nature genetics

Supersequencing the supercontrols

The $10m Archon Genomics X PRIZE presented by MEDCO will reward rapid and accurate sequencing of the genomic DNA of 100 centenarians. With this choice, the technological competition will provide highly scrutinized and publicly available reference sequences that will let us focus on the genes behind healthy aging.

The start date and rules of competition have been announced for this long-awaited prize contest (p 1055) together with the contest validation protocol developed by community consultation and expert review (see Editorial, *Nat. Genet.* **43**, 173, 2011). As the prize contest might well have been carried out using established cell lines, it is gratifying that the case for new scientific and medical discovery has been built into the revised plan for the competition. It is particularly pleasing to us that the consultation process that we helped enable has resulted in the choice of well-phenotyped men and women who have led exceptionally long, healthy lives to participate in donating their genomic information to this contest that challenges our human ingenuity.

There are several established ways to incentivize research with funding, tools and public goods. Resource generation projects such as the Human Genome Project and the International HapMap Project have released enormous research potential and have generated unprecedented insights, methodologies and articles. Commercial investment turned sequencing and genotyping experiments into the successful machines of today's genomics research. Lastly, contests such as the Grand Challenges and X PRIZES aim to make the impossible possible by tapping into our competitive spirit, providing an incentive while leaving competitors free to find a route to the goal. However, much biomedical funding is tied to earmarks and donations from groups with an interest in researchers tackling a particular disease, for example where no therapy exists. Many groups now study collections of sick individuals with the aim of understanding the genetic mechanisms of each disease one at a time.

A contrary argument says that protective gene variants often provide better insights than disease-causing ones into mechanisms at which to target future therapies. This means that it is worth studying the genomes of very healthy, very old people who may be depleted for common risk variants or even enriched in rare protective variants. Such individuals who have evaded all of the common diseases associated with aging are effectively supercontrols whose genomes deserve to be scrutinized in contrast to the genotypes of the many disease cohorts currently under investigation.

Other intended consequences of the contest include the development of tools for the better display and visualization of the assembled and aligned genomes—because the greater the number and diversity of readers thinking about their content, the more chance we have of sparking medically useful insights. We think that one way the unique resource generated by this contest could add momentum to human genomics research and translation is if we could collect ideas for the potential uses of the centenarian sequences from young researchers working in genomics internationally together in dialogue with some of the experts and pioneers of genomics. As the technology nears the state where the prize objectives may be realistically met, we need to be ready to turn the best-scrutinized sequences in the world into usable information. ■