

## A Genome Commons

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Revelation of the complete DNA sequences of pioneering geneticists James Watson and J. Craig Venter recently elicited headlines, but most press reports offered little meaningful interpretation of those sequences. The most significant observation was that Venter has a mutation predisposing him to cardiac disease, although his family history was enough to let him know about this general risk.

If the genome is so revealing, why was so little revealed?

It is telling that Venter learned about the cardiac disease gene in a newspaper report. Put simply, even we in the scientific community can't easily come to grips with what we know. The effects of gene variations are scattered in hundreds of databases and amongst millions of manuscripts and patent applications. And while some papers discuss the precise effects of a single nucleotide change, many analyses typically offer simple rules of thumb rather than specific detail and guidance.

Visionary geneticists have long contemplated building a resource to integrate much of this information, but academic squabbles caused the most comprehensive effort — involving hundreds of scientists backed with millions of dollars — to founder. Perhaps they were premature? Until recently, it was rarely productive to look beyond a single gene known to be of research or clinical interest. Today, with the prospect of inexpensive personal genome sequences, there is profound impetus for integrating our knowledge.

I propose establishment of a Genome Commons, a public knowledgebase of human genetic variation and its effect, culled from databases and the scientific literature. Building on master curation of hundreds of small databases today, quality controls in the Genome Commons would be provided by experts overseeing entries in their domain of expertise. Entries would be systematically compiled by anyone with an Internet connection, access to academic journals, and appropriate training. Ultimately, such a repository of our common human inheritance would be a vast resource for research, medicine, and understanding ourselves.

Private enterprise would play a vital role by contributing discoveries to the Genome Commons and making its contents accessible to clinicians and the public. As a central clearinghouse of intellectual property, the Genome Commons would reduce transactions costs, making more assays affordably available to patients and offering new revenue models for promulgating genetic discoveries.

Any individual genome will typically have millions of differences from any reference genome; most are of little consequence, but some single mutations can be fatal. We need a navigation tool to relate each individual's variations to the knowledge compiled in the Genome Commons. A technical challenge is that our genomes don't come indexed for such analysis and that our knowledge is so multi-layered. Perhaps even more daunting is sifting through the millions of variations and ranking them so that we are not deluged with genomic marginalia. The Genome Commons navigator would present a status report focusing on genetic differences of greatest medical or personal importance.

Even as we celebrate what we will learn from our genomes about ourselves, we should maintain realistic expectations. Given that most medication prescriptions don't even take our weight into account, it is unclear how many pharmaceuticals will depend upon minutiae of our genomic complement. Indeed, it remains to be seen whether we will typically learn anything more important from our genomes than that we should use sunscreen, eat better, and exercise more.

Yet, a Genome Commons could offer a breakthrough for translating knowledge into good health. For example, after learning of a genetic mutation that renders him particularly susceptible to cardiac disease, Craig Venter assumed a new level of personal responsibility by altering his diet and taking a cholesterol-lowering statin.

In a world of limited time, resources, and personal restraint, a Genome Commons would enable all of us to make productive use of the wealth of information available, helping us to similarly prioritize healthful activities and therapies to give us the most productive and enjoyable lifespans.