Genetic Testing for Sale

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Population-based genetic research has many purposes, one of which is to develop practical applications of prevention and therapy. This obviously includes the possibility of commercial uses. Although commercialization of genetic testing is not a matter of concern in itself, there is reason to be concerned about premature transfer from research to marketing. We describe 2 examples of a clearly premature use (or misuse) of genetic testing for low-penetrant genes.

GENELEX

Genelex is a private enterprise that offers genetic testing. According to their web site (www.genelex.com), "The selected genes that make up the Genetic Nutrition Analysis Panel were chosen because they have strong links to health and can be influenced with lifestyle changes. We assess 7 genes that relate to the following physical aspects within your body: skin and hair repair—*MTHFR* gene; free radical damage—*MnSOD* gene; detoxification—*CYP1A1, GSTM1, GSTP1,* and *GSTT1* genes; and alcohol metabolism—*ALDH2*. Your DNA sample is obtained in an easy and completely painless way that can be performed in the home. Simply rub a brush swab on the inside of your cheek, complete the lifestyle questionnaire and return them for assessment. What do you get? You'll receive a personalized report describing your lifestyle results and genetic results with nutrition advice based on a detailed analysis of your current diet and lifestyle combined with an understanding of your unique genetic profile. Included with the results is a consultation with a local nutrition expert who will help you interpret the results and modify your diet accordingly."

The price for this service is US $445.

The 7 genes mentioned here will be familiar to many epidemiologists. They are well-characterized metabolism genes studied in connection with a range of diseases. The associations between allelic variants of these genes and specific diseases are typically weak (low-penetrant), inconsistent, and sometimes found only in the presence of exposure to a primary causal agent (eg, polycyclic aromatic hydrocarbons, aromatic amines, ethanol). Review articles have been cautious in drawing causal inferences from these genetic associations, pointing out methodologic problems of study design, test accuracy, linkage disequilibrium, and population admixture.[1,2]

SCIONA /BODY SHOP

Sciona is a private company offering genetic testing in the United Kingdom. The Sciona web site (www.sciona.com) promises the following: "These days there is plenty of good healthy-eating advice available—too much for most people to take in. We all know

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that we are different, so why is the advice we're given exactly the same for everyone? Wouldn't you prefer advice that's specific to you?"

More expansive claims appear in advertisements for Sciona found in the European Body Shop stores: "Find out how your body copes with the following and what you need to eat to improve your body's efficiency: Detoxifying—Is your body as efficient as it could be at removing toxins? Antioxidant Capacity—Does your body cope with free radicals as well as it should? Tissue Repair—Do you need to boost your vitamin intake to ensure effective tissue repair? Alcohol Metabolism—Can your body cope with alcohol consumption?"

The genes offered for testing are the same 7 genes as in the previous example. The current web site does not provide information on cost, although an earlier version of this web site listed genetic testing with nutritional counseling for up to US $1000.

The Sciona case has attracted strong criticism in the United Kingdom. In an article in the *Guardian* (March 12, 2002), researchers claimed that the public was being "misled by gene test hype": "A government-backed firm which sells genetic tests direct to consumers through the Body Shop chain is misleading the public by 'irresponsibly' exaggerating the strength of research about the relationship between genes, diet and health, and downplaying the potentially serious consequences of gene testing, scientists have warned the Guardian."

In response to such criticism, Sciona has changed its web site to address several potential ethical issues (http://www.sciona.com/coresite/about/ethics.htm). However, the product and marketing remain the same.

WHAT IS THE PURPOSE OF TESTING FOR "SUSCEPTIBILITY GENES"?

The marketing of genetic testing creates heightened expectations about the benefits of genetic information and understates their negative implications.[3,4] An "evidence-based approach" to genetic testing would take into account the population prevalence of the "high-risk" genotype, the penetrance (or, in epidemiologic terms, the relative risk) of the genetic trait, the amount of benefit that can be provided (through prevention or therapy) to an identified carrier of the gene variant, and the possible harm associated with testing.

In the absence of such assessment, gene testing can cause more harm than benefit; for example, by misdiagnosis of genetic status, by promoting unhealthy behaviors, or by stigmatization from the results of gene testing. We briefly list some arguments against population genetic testing for these metabolism genes (and by implication, the arguments against their general marketing for commercial purposes).

1. Carriers of a low-penetrance allele that predisposes to a disease nonetheless have only a modest absolute risk (often very small) of developing the disease. This is true even for alleles that have well-established associations with disease, for example, the apolipoprotein-E e 4 allele and Alzheimer's disease[5] or the susceptibility alleles for insulin-dependent diabetes.[6] This is all the more true for the variants of metabolism genes tested by Sciona and Genelex, which have weaker associations with specific diseases.
2. Contrary to popular opinion, genetic testing is not 100% accurate. A minimum requirement would be to require that these commercial companies have laboratory accreditation such as that offered by the Clinical Laboratory Improvement Amendment in the United States and similar institutions in Europe. Even with the best laboratory practices, current evidence suggests that the widely used Taqman assays have a sensitivity of 96% and specificity of 98%. Depending on the prevalence of the alleles under study, the inevitably imperfect sensitivity and specificity of gene testing can mean substantial errors on the population level.
3. Genetic traits can relate differently to different diseases. For example, subjects with the NAT-2 slow genotype have an increased risk for bladder cancer but a decreased risk for colon cancer. This is not likely to be an unusual situation and complicates any recommendations based on common metabolic genotypes.
4. An almost entirely unexplored issue is the psychologic and social impact of genetic testing for low-penetrant genes.
5. Perhaps most importantly, there are no specific interventions for carriers of low-penetrance polymorphisms beyond the promotion of good nutrition and avoidance of hazardous exposures that benefit all persons. Conversely, subjects with the "protective" gene variant can feel a sense of invulnerability and become resistant to changes in diet or smoking that could help protect them from disease.

ETHICAL ISSUES

It is an irony that researchers in molecular epidemiology are held to a higher standard of ethical practice than those who work for enterprises such as Genelex or Sciona. Epidemiologic research is strictly regulated in the conduct of studies that involve genotyping.[7–9] In contrast, gene testing by commercial entities is not "research," and therefore is exempt from Human Subjects Protection oversight and regulations. Although these companies make convincing promises of confidentiality, there is no apparent penalty if such promises are broken.

Ethical issues become even more complex when the boundaries between commercial ventures and national governments are blurred. The U.K. government has a financial

interest in Sciona. It would seem prudent that a company with links to government use exemplary practices, protecting the public's health through efforts that exceed merely legal requirements. Such prudence is not evident.

Some could regard the commercialization of testing for common alleles as no more worrisome than the overblown health claims that accompany nutritional supplements or herbal medicines. We disagree. Molecular genetics comprise a unique and volatile combination of high-profile science and highly personal information. The exaggerated claims of the marketplace that we describe here are corrosive to the public's trust in genetic research. Public disillusionment over claims by these companies could damage not just the commercial ventures, but research studies as well. Furthermore, if the unregulated activity of these businesses leads to even a single abuse of genetic information, this could undermine the trust between research scientists and study participants that allows us to do our work.

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