Industry Watch

Biobanks: Will They Help Promote the Genomics Revolution?

Ethical concerns notwithstanding, gene databanks are beginning to spur scientific debate about their utility in deciphering disease and furthering the cause of personalized medicine.

Stan N. Finkelstein, Anthony J. Sinskey and Scott M. Cooper

A recent Google™ search on the word "biobank" yielded close to 40,000 hits. It's hard to say when the word — which combines "biology" and "databank" — first was used, but there's little doubt that it is fast becoming a staple in the vocabulary of life science researchers.

What is a biobank? Essentially, it's any collection of biological samples and associated clinical data. There are biobanks for diagnostic purposes, such as pathology; for therapeutic treatment, similar to blood banks (which means that biobanks have been around for quite a while, even if that's not what they've been called traditionally) and — increasingly — for pure research into specific populations or specific diseases. It's this third type of biobank that is on the lips of the genomics world. And that's where we see the link to a topic about which we've written many times: personalized medicine.

Of course, you don't need to take our word about the link. Researchers everywhere are spelling out the connection. According to *Science* magazine, "Hoping to jump-start an era of personalized medicine for black Americans, researchers at Howard University in Washington, DC, USA, want to build the first large DNA and health database on people of African descent. The project…aims to collect samples from 25,000 volunteers over five years and use the data to probe how genetics and lifestyle factors contribute to common diseases" (1). It will be known as the Genomic Research in the African Diaspora (GRAD) biobank.

On the other side of the globe, the BioBank Japan Project began in fiscal 2003 with the support of the nation's Ministry of Education, Culture, Sports, Science and Technology (Tokyo, Japan). It aims to provide researchers with a means to clarify the causes of disease and side effects on a wider scale than ever before, focusing on different genetic codes and with the ultimate goal of developing new drugs and diagnostics.

Biobanks offer an approach to overcoming something we wrote about two years ago in this column: the "tyranny of data" faced by researchers who have made such tremendous genomics-related advances in drug discovery but who, for completely legitimate reasons, are finding it to be a daunting challenge to figure out everything that's necessary for drug development. A biobank can supply the scientific community with biological samples and associated clinical data that can be used specifically to research a disease's genetic basis. From that, biomarkers can be identified for developing diagnostic tools to predict and monitor the disease optimally. All of this gets us closer and closer to the ultimate day of personalized medicine, where an individual patient's health needs can be addressed with medicines that are right not for the patient's broader "class" but specifically for her or him.

It all sounds great. But not everyone is convinced. Consider this headline from the Institute of Science in Society (ISIS, London, England, United Kingdom): "Human DNA 'BioBank' Worthless" (2). That's a specific reference to the UK Biobank (Manchester, England, United Kingdom), one of the larger and more public biobank projects underway. But the sentiment could apply to any biobank. They are generating a lot of controversy — about ethical and scientific considerations.

Ethical Controversy Abounds

A survey article in *Science* (published by the American Association for the Advancement of Science, Washington, DC, USA) two years ago catalogs nearly every controversial aspect of biobanks (3). It's worth reviewing these aspects.

In the realm of ethics, concerns revolve primarily around how donors of biological material or data will be assured that their privacy and interests will be protected. This is especially prob-

Stan N. Finkelstein and **Anthony J. Sinskey** are co-directors of the Program on the Pharmaceutical Industry (POPI) in Cambridge, Massachusetts, USA and members of the Pharmaceutical Discovery editorial advisory board. Finkelstein is a senior research scientist at MIT Sloan School of Management in Cambridge. Sinskey is a professor of microbiology at MIT in Cambridge. **Scott M. Cooper**, an affiliate and frequent collaborator of POPI researchers, is a visiting scholar in the MIT Department of Biology.



lematic given the increasing number of private companies that are amassing large and entirely private biobanks of DNA and tissue samples. A perusal of Web sites reveals that in the "world" of biobanks, there are pharmaceutical firms amassing their own data, as well as companies whose primary business appears to be amassing data to provide to researchers, whether in commercial firms or in academia.

The *Science* article notes that, "companies say they provide secure data systems for ensuring patient confidentiality, and voluntarily follow federal rules for protecting human subjects. But…these procedures often are shrouded in secrecy. Some private biobanks, for example, consider key documents, such as consent forms, to be proprietary. And if companies go bankrupt, critics contend, tissue and DNA samples might be sold off to practically anybody" (3). That's exactly what happened in Japan in 2001, when a bankruptcy court auctioned off a human cell collection that had been used by a scientific society as collateral for a loan (3).

Serious contention over biobank privacy has occupied Icelanders for years now, ever since an company called deCODE Genetics (Reykjavik, Iceland) announced that it was contracting with the Icelandic government to put the health records of the entire 270,000 person population into a single database that would be linked with detailed genealogy and genetic data collected from volunteers. deCODE's contract allows it to provide drug companies with access to the data for a fee and to academic researchers pursuing "noncommercial" projects at no charge. The data is being encrypted, but the main controversy has been over the issue of "presumed consent" — that is, government health records on every citizen are included in the database unless individuals specifically opt out (sort of like the "Do Not Call" list for telemarketers here in the United States).

In Iceland and elsewhere, safeguards have been or are being created to ensure privacy, but some bioethicists wonder how much really can be done and whether privacy really can be verified. But privacy isn't the only problem. Consent looms large as an ethical issue, as the "presumed consent" approach in Iceland would indicate. For instance, when patients agree to have their data studied, should they be able to give consent only for specific diseases? As the ISIS report states, "proper informed consent must be obtained, and…it must be made clear to the participants as to what they are consenting to. But what if the collection is to be used for a different purpose in the future, to study other diseases, or intelligence as was suggested for other behavior? Would participants be required to give carte blanche consent" (2)?

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Another ethical issue is genetic discrimination. GeneWatch UK (Buxton, Derbyshire, United Kingdom), which has been organizing opposition to the UK BioBank, notes that Britain has no laws banning genetic discrimination as a justification for refusing insurance coverage or employment. "Public trust in doctors could be severely damaged if patients are harmed instead of helped by this research," the group's deputy director, Helen Wallace, told *The Scientist* (Philadelphia, Pennsylvania, USA) (4).

These are some of the ethical concerns most biobank projects face. Whether they can be allayed is a question we'll leave to the experts. It is the scientific controversy to which we'd like to turn.

Does the Science Make Sense?

The ISIS report makes a claim that really goes to the heart of the scientific controversy surrounding biobanks. "The quest for 'personalized' medicine based on individual genetic makeup," the authors write, "is simply scientific nonsense" (4).

That's the starkest among many statements from scientists and others suggesting that the goal of personalized medicine is not simply elusive, but downright unattainable. We disagree — but let's look at what others are saying.

The scientific argument for biobanks boils down to how genomics data can be made useful. The idea of a biobank is to put the data into context. As we've written in these pages, one of the key challenges for translating genomics information into something useful involves understanding a disease by examining its pathway and its phenotypical expression. This is crucial if good choices are to be made about which targets are involved in the establishment of disease.

Helen Wallace from GeneWatch concedes that a biobank in a place such as Iceland, which has an "isolated" gene pool, offers tremendous potential for research. But she questions whether similar benefits can come in Britain or any multiracial, multicultural society where genetic information is likely to be more complex. Referring to UK BioBank, Wallace says, "There will be medical advances, but they will be mainly in single-gene diseases, or inherited diseases…Once you start moving on to multi-factorial conditions like heart disease and cancer, you might gain some understanding of the mechanisms of the diseases but it's questionable whether studies on these half a million people will tell us any more than we already know" (4).

This perspective is shared by Sir Alec Jeffreys, the scientist who invented DNA fingerprinting in 1984. "My concern with the project is with basic scientific doability. Whether a study constructed in that way will be effective at teasing out really quite subtle genetic factors influencing disease, whether that is more cost-effective to use focused studies on diabetes, or specific cancers, which already has been done" (5).

Proponents have answers, as you might have expected. At BIO, a biotechnology conference held this past June in San Francisco (California, USA), Francis Collins reiterated what he had written in *Nature* (London, England, United Kingdom) just a week earlier — that the United States should establish its own biobank. He argued for creating a longitudinal database, publicly accessible, with the biological material of at least a half a million people.

Collins, the director of the National Human Genome Research Institute (Bethesda, Maryland, USA), wrote, "In the United States, a gene-environment cohort study could be assembled by building on, at least in part, already existing large studies such as the Women's Health Initiative, the Framingham Study, the Harvard stud-

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A Sampling of the World's Biobanks, Existing or Proposed

The following is a very small sampling of some of the biobanks currently proposed or operational, to show readers that these are becoming a part of the public, private and academic sectors.

deCODE Genetics
Private-sector company banking genetic samples of 100,000 Icelandic volunteers linked to Icelandic Health Sector Database and genealogical records (www.decode.com).

Estonian Genome Project
Government effort to establish a national genetic/medical database of 1 million volunteers (www.geenivaramu.ee).

Genomic Research in the African Diaspora
Howard University project to collect DNA and health information from 25,000 Americans of African descent (www.genomecenter.howard.edu).

Karolinska Institute (Stockholm, Sweden)
Swedish academic bank collecting human biological material for molecular and genetic research (http://www.ki.se/corefacility/biobank/biobank.htm).

UK Biobank
Government plan to collect genetic samples from 500,000 volunteers between the ages of 45 and 69 (www.ukbiobank.ac.uk).

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ies of health professionals and some of the many large cancer cohorts. The obvious advantages are that many years of follow-up already have taken place in these cohorts and, for many of them, DNA already has been collected. But serious consideration must be given to whether the disease-specific focus of many of these studies has limited the phenotyping and exposure measures, whether the minority representation is adequate, whether the consent obtained is sufficient for broad access to data and biological materials and whether the study design is appropriate for the ambitious goals of a national gene-environment study. If those limitations turn out to be significant, an entirely new cohort project may need to be contemplated. Although the challenges in undertaking such a prospective population study in the United States would be considerable, a serious evaluation of its merits now is in order."

His scientific argument boils down to this: "If the conclusion is that this resource is needed, then we must collectively seek ways to organize and implement it quickly and efficiently — or face the real possibility that a decade from now the promise of genetic and environmental research for reducing disease burden on a population basis will remain out of reach" (6).

For its part, the UK Biobank argues that it will be "the world's biggest resource for the study of the role of nature and nurture in health and disease," and that without the biobank the opportunity simply won't be there for "researchers to carry out case-control studies in which environmental exposures, lifestyles and genetics can be compared in those with a disease or condition (cases) and those without (controls)." Further, "Our scientific understanding cannot be considered complete until we know how genes and environment impact on these complex pathways, and this understanding could produce important clues to possible new therapeutic interventions" (7).

Awaiting an Answer

Until the research is underway, the jury will be — and should be — out on the science issues. yet, the ethical questions are substantial and real. It will take a lot of work — undertaken with complete transparency — to resolve the concerns about privacy and consent.

We don't know the answer to any of these questions, but we're going to keep looking for them — and we hope to report what we find in a future column. In the meantime, we do know that the general issue of biobanks is attracting increasing attention from practitioners and thought leaders, who are meeting both informally and formally to discuss how best to move forward.

Those of us who advocate personalized medicine will be watching closely. There's a lot at stake, just as Francis Collins wrote. We want to realize the promise of reducing disease held out by genomics, not let it slip from our grasp.

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