides reducing power NADH and pentose phosphates for fatty acid and nucleic acid synthesis), GAD1 (12, pyridoxine deficiency and seizures), GAD, GAMT (converts guanidinoacetate to creatine using S adenosylmethionine as a methyl donor), GIF (gastric intrinsic factor, deficiencies in B12 > pernicious anaemia). In some cases these other alleles could be relevant to the individual's well-being. In particular, with MTHFR SNiPs it would be good to know if a GIF allele exists, because this will impact on how methylcobalamin/adenoslycobalamin is administered.

History, not just SNiPS

This report also encourages learning rather than relying on interpretation from an external source. Laboratory interpretation can be problematic because the interpreter invariably does not know the client. In inexperienced hands there is a danger of treating the SNiP only, which could be detrimental to the client's health. Practitioners should avoid this at all costs. In fact, according to Dr Ben Lynch, ND, the history is as, if not more, important than the SNiPs.

To offer balance here it is worth noting that MTHFR Support report does not consider TH (tyrosine hydroxylase), responsible for the conversion of tyrosine to dopamine, nor TPH2

(tryptophan-5-hydroxylase), which catalyses the rate-limiting step in the biosynthesis of serotonin. TH would lead to low dopamine levels, associated with Parkinson's disease (CNS Neurol Disord Drug Targets, 2012), while TPH2 has been associated with CFS and ADHD (Molecular Psychiatry, 2005).

Perhaps because DAO and GAD are part of methylation in the MTHFR report, subsequently affecting neurotransmitter balance, the MTHFR Support report– aka Sterling's app – is not unduly concerned with this omission. NR3C1 is a stress hormone receptor that mutated could create high cortisol and presumably high epinephrine. This is also associated with CFS (Genes Brain Behaviour, 2007) and bipolar disorder (Int J Neuropsychopharmacol 2013, doi: 10.1017/S1461145713000102), and has been omitted from the MTHFR report. However, MAOA genotypic variations may adversely affect the extent of NR3C1 methylation, so could this be enough reason to omit the SNiP?

Messy

I am not in favour of the NutraHacker report in its current format, because until it is laid out neatly it cannot be given to a client. I also think there is a danger of SNiP-treating in inexperienced hands. While there is comprehensive information on a limited number of SNiPs (compared to MTHFR), it is messy. The added webpage extra contains the individual's personal supplement options. You need to click on certain points, which opens up a mind map. This opens across many pages when you click on the points to open each part, so you have to scroll all over to read it. In addition, some of their information is incorrect, in particular the use of lithium orotate. This is not a widely-understood nutrient and can have risky side-effects. This supplement would be contraindicated in a case of autoimmune thyroiditis, but no such guidance is given to the end consumer in its current format. NutraHacker are working to improve the presentation and the information. I look forward to reviewing the new look. Out of them all, this one could show promise.

Genetic Genie, although compact and reporting 26 rather than the 200 from MTHFR, is presented well. Only the SNiPs relevant to the client are reported, and these are colour-coded. Gene variation, alleles, rs ID and results are clear. There is no comments box, however there is a clear commentary, which could be given to the client. The commentary is very simple, working from the basics to the individual SNiP mutations. This could be useful information for the client.

Quirky

Livewello seems to be a new addition to the mix that is quite a quirky tool. It offers all the features of the MTHFR/Sterling's app report, with one really excellent feature of its own. Instead of the comments box for practitioners to deliver their impressive homework by hand (MTHFR), you now have the option to click on the gene or the rs ID and that takes you to the appropriate section in SNpedia (www.snpedia.com), where a full explanation of the merits and risk for that gene SNiP await your perusal. In addition you have the option of comparing SNiPs with family members and/or adding your results from other tests such as organic acids, general labs, heavy metals and various health diaries to complete your health profile. Again my concern would be that in inexperienced hands there is a safety issue, in that it might encourage practitioner and clients to address the SNiPs in isolation from history and symptoms. However the comprehensive nature of this programme does stand out from the crowd.

Hats off to Yasco

All these reports seem to have originated from the work of Dr Amy Yasco (www.dramyyasko.com), which in itself is thorough and evidence-based. However we do need other knowledgeable practitioners to provide a well-rounded appraisal. The reports from Laboratoire Reunis and Genova are very limited in the number of SNiPs reported, although they are said to comply with the four "Culp conditions", which is not the case for some of the other reported SNiPs.

Both these companies also offer extensive reports on the alleles themselves, disease risk factors and have appropriate nutritional diet and lifestyle advice. To cover detoxification and methylation with Genova would mean two tests (Detoxigenomic and Neurogenomic, Estrogenomic or Cardiogenomic dependent on client requirements). The cost could be £593 or £826. This takes genomic testing far away from the pockets of the majority, so we do need alternatives that comply with the four conditions set out by Culp.

How much information, how much training?

As usual the choice is individual. If you have someone very sick, then the more information the better. If you know exactly what you require, then it may well be that less is more. Yasco states that Beadchip technology offers as low as 75% accuracy, while massarray technology offers above 99%; Hu et al report a comparison figure of 88.8-99.1% (PLoS One 2012, doi: 10.1371/journal.pone.0033968). I have been unable to source other papers in support of Dr Yasco's information, so this still leaves a question mark.

Good training is paramount to gaining confidence in nutrigenomics. However the training in the UK could be improved significantly. At the workshop I attended with Dr Culp, he was very entertaining and gave some delightful background and clinical pearls, but his references were mostly 10-15 years out of date. The Regenerus training was disorganised and poor overall. Last-minute changes to the date left a lot of practitioners out of pocket. One speaker was unable to make the new date, and the other three were uninspiring and focused purely on the tests. Test results shown were different from mine, taken only months before, and were about to change again.

On the other hand, Dr Ben Lynch's two-day training was exceptional, and delivered by a practitioner constantly using the approach. Having undertaken Ben's training, I'm not convinced that current UK training events offer an understanding commensurate with BANT's expectations of practitioners.

I am all in favour of not missing the boat when it comes to nutrigenomics. However, there are many ethical and safety issues to consider. Treating SNiPs can be detrimental without an appreciation of the full client history. The current level of training is wholly inadequate. The question needs to be raised: are registered nutritional therapists the correct people to deliver the news of health risk factors to clients? We have so much more to offer than ever before, by manipulating gene expression, but this has to be undertaken seriously, ethically and safely if we are to remain credible and professional. We need to know how to respond when clients approach us having found their own SNiPs and risk factors. Training at an appropriate postgraduate level should be paramount.

CAM's April initiative, in collaboration with BANT, in bringing over Dr Ben Lynch – a conference at which I will update this information as well – is a major step in the right direction.

*** Full references (with live links to abstracts where available) online at www.cam-mag.com/references.**
*** Dr Ben Lynch has an outstanding video course available – Methylation and Clinical Nutrigenomics – via Seeing Health: www.seekinghealth.com/methylation-conference-dr-lynch.html.**

About the author

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