

10 DNA AND HEALTH

Tapestries of Illness

By Phyllis Starnes

Some trips we take are of the mind and not the body. Sometimes all you know about yourself, or think you know about yourself, changes or gets such additions as to make the picture different enough to feel like a change. It's amazing how the catalyst for such a moment can be something as simple as a clipping from a newspaper.

In 2002 my mother sent me a copy of a clipping from the Kingsport Times-News because it mentioned a friend from my school days. "I thought you and Billy might be interested in reading this ..." she had written in blue ink across the article right under the title "Solving a puzzle to relieve the pain." She thought our only interest would be in the fact that the article featured someone that we'd known. I don't think that she realized that she had set my feet upon a path that would carry my family and me to the other side of the world and back again.

I found the article to be of interest for a very different reason than the one my mother had thought would interest me. It was my first introduction to Brent Kennedy and to the term familial Mediterranean fever (FMF).

For as long as I can remember I have never felt good. There are days that it's a challenge to put one foot in front of the other. My daughter says that some days you operate on the principal of "might as well ..." as in, "I'm up so I might as well do what needs doing," she says. I read that article, and I heard every ache and every complaint I'd ever had in it.

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I was driven to learn more, but the more I learned the more there was to know.

I bought Brent's book, *The Melungeons: The Resurrection of a Proud People*, because I wanted to know more about how he came to be diagnosed with FMF—a genetic disorder found most often in people of non-Ashkenazi Jewish, Armenian, Arab and Turkish backgrounds. As I was reading the book, I kept thinking that his family names sounded so familiar. A look at a family tree that had been kept up away from sight revealed that Brent's ancestors were the brothers, sisters and cousins to my own ancestors. If nothing else—I had found a new cousin.

My mystery illness might finally have a name! Armed with the newspaper clipping, my family tree, and Brent's book I returned to my primary physician. A few months earlier in a state of frustration at not being able to find a reason for all my aches and pains he had at last said, "Don't come back, Phyllis; there's nothing I can do for you." On the basis that I was related to Brent and had suffered the same symptoms, my doctor gave me a referral to Dr. Christopher Morris in Kingsport, Tennessee, who had been mentioned in the article. I think he figured that this might at last put a name to my condition or at least prove that it was "all in my head."

I found out in my appointment with Dr. Morris that diagnosing familial Mediterranean fever is often a process of eliminating anything else that might explain the symptoms. There has to be the genetic connection—at that point to Brent and some few other patients that had also been diagnosed—and then all the tests to eliminate other illnesses that have similar symptoms. Once the other possible culprits are eliminated then a trial of colchicine could be prescribed. A positive reaction to the medication is a positive indicator of FMF. I have been taking colchicine for six years now. There are still days that are challenging, but the episodes of joint pain, sore throat, low grade fevers, pleurisy, and unexplained abdominal pain are less frequent and shorter in duration than before my introduction to colchicine. My husband and two of three children are also taking colchicine. It has made life better for all of us. Only someone who has suffered a nameless condition can ever truly appreciate how it feels just to have a name for what ails you. It's not enough to know the what, though; I had to know the how. How could a family from southwest Virginia be diagnosed with a condition for

which there was no connection to our known origins?

This was the start of my travels down paper trails, to county courthouses, family reunions with people I hardly knew or didn't know at all. The names keep multiplying as I go back through time tracking generations. Adams, Berry, Beverly, Bowling, Campbell, Carter, Caudill, Cole, Counts, Cox, Coxe, Fields, Freeman, Gibson, Hill, Jackson, Kiser, Lawson, Lucas, Mosely, Mullins, Osborn, Osborne, Powers, Pruitt, Rasnick, Robinson, Shephard, Short, Stallard, Stanley, Stewart, Taylor, Tipton, Turner, Williams, Williamson and others.

My family has lived by and played in and on the banks of the Clinch River and Stony Creek for generations—the same Stony Creek where the old Primitive Baptist church of the same name once stood—the same Stony Creek church that is often put forth as the place where the earliest known written reference to the word “melungins” occurred in 1813. The listing of membership from that time is a “Who’s Who” of mine and my husband’s family trees. The original church building was washed away by floods a long time ago. My husband’s family and my mother were members at the Pine Grove church that replaced it. My mother sometimes took my daughters to services there when they stayed with her during summer breaks. It was still a one-room church house with a curtain to pull for Sunday school, and an outhouse. Baptisms were still performed in the deep spot right behind it in Stony Creek—the same deep spot that served as a swimming hole on Saturdays.

Our family trees have long and deep roots; I am still following threads here and there trying to sort them out. The roots and branches are intertwined so that in some places it’s hard to tell where one tree ends and the other begins. I have reached some ends that I can no longer follow. I am sometimes like a squirrel whose weight bears down on the branch too much so that I must leap to another one for a while. My search has led me to counties outside of Scott County, Virginia such as Lee, Wise, Russell, Dickenson, Patrick, Louisa, and Cumberland, Virginia. I have crossed the border to Tennessee to Hawkins, Hancock, Grainger, Greene, Claiborne, Sullivan and Washington Counties. I’ve made trips to Letcher, Perry, and Clay counties Kentucky chasing down a name or a possible ancestor. I have found that at some point the paper trail runs thin—fires, floods, and politics can be blamed for records being lost or destroyed. In all of the trails that I can follow this way, I still

haven't found out how a Southeastern Appalachian family could possibly have a Mediterranean medical disorder.

My husband and I attended the Fourth Union hosted by the Melungeon Heritage Association (MHA) in Kingsport, Tennessee, in 2002 right after I had first visited with Dr. Morris. I had only been taking colchicine for a few weeks at that point. This was the event where the preliminary results of the first Melungeon DNA project were announced by Dr. Kevin Jones. It is unfortunate that project wasn't able to be followed to its end due to Dr. Jones' illness, but this event did have some lasting effects for my family in a personal way. I met Cousin Brent and found cousins, Beth (Caldwell Hirschman), Donald (Panther-Yates), and Nancy (Sparks Morrison) among others; although, at the time I didn't realize that they were my cousins. Their research has added to that of my own, and we have all been able to fill in pieces of the puzzles that we have been working to put together individually. Subsequent MHA events for many years have been like extended family reunions.

The first time I ever saw Donald Panther-Yates, before he'd even spoken, I told my husband, "I don't know who he is, but I want to pick his brain." Once I heard him speak at Fourth Union—his topic, "Jewish Indian: Who'd've Thunk It!"—I knew he was right. If you've ever had an epiphany—a moment when you *know* the truth when you've heard it, this was one of those moments. I had never thought about it. It can only happen if you are willing to accept the possibilities—I was willing to accept this new aspect as to who my ancestors might have been: Jewish, Muslim, Christian, Native American, Mediterranean, Middle Eastern, Romani, Northern African, as well as northern European. I went from being a white, middle class Appalachian American to multiracial. It was a huge leap, and yet I am so much richer for having made it. My family doesn't look any different from everyone I grew up with in Fort Blackmore, Virginia.

At one point in history, though, a Virginia state official apparently thought that families with my ancestors' surnames were different enough to warrant being treated differently. Did Walter Plecker cause some members of my family to "whitewash" the family lore? At what point in time did my Native American ancestors decide not to be Native American? Why did my Romani ancestors decide that they weren't Roma? When did my Mediterranean forefathers and mothers decide that

they had to be the same as their neighbors? The truth is lost irretrievably from the prospective of paper records and my family lore has long since forgotten the answers to any of these questions. I now had more clues about our origins, but how to prove it? Science provided me with another avenue to follow. Where a door closes, often a window opens.

The new and upcoming thing in genealogy for a few years now has been the use of genetic and DNA technologies. Once I accepted that the paper trail was never going to go back far enough to find my family's origins or to explain our medical condition, I decided that this new path was the only one that might possibly provide the links. Paper trails can definitely be lies; blood trails don't lie but neither can they always be taken at face value and some results only create more questions.

We chose to support Donald's new venture, DNA Consultants, and ordered the mtDNA test for myself and both the Y-DNA and mtDNA test for my husband. My husband's Y-DNA results showed an Albanian or Macedonian modal (R1b). His mtDNA results (T*) had an exact match in Iceland. My mtDNA came back U2e, which is normally considered a European haplogroup, but I have no HVS1 matches and my HVS2 region matches that of a documented Cherokee woman. Answers? Yes. Questions? Yes.

I have continued to chase down paper trails, but my thirst for knowledge has not been quenched. A new type of DNA testing has become feasible for public consumption—autosomal testing has become affordable. DNA Consultants offers a DNA ethnotyping test that matches CoDIS markers to contemporary populations. It is the same test used to match evidence to victims or suspects in crimes. It is the same test that is used to prove maternity and paternity. The numbers alone won't give you much information; the profile and map provided with the test answer many questions. They also gave me new topics to research—I've found it interesting that many of our individual matches can be connected through historical events and shared borders. I have, at this point, had a few of my maternal and paternal family members tested as well as my husband, my three daughters and one grandchild. My family's common matches show that we are, indeed, of northern European descent—with many members having matches in the United Kingdom, France, several Scandinavian countries and the Iberian Peninsula. However, this wasn't the whole story as the history books would have us believe.

We also had common matches in Morocco, Tunisia, Syria, Saudi Arabia, Turkey, Greece, and Afghanistan to name a few Middle Eastern matches. Every family member had at least two or more of these countries on their matches, and the matches occurred for at least three or more members. There are also matches in several scattered countries including northern India that would indicate a Romani or Gypsy ancestry. There were even some Australian Aboriginal matches and some Sub-Saharan African matches.

What may be the most recent additions to the family history are our numerous Native American matches—the top or second match of many family members being a Lumbee match. There are other Native American matches all over North, Central, and South America. None of these can be interpreted as a specific tribal affiliation.

I have at least proven that it's possible for me to suffer from familial Mediterranean fever. I have the ethnic backgrounds most often affected in my genetic makeup. If for no other reason, the decision to have my DNA tested was worth knowing/proving this to be the case. There is one thing that anyone thinking about taking this path should consider—it may disprove as easily as it may prove any stories of origin that your family may have. I do not think that I would have gotten as much out of it, if I hadn't been willing to accept all the possibilities.

Will I ever track down which ancestors came from where exactly? Most likely not, because I think many of the ancestors that you could say came from here or there are probably hundreds of years back. I believe that most of the mixing of various ethnicities happened before my ancestors came to the Americas. I now believe that I have ancestors that were here prior to my ancestors that I know came before or during the Revolutionary War. I am more firmly than ever an Appalachian American. And I am also Native American, northern European, Mediterranean, Middle Eastern, and Romani (Gypsy). And yet since my ancestors chose (perhaps freely, perhaps out of necessity) to become Anglo-American—I am none of these things. I sometimes feel like I am an "orphan of the world." I know that many people from the cultures and heritages that are a part of me wouldn't accept me as a part of them.

It seems to be human nature to want to label and categorize things—including people. It is most definitely human nature to want to belong and to be accepted. I think the greatest challenge in being a multiracial

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person in a time when society is supposedly more enlightened is resisting pressure to choose to acknowledge one facet of your heritage over the others in order to wear a certain label. That pressure comes from those that are uncomfortable with you defying their attempt to put you in one category or keep you out of another. It seems to me that if I reject one part of myself to satisfy anyone's desire to label me or my own longing to belong then I repeat history. I start down the same slippery slope that some ancestor slid down long ago. I hope not to repeat the decision that I consider in the present to have been a mistake in the past.

It is my hope that one day the world will be able to accept the diversity that makes up the foundations of America. It is my hope that one day the average American will recognize that our history is much deeper than what we thought it was. I think that groups like the Melungeon Heritage Association are the best way to start. If we can hold to the belief that the purpose of the MHA is to celebrate the richness of culture and the diversity of heritage that is Appalachia—if we can keep to the belief that we are "one people, all colors," then we stand the best chance of finding belonging and acceptance for how we are different. We will finally be able to be true to ourselves.

The beauty of Appalachia's people is that we are much like a tapestry, a kilim or a quilt—it takes many threads of many colors to make a whole.

September 15, 2003

Children of Parents with Alzheimer's Want to Know If They Have the Gene

Genetic screening for the apolipoprotein E gene associated with Alzheimer's disease appears to be beneficial and welcome to nonsymptomatic adult children of people with the disease, according to an article by Kerri Wachter in this month's *Adult Psychiatry*. Dr. Robert Green made the announcement at an international conference by the Alzheimer's Association.

Dr. Green said he was surprised by the results of his study, which determined that knowledge of having the gene, not having the gene and not wanting to be screened for it made no difference in levels of

depression or anxiety.

Revealing such genetic risk information to asymptomatic patients is not usually done, because the gene is only a marker for susceptibility, not for the disease itself.

Another reason for not sharing knowledge of the gene's presence is that there is no treatment at present, and it was feared that screening might increase people's anxiety.

Happily, Dr. Green's study showed that people want to know and can seemingly deal with the results of that screening.

March 31, 2006

Linkage Disequilibrium Lower in African-Americans?

Referencing *Genes and Immunity* 6 (2005) 723-727

Linkage disequilibrium across the human genome is generally lower in West Africans and African-Americans than Europeans. However, in one region of the DNA rich in immune genes, scientists have found significantly more examples of apparent positive selection in West African and African-American populations.

July 28, 2005

My Genome. So What?

According to an editorial in *Nature* with this title, recent additions to the growing database of personal genomes dictate that research be undertaken on how people are using the new genetic clues about their health.

November 6, 2008

Putting the Test to a Test

In the last blog post, we responded to the call of *Nature* in "Genetics without Borders." In this, we examine the second of three editorials in this week's issue concerning regulation of DNA testing companies: "Putting DNA to the Test."

It should be pointed out at the beginning that the wrath of the editors

descends in unequal fury on commercial enterprises. They are not as irate at ancestry companies as “personal genomics providers.” They seem to have in mind mostly concerns like 23andMe, which promises for \$399.00 to sequence your personal genome and give you “access to all health, disease, and trait reports” maintained by its staff, together with “all ancestry features and raw data download.” To the editors of *Nature*, this is akin to practicing medicine and genetic counseling on the Internet. Spit into a cup, discover your personal DNA sequences and get an email when a medical article mentions your nucleotide position.

The presumptuous and condescending attitude of the editors is evident in their first paragraph (*italics added*): “The availability of affordable, direct-to-consumer genetic tests has *mushroomed*, leaving regulation lagging behind. Dozens of companies now offer *inexpensive* (elsewhere: *cheap*) home kits that allow people to *spit* into tubes, send the samples for DNA analysis and receive a report that *allegedly* details their ancestry or their *possible* susceptibility to a *long list* of disorders that have been linked—*often tenuously*—to particular genes. But the value of these tests remains *debatable*, which is why (*bad predication in our grammar book*) the *industry* needs a strong set of quality standards and codes of conduct to protect both *its consumers* and its own *credibility*.”

Aside from poor writing (which seems to be a requirement for an advanced degree in the natural sciences today), there are numerous examples of logical fallacies in this and the rest of the article. Perhaps Ludwig Wittgenstein was right. What cannot be put into words cannot be thought. What can only be poorly expressed is poorly thought.

It is unclear whether the regulators would extend the same benevolent protection to the academic researchers who also consume genomics laboratory services. A case can be made that even *their* understanding is not always perfect and up-to-date. Elsewhere in the same issue of *Nature*, are warnings to fellow scientists who make exaggerated claims about their research. The editors also reprove wayward brethren who seek to dip more than once in the immortalizing waters of the Pierian springs, by submitting their work to multiple journals, often under different guises or false pretenses.

The world of science has so much dirty underwear of its own, it is surprising it wishes to examine that of others. Credibility seems to be in short supply everywhere.

Without dissecting what is a mess of snips to start with, let us draw attention to one scenario the would-be regulators raise. "Customers," they predict, "will frequently receive results telling them only that they face the ambiguous possibility of a somewhat elevated risk of a little-understood disorder. ... If the ambiguous, slightly elevated risk relates to a frightening condition such as breast cancer, some individuals might feel compelled to undertake drastic and perhaps needless measures, such as prophylactic mastectomy (surgical removal of a breast to avoid cancer)."

I read this horrific statement to a friend of mine over the phone, who said she had been in that exact situation. Doctors found a lump in her breast. Knowing that ancestry testing had placed her in a category of predisposition to developing breast cancer, she underwent, after due deliberation, "prophylactic mastectomy." "I was thankful I took the DNA test," she said, "because it gave me information that helped me evaluate my risks." She says she is sure that if she had not taken the step she did, she would have breast cancer today.

It is arrogant of scientists to think they must protect people from information. This is the stance of a totalitarian state that controls and censures the information consumed by the populace, or of a state religion such as that which ruled supreme during the Middle Ages. It was attempted with disastrous results in so-called "activist era" of the Federal Trade Commission during the 1960s and 1970s under Commissioner Mary Gardiner Jones. An institutional ideology of this sort assumes that consumers require protection from scientific information that they may misinterpret and that may lead to personal or social distress. For example, misplaced information like this might lead historically disadvantaged communities to increase their distrust of the scientific establishment ... as though the scientific establishment didn't do enough in that direction!

Another of the editors' arguments against releasing genetic information to the populace is that genetic information is always evolving and may not be complete. Quoadusque, we may well ask with Cicero. When will it be complete? Or complete enough? And who is to make that judgement?

Instead of mad, speculative and needless worry about consumers who are supposedly ignorant and defenseless, why don't we let reason and the

unimpeded flow of information take their course? Those two forces educated, up to a point, the scientists who are now trying to second-guess the rest of us. While it may have taught them a lot of facts, it did little apparently to sharpen their powers of philosophical reflection.

October 8, 2009

To Do or Not to Do DNA?

Mad Hatter's Tea Party at California Colleges

American education is in such a state of decline and confusion that the following new program, with all its pros and cons, seems tantamount to a mad hatter's tea party. We reproduce a description of it from *Nature* in all its carefully nuanced and agonizing detail. We suggest that rather than fretting over whether DNA testing companies might use predatory marketing on teenagers or students be pressured into making purchases and be psychologically damaged by DNA results, the school authorities worry about real threats like the fast-food poisons served up in the cafeteria franchises on their campuses. Or overpriced and watered down textbooks. Or alcohol in dorms. Or date rape. Or just about anything else.

A DNA Education (*Nature* 465: 845-46 16 June 2010)

"Taking personal genetic testing into the classroom brings ethical and legal sensitivities to the fore. Although personalized genetic testing is still very new and controversial, its increasing use in health care seems inevitable—a trend that makes it essential to give consumers and physicians a better education in the technology's strengths and weaknesses.

"That was the rationale behind an announcement made last month by the College of Letters and Science at the University of California, Berkeley. This year, instead of sending its incoming students a book for later discussion in class, the college will send them a kit to swab their DNA. If they so choose, students can send in their sample to be analysed for three common gene variants that indicate how an individual metabolizes alcohol, lactose (found in dairy products) and folic acid, a vitamin common in leafy green vegetables....

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University in Palo Alto, California, which announced a similar course designed for medical students shortly after Berkeley announced its program. Recognizing the potential for controversy from the outset, Stanford officials first appointed a task force of basic scientists, clinicians, legal professionals, genetic counselors, ethicists and students who spent a year designing precautions against coercion and conflicts of interest by the institution, and working out access to counseling.

"That said, the Berkeley and Stanford programs are both still experimental ... these two programmes are only the beginning of a long conversation that needs to happen on campuses worldwide."

June 16, 2009

Officious or Official?

Council of Europe Adopts Protocol on Genetic Testing for Health Purposes

In this report by Laurence Lwoff in the *European Journal of Human Genetics* (2009) 17, 1374–1377, first published online July 1, it is noted that the Council of Europe has weighed in on one of the most controversial areas of DNA testing, whole-genome sequencing and SNP testing to find genetic predisposition to disease for individual customers. Recent editorials in *Nature* have called for similar measures in the United States, which is home to 23andMe and other companies offering such services.

So far, no regulatory proposals have been aimed at genetic ancestry testing, only medical and health-related screening. One of the warnings often raised in the public discussion on genetic testing for health purposes, however, is that results may confuse and unnecessarily alarm consumers—a criticism that could apply equally to ancestry services. Another is that commercial research scientists and business operators may jump the gun with findings and peddle bad science, although critics admit that the state of knowledge on nearly every topic of interest to geneticists and medical researchers is in a constant state of flux. A finding about a gene for Alzheimer's will be trumpeted in the pages of a major journal one week only to be updated or withdrawn in the next.

This being the case, one wonders when discoveries will ever be fit to

be commercialized or made available to the public. Should science only serve scientists?

We have always maintained that the would-be regulators underestimate moderately educated people's ability to understand emerging science. They overestimate commercial companies' disregard for professional practices and responsible communications. Most of the measures under discussion will have the effect of denying people access to valuable information. Regulation will also hamper growth in a direct-to-the-consumer business with unimaginable promise for society at large. A home paternity test purchased at the corner drugstore may make all the difference in the life of a family. Discovery of varied ancestry through a DNA test can be an important factor in furthering a consumer's interest in other peoples and countries, in history, and ultimately in tolerance of others. DNA testing can help bring peace of mind, but it can also help bring peace in the world.

Many, if not most, of the innovative contributions to society have come from non-specialists. The scientific establishment is not oriented toward practical applications of knowledge. The Croatian engineer Nikola Tesla dropped out of college and never received any formal training. Driven entirely by his natural aptitude, he patented some of the most important inventions in the birth of commercial electricity, including alternating current (AC) electric power systems and the AC motor. He died penniless at the age of 86 in 1943. No government program or university gave him any support or assistance.

Whatever else the Council of Europe deliberated about, we hope they were not cynical or self-important enough to discount the possibility there may be many more popular scientists like Tesla in Europe's future. Science and technology are increasingly becoming a way of life for millions of people around the world who do not happen to have an advanced degree. It is a positive sign that consumers are so eager to take responsibility for their own health they will use the latest innovations from genomics to gain knowledge and control. Scientists should be glad they have such an impact. They should not squander the respect they enjoy in our eyes with pedantic discussions.

October 22, 2009

Future Shock or Future Letdown?

Does deCODE's Bankruptcy Signal False Promise of Genetic Medicine?

New York Times reporter and DNA book author Nicholas Wade raised an interesting question in his report on the bankruptcy last month of Iceland's deCODE Genetics, which attempted to make it possible for an ordinary consumer to buy the latest applicable information on the connection between their personal genes and their personal disease risk. The article was titled "A Genetics Company Fails, Its Research Too Complex."

In the November 17 edition in the Science and Technology section, Wade wrote, "The company's demise suggests that the medical promise of the human genome may take much longer to be fulfilled than its sponsors had hoped." But there may be more to the story." The discovery that major diseases do not have any simple genetic pattern of causation has dealt a serious setback to the gene-hunting field as a whole," he added.

Signs of the deflation in the field of "gene hunting" over the past 10 years since the Human Genome Project was completed and the second phase of the HGP was announced as focusing on the "conquest" of disease are:

- Discovery that genes are not found in continuous sequences or segments or even on the same chromosome.
- Realization no DNA can be considered "junk DNA" and even "non-coding" loci have at least place-holder functions and hence their values are not neutral.
- Greater respect for the role of environment in inheritance, including the nano-environments within the cell where DNA is stored and replicates.
- Jumping the gun on numerous claims concerning genome-wide association studies in scientific journals like *Nature* and *Science*, and subsequent retractions by editors and authors.
- Ever-increasing sample sizes with ever-increasing lack of robustness for the data and clarity for conclusions.
- A push for extending genetic surveys to rare and under-represented populations, with few surprises in the analysis of the

implications for medical research or consequent benefit for public health.

- Diminishing returns on research investment (ROI) on nearly every front.
- Not a single viable gene-therapy product ever introduced.
- Realization that only very rare genes are discoverable and selection usually takes care of them and extinguishes them over time; hence the bulk of medical research funds goes toward the rarest of cases and not widespread disease such as cancer or diabetes.

Harvard biology professor Richard Lewontin maintained as long ago as the 1960s, and continued to warn even on the eve of the completion of HGP I in 2000, that gene hunting was essentially a scientific fetish with little true power or efficacy. In 1992, he wrote "The Dream of the Human Genome" as a review article in response to *The Code of Codes: Scientific and Social Issues in the Human Genome Project*, edited by Daniel J. Kevles and Leroy Hood, and seven other recently published books on the subject of genetics and medicine. The essay was reprinted in Lewontin's own book *It Ain't Necessarily So* (second edition, New York Review, 2001).

I think it is time to elevate gene hunting to the danger of something beyond a harmless fetish for the members of a narrow profession or scientific sect. Its waste and failures have taken on the proportions of a national form of folly and collective denial. While huge expense and sensational efforts continue to be thrown away on the molecular biology revolution, the need to renovate our neglected infrastructure and reform political mechanisms goes unanswered. Resources that might be better allocated keep dwindling. The supposedly most-advanced society in history turns a blind eye on such relatively easy measures of public health as universal health care and uncontaminated chemical-free food and water supplies. While geneticists continue to cackle about inch-sized strides in their progress toward scaling the distant peaks of genetic medicine we are slipping into the abyss of logical disconnects.

December 6, 2009

The New Science of Epigenetics

The sequencing of the human genome capped off the 20th century's tireless search for genetic causes for all diseases. But epigenetics is the hot new science now. Dr. Anne Marie Fine, a Scottsdale physician, certainly thinks so. Dr. Fine spoke in Paris recently on Epigenetics and Beauty and next month will present a paper called "Dining at the Epigenetic Cafe" in Monte Carlo, Monaco, at the largest European physicians' anti-aging conference. In June she will present a paper titled "Epigenetics and the Autosomal DNA of Human Populations: Clinical Perspectives and Personal Genome Tests" at the University of British Columbia, Canada, with Donald Yates, principal investigator at DNA Consultants, along with participating in a 90 minute colloquium on epigenetics, autosomal DNA and ethnic identity. Clearly, epigenetics is stealing the show!

From the Fine Center for Natural Medicine News, here is how Dr. Fine describes epigenetics and its promise:

"Epi" literally means "above" so epigenetics are the influences from above that affect the DNA. Epigenetics refers to modifications to DNA and chromatin, the protein scaffolding that surrounds the DNA, that persist from one cell division to the next, despite a lack of change in the underlying DNA sequence. So, the "epigenome" refers to the interface between the environment and the genome. This is the basis behind the new science of epigenetics— how the environment affects the cellular DNA. Cells are bathed continuously in a sea of changing environmental conditions. This means the epigenome is dynamic and responsive to environmental signals especially during development, but also throughout life. It is becoming increasingly apparent that stress, environmental chemicals, and nutrient deficiencies are some of the biggest factors that promote epigenetic changes to the DNA. In addition, some of these changes in gene expression persist long after the exposure has stopped. What this means is that these changes can transcend generations.

Researchers at the University of Pittsburgh stated in the journal *Medical Hypotheses* in 2009:

It is becoming clear that a wide variety of common illnesses,

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behaviors, and other health conditions may have at least a partial epigenetic etiology, including cancer, respiratory, cardiovascular, reproductive, and autoimmune diseases, neurological disorders such as Parkinson's, Alzheimer's, and other cognitive dysfunctions, psychiatric illnesses, obesity and diabetes, infertility and sexual dysfunction. Effectors of epigenetic changes include many agents, such as heavy metals, pesticides, tobacco smoke, polycyclic aromatic hydrocarbons, hormones, radioactivity, viruses, bacteria, basic nutrients, and the social environment, including maternal care. It has even been suggested that our thoughts and emotions can induce epigenetic changes.

"Incredibly, only about 2 percent of diseases can be attributed to locked-in single gene mutations," says Dr. Fine. Most disease occurs as a complex interaction between genetic susceptibility and the environment. This means, while there are genetic predispositions, there are environmental triggers that actually start the disease, but also environmental factors that protect against developing the disease. The key is to understand which factors promote disease, and avoid them, and which protect, and seek them out. Our genetic makeup doesn't necessarily determine our biological fate. "Genes may load the gun, but environment pulls the trigger," says Dr. Fine.

James Watson once said that the double helix contains a library of detailed information about all generations of our ancestry "if only we could read it." Combining epigenetics and the advances in autosomal DNA tests, we are *beginning* to read the whole of human medical, evolutionary and ethnic history, at least in outline form.

February 14, 2012

Tommy Dionisio commented on 16-May-2012

Very well said. High time we began looking closer at the environmental factors associated with disease. The more we understand, the greater our knowledge, the more empowered we become to exercise prophylactic exclusion of many of the harmful chemicals we expose our genome to in the products we eat, apply to our skin and inhale on a daily basis.

How Good Is Direct-to-Consumer Genetic Screening?

Not Very, According to Study

Direct-to-consumer Genetic Testing Services: What are the Medical Benefits?

Thierry Frebourg

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It is clear that consumers, and many geneticists and medical professionals, underestimate the complexity of genetically determined diseases and their risk levels as measured by genomic testing. The question is whether it is ethically sound to sell consumers packaged DNA tests that could exaggerate their risk for say, heart disease, or render a false negative result.

In one study, DTC testing on average handed out very slight risk factors across the board, lower than those known to be in the general population. Another study, the first of its kind, performs an experiment comparing traditional genetic screening by counselors to "insta-testing" by Navigenics. It looks like the technology of DTC has a long way to go, while our understanding itself of genetically inherited disorders is still in a rudimentary stage of development. Rather than exploring new sites and new tests the emphasis needs to be on interpreting the studies and data we already have.

April 19, 2012

The Sins of Science

Science, it seems, has been "the new religion" for a long time. It has always had its apostates and heretics, even its unremarkable and quotidian sinners.

In an article titled "Disgrace," Charles Gross, a professor of psychology and neuroscience at Princeton University, reviews the whole matter of contemporary and historical scientific misconduct (*The Nation*, Jan. 9/16, 2012, pp. 25-32). He finds nothing new in the shocking case of Harvard's Marc Hauser, who was exposed two years ago for scientific

misconduct, in of all fields, the biological basis of morality and genetic inheritance of doing evil. Hauser apparently was guilty of the very venial sin of fudging facts. The three ways to do that, all frowned upon, are by fabrication (making data up), falsification (altering or selecting data, cherry picking) and sheer plagiarism (which all but entering freshmen understand).

In 1830, computer science pioneer Charles Babbage published a book in which he distinguished "several species of impositions that have been practised in science ... hoaxing, forging, trimming, and cooking."

Gross classifies the Piltdown man as an example of hoaxing. This fossil combining parts of an ape and human skull was discovered in 1911 and not discredited until the 1950s. Most hoaxes are intended to poke fun at the public's credulousness, but the Piltdown hoax was undertaken by well-meaning British imperialists who hoped their construction would fill an awkward gap in the record. Like God, if the missing link did not exist, we should have to invent one. Pip pip for the Royal Society!

Babbage believed that forging was uncommon. Rarely are results completely counterfeited and pulled out of thin air.

"Trimming" is probably a form of scientific misconduct that few scientists confess to their most exacting monitors such as the National Science Foundation but rather quietly cover up in bland hypocrisy. It consists of "eliminating outliers to make results look more accurate, while keeping the average the same." Who has not committed that little white sin? Let him who is without self-assurance cast the first chad.

"Cooking," on the other hand, the purposive selection and distortion of data, might be a real concern for all of us.

Gross goes on to inspect the career of Harvard's "war crimes professor" Richard Herrnstein, who became a co-author after his death of the book *The Bell Curve* about racial differences in intelligence. It is not a very pretty kettle of fish.

Charles Darwin essentially stole the idea of natural selection from Alfred Russel Wallace, the father of biogeography, did he not, and if he didn't, certainly failed to credit some of his predecessors in his rush to fame and self-glorification.

In genetics, we are reminded that the saintly Gregor Mendel probably falsified the suspiciously exact 1:3 ratio he "observed" in comparing pure dominant with hybrid peas (p. 26).

Alarmingly, we learn that "the modal scientific miscreant is a bright and ambitious young man at an elite institution," just the sort of role model worshiped by the popular press.

Maybe our society should be examining a few of science's feet of clay rather than pompously setting more laurels on the heads of its exalted heroes.

April 21, 2012

Undying Memories

The next time you experience déjà vu think about this. It might be more than a trick of the brain. Scientists have recently confirmed that genes can pass down the memories of our ancestors to us.

It sounds like something out of "Lord of the Rings," but medical researchers at the University in Cambridge have determined with experiments that DNA might pass down some genetic markers from generations ago (David Cornish, *Wired Science*, "Study: Genes Could Retain 'Memory' When Passed to Offspring").

This means that if you have a phobia about boarding an airplane it might be because your great-grandfather had a fear of flying. It also might mean that if you have a certain condition or disease, it could be because someone in your family history had that disease. We have had the latter idea of genetic inheritance being linked to disease for some time. That is why, with women, doctors might ask who in their family had breast cancer. Doctors even know that it is a greater risk if it is on the mother's side of the family.

Until now, scientists did not understand this process of passing epigenetic markers on, piggy-back style, through generations. Epigenetics was the mystery person in the room no one wanted to question or talk about, whether out of politeness or ignorance.

First, what do epigenetic markers do? They are like the managers in a factory telling the cells to either "use or ignore a particular gene." For this reason, although it should not be ignored, it is not the entire story if you discover with genetic testing that you, or someone you know, have a genetically high risk for a certain disease like breast cancer. It is possible to get lucky and have an epigenetic marker that is telling a gene to just sleep a few decades and not turn into cancer (Carl Zimmer, "Hope,

Hype, and Genetic Breakthroughs”).

But how are epigenetic markers passed down through generations? Most of them are erased from one generation to the next (Cornish). However, James Gallagher, in his article, “‘Memories Pass Between Generations,’” says that traumatic events can alter DNA and affect both the “brains and behavior of subsequent generations.” Reputable publications now suggest that genetic memory is not science fiction. Genetic memory is stored in your DNA. Both genetic memory and epigenetics are now considered mainstream science.

December 6, 2013

Carried Away on the Red Balloon

We are now in the DNA age. What can DNA testing reveal today, and what will it reveal tomorrow? Genetics testing is an exciting field as it has just now become accessible and affordable, and the science is advancing at an unprecedented level. How can anyone not be in awe of the cutting-edge advancements in this field? After all, DNA testing is fast becoming a more important tool for understanding one’s health conditions.

However, it is as important to be cognizant of possible limitations in this field as it is to understand what it can tell us. Genetic testing results can tell us a great deal. And we should be aware of this important resource to acquire what knowledge we can about ourselves, but we need some perspective. Otherwise, our outlook is one more akin to pure blind and deterministic faith than a scientific one. We should not be like the boy in the movie, *Red Balloon*, where we get carried away into the clouds because we think DNA testing can do anything we desire. We need to come down to Earth once more and analyze what it can and cannot do. To go too far down the path of thinking DNA testing for medical purposes provides all answers can be as much of a problem as shunning genetic testing science altogether out of unfounded fears. Genetic testing is an innovative tool. But it is still a scientific tool—not a religion.

And if genetic testing is a tool, aren’t there other tools in the toolbox? Many have pondered about the role that epigenetics and the environment play on the genetic level. Surely it is not a life sentence to get a certain

gene for cancer, and there are other factors like this to consider, at least in some cases. The formula then may not always be so simplistic: If one has X gene, one contracts Y disease in a pure deterministic fashion. Instead, perhaps we should view genetic markers as a pattern of guideposts warning us of greater health risks.

This is important and is not to make light of what genetic testing can do, because we could all use such warnings. In other words, even if we are unable to establish individualized medicine based on some futuristic, genetic testing system on the level that many hope for in the foreseeable future, that is no reason not to embrace what genetic testing can do for us today. And it has already saved lives and solved mystery diseases according to Marilyn Marchione's *Time* article, "Gene Scans Solve Mystery Diseases in Kids, Adults." That is plenty enough for me for now.

October 2, 2013

DNA Vaccines

What do you first think of when you think of DNA? DNA tests for ancestry, paternity, and forensics come to my mind first. Drugs and vaccines were not on my list, but they should have been. In the future, DNA will help advance drug delivery. We are living just at the dawn of the Genomics Age.

It sounds like a scene from the science-fiction show, *Continuum*, but it isn't. Nanoscale-sized DNA "cages" have been shown in recent clinical trials to be effective for a more optimal delivery of drugs. These miniscule DNA cubes are made from actual strands of DNA. The DNA cube carries cargo like a UPS box carries the phone you just bought, and it is carried to your door. Just like any package, it is shipped to its source. But like a Trojan horse, opening it means it will attack diseased cells by dispensing medicine. How does it open? The cancer cells, or other diseased source, trigger the release of the DNA cargo full of medicine. ("DNA 'Cages' May Aid Drug Delivery" *Science Daily*). Like the soldiers surrounding the Trojan horse, it seems, they have to see what is inside, and it is their undoing.

Why use DNA to deliver drugs? According to Thomas Edwardson, a McGill doctoral student, "DNA structures can be built with great

precision, they are biodegradable, and their size, shape, and properties can be easily tuned" ("DNA Cages"). They are, after all, building blocks, and it seems that we can use them to build in other ways that we never thought possible.

In fact, the future is now. Though they are not yet on the market, vaccines that are currently being developed use DNA ("Biologicals" *World Health Organization*). What could the future look like? It could be that in the near future you will get a genetic test that shows you have cancer, and then you get a DNA-delivered drug or vaccine to help cure it.

September 3, 2013

Born to be Vulnerable

Little doubt exists that genetic testing and sequencing of infants is an extremely innovative and valuable tool. The amount of knowledge that we can garner from this cutting-edge technology is far beyond what we have been able to do up to this point with a medical diagnosis. It reminds sci-fi fans of the scans on *Star Trek, The Next Generation*. Truly we are living in the future. But are we ready for it?

The NIH, National Institutes of Health, quotes Alan E. Guttmacher, M.D., director of NICHD, as saying, "Genomic sequencing has [the] potential to diagnose a vast array of disorders and conditions at the very start of life, but the ability to decipher an individual's genetic code rapidly also brings with it a host of clinical and ethical issues, which is why it is important that ... the trio of technical, clinical, and ethical aspects of genomics research ... (is part of the research for treating newborns)." Now, we just have to decide how to use this tool.

If DNA testing is used to diagnose a baby with a disease or disorder at the start of life, and the infant can be better treated and evaluated from the start of life that would be a great advantage for all concerned. We could save lives. We could catch rare genetic conditions earlier. That is the desire of those in the genetic testing field, and the hope many have discussed is that this will become common for these reasons.

However, what if like *Gattaca*, a child is found with genetic testing to have a high probability of having a heart problem or other disorder or disease later in life? Should the parents be told? Should they later tell the child? Would they treat a child differently like the parents in *Gattaca*? It

seems that many parents do tend to overreact if their child's DNA testing results show high probabilities of genetic disorders or diseases. Rob Stein in his *NPR* article, "Genome Sequencing For Babies Brings Knowledge and Conflicts," quotes bioethicist Mark Rothstein of the University of Louisville as saying these test results can sometimes lead to the so-called "vulnerable child syndrome" where a child is not allowed to have a "normal childhood" including "... riding bikes and climbing trees." Perhaps, some children would not even be wanted.

However, is this a problem with the science of genetic testing? There have always been overprotective parents. Sadly, there have always been unwanted children. It seems that what is needed is more education about genomic sequencing and possibly guidelines for all involved in the process, including the parents.

October 18, 2013

Lazy Genes

Lifestyle choices play a part, but DNA tests now show it isn't just how much fast food you eat that causes obesity. Some claim they cannot lose weight because of their genes. And many stigmatize people who are larger than average, like the Republican hopeful for the U.S. 2016 election, Chris Christie, because they assume it is easy to control weight. However, we are all unique. Now science and genetic testing is backing them up and coming to the rescue. Genetic testing shows that we have unique genetic variations, and genetics plays a larger role than many formerly thought when it comes to how much we weigh (Jacque Wilson, *CNN*, "5 Cool Things DNA Testing Can Do").

How do our genes differ? They differ in many ways, so this is just one more reason that it might be good to get to know your genes and your genetic profile with genetic testing. Scientists have determined with genetic testing that some people's genetic profile may predispose them and their children more to obesity (Wilson).

Also, genes regulate about 80 percent of our body fat (Alexander Sifferlin, *Time*, "What Mice Can Tell Us about Obesity and Genetics"). Why should that concern us? Genetic testing on mice shows that some of our genes are better at the job than others. In other words, some genes are better at turning calories into energy than others. Some sit down on the

job.

How can we use this information to lose weight? It might be all the rage in the future, but there is no diet plan according to your genetic profile. "While there is a genetic component to obesity, our understanding of it is limited," says CNN diet and fitness expert Dr. Melina Jampolis (Wilson).

What can I take from these findings then? Certainly, one should just not use it as one more excuse to eat whatever one wants and sit on the couch instead of exercising. Exercise, like it or not, seems to be the more important factor. "In the case of the mice, it looks like the metabolism and activity is way more important than the amount of food consumed," says Jake Luis, a part of the team doing genetic testing on the mice, and a professor of medicine and human genetics and of microbiology (Sifferlin).

It looks as if we will have to wait for a specially selected diet based on our DNA testing results, but we might not like it anyway. For now, it looks as if we will have to keep putting on our running shoes to make up for our lazy genes.

April 25, 2013

Reversing Aging

What if you could reset your DNA biological age and become ever younger like Benjamin Button in the recent film with Brad Pitt? Sound too much like science fiction? Actually, scientists have just discovered the DNA biological body clock. Now, they are set to work on how to reset it to reverse aging. Of course, we are not talking about actually reversing one's actual age but using genetic testing and genomic science to reverse the age of one's cells and organs.

Is this possible? Not now, but scientists think this discovery brings them a step closer to finding this DNA Fountain of Youth. Why? First of all, they have revealed through genetic testing that not all of our organs age at the same rate. Tissue within and surrounding diseased organs may be decades older than healthy tissue found in the same person. (Ian Sample, *The Guardian*, "Scientists Discover DNA Body Clock")

Now, they just have to figure out how to slow it down. Actually, they are on the way to doing that using genetic testing and stem-cell research.

Steve Horvath, professor of genetics and biostatistics at the University of California in Los Angeles, in the journal, *Genome Biology*, said they managed to reset cells back to zero by “converting adult cells into stem cells, which can grow into any tissue in the body” (Sample). Ever said you wanted a new body? We might be just around the corner of doing just that and living longer lives.

Perhaps, not far in the future, we will go to the doctor to have genetic testing done to see which old or diseased parts of our body we need to reset. Puts a whole new meaning on the phrase “recreating your life.”

October 21, 2013

Genes Are Not Contagious, Though Genetic Testing May Be

With any new science, there must be guidelines. With the advent of the first automobiles, there were no speeding signs until we discovered that driving fast is equally fun and dangerous. There are now emerging new and more sensible guidelines for genetic testing for children and newborns. The panel composed of the American Academy of Pediatrics and the American College of Medical Genetics and Genomics recommends genetic testing for childhood diseases for children and newborns. Diseases that wait to strike in adulthood—like Alzheimer’s—are only to be tested depending on the parents’ wishes and what is in the best interest of the child, according to Denise Mann in her *US News & World Report* article, “New Guidelines Issued for Genetic Screening.”

There are exceptions. For instance, it might be reasonable to do genetic testing if there is a family history of a rare, genetic disease, even an “adult-onset” one, Mann quotes Dr. Joyce Fox, a medical genetics doctor at North Shore Hospital in Manhasset, N.Y. Mann also quotes a Dr. Helaine Ross, pediatrician at the University of Chicago as saying, “The focus should be on the education of families, counseling them and helping them make decisions that focus on the child’s best interest.”

What is not in the child’s best interest when it comes to genetic testing? Genetic testing done out of placating the adult’s morbid curiosity is not in the interest of the child. However, the panel did leave it up to the parents to do further genetic testing, and “what is in the best interest of the child” could be interpreted differently. It is conceivable that some parents could, as a consequence of genetic screening, treat a child like

DONALD N. YATES and TERESA A. YATES

Vincent was treated in *Gattaca* by being overly protective. However, there have been plenty of overprotective parents without genetic testing. Still, this could be problematic for some children and families.

My best friend died of leukemia when I was a child and though my mother was brilliant, she somehow became convinced I could get it as well and demanded my pediatrician do genetic testing to look at my white blood-cell count. It was normal. I am not sure what she would have done with this tool. Nevertheless, it is an incalculable scientific breakthrough to have such an advanced level of genetic testing. We now have genetic tests for more diseases and can provide a better treatment plan and diagnosis for many children and even save lives. We didn't stop making cars because some people speed.

October 28, 2013