



Living with my personal genome

"Many, many more individuals will have to make their personal genomes publicly available before we begin to get a real feeling of where we want to go."

I have benefited a lot from being the first human to have his or her personal genome made publicly available on the web. So far, knowledge of my personal genetic risks has not cost me an hour of sleep. I doubt, however, whether I would feel so positively if this knowledge had been given to me at a much earlier stage of my life. If I were now much younger, I would not be welcoming the fact that I am a bearer of mutant alleles in several of my DNA repair genes, including the now too well known *BRCA1* (breast cancer) gene. Knowing of them at the age of 30 might well portend a later life with cancer. However, at 81 years of age, I suspect that any cancer-causing mutations that my mutant DNA repair genes may have generated are likely to have been neutralized by my possibly possessing a larger than normal number of tumor suppressing genes.

Initially, I felt that I had to tell my nieces that I had a nonsynonymous base pair change in my *BRCA1* gene. Earlier, my now deceased sister was a victim of breast cancer, raising the possibility that she and her daughters might have shared (or now share) with me the bad *BRCA1* allele that bedevils too many Jewish and French-Canadian women. However, before possibly needlessly worrying Holly and Lynn, I called Mary-Claire King in Seattle (University of Washington School of Medicine, WA, USA) to look over my *BRCA1* sequence. To my relief, she said I had a nondisease-causing Irish base pair change.

Whether isolated human populations bearing DNA repair mutations, like *BRCA1* and *BRCA2*, have inherent advantages over groups in which DNA sequences are more stable remains to be seen. The births of small numbers of exceptionally talented individuals may more than compensate for larger numbers of less functional persons.

Less speculative has been the gain to my life resulting from my genome reaffirming my long held suspicion that I do not handle milk well. Unlike Charles Darwin, who was probably

homozygous for lactose intolerance, I have one good lactase gene, so the occasional dish of ice-cream only causes me minor inconveniences. More important is the realization brought to me by a comparison of my genome with that of Craig Venter (J Craig Venter Institute, MA, USA) – that I am homozygous for the '10' variant of the cytochrome P450 drug metabolizing gene, *CYP2P6*. As a result, I metabolize β -blockers much more slowly than most other Caucasians, like Craig, who largely carry the more efficient metabolizing 1A/1A genotype. Before I had this knowledge, my use of β -blockers to control my blood pressure caused me to constantly fall asleep at inappropriate moments. Instead of a daily pill, I now take one every week.

Whether Craig Venter will later regret that he and the whole world knows that he possesses one copy of the Alzheimer's predisposing apolipoprotein E4 allele remains to be seen. Being 20 years older, I instinctively saw that my *APOE* gene sequence was not revealed to me or later put on the web. I continue to live as if I will not be victimized in my 90s, as was my Irish grandmother, with this most pernicious brain-destroying affliction.

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Jim Watson

Chancellor Emeritus,
Cold Spring Harbor
Laboratory, Cold Spring
Harbor, NY 11724, USA
Tel.: +1 516 367 8455
Fax: +1 516 367 8480