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Genomics company formed from Framingham heart study

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In late June, Boston University (BU; Boston, MA) announced that it had formed Framingham Genomic Medicine (FGM) to capitalize on data from the Framingham Heart Study, a project credited with fundamental discoveries such as linking smoking and high cholesterol to heart disease. Those involved with FGM say the high quality of the data will be extremely useful in connecting gene markers with clinical records in the search for new drug treatments, but others say that the data, like those from most gene linkage studies, have their limitations.

The aim of FGM, according to chief scientific officer Fred Ledley, is to develop bioinformatics tools for use in the search for genes related to disease. FGM, which was set up with $21 million in venture capital, will also conduct linkage studies similar to those being done by Gemini Genomics (Cambridge, UK) and deCODE Genetics (Reykjavik, Iceland): It will correlate clinical records with DNA analysis from blood samples collected in the Framingham study to look for genetic markers. The company will map 50,000 markers related to diseases, and Ledley predicts those markers will yield much information on their own, also allowing pharmaceutical companies using the data to further narrow-in on genes. He says the Framingham data will complement those generated by the Human Genome Project and the SNPs Consortium.

FGM's software will enable pharmaceutical companies to conduct "virtual clinical trials," says Ledley, who was formerly president of pharmacogenetics company Variagenics (Cambridge, MA). For example, if a company is developing a gene-based drug for hypertension, it will be able to search the Framingham data to determine if the gene targeted by the drug has effects on other areas, such as the central nervous system.

The Framingham Heart Study was begun in 1948 by the National Heart Institute (now the National Heart, Lung, and Blood Institute, or NHLBI) at the US National Institutes of Health (NIH; Bethesda, MD) to look at environmental, hereditary, and lifestyle factors related to cardiovascular disease. The original study enrolled 5,209 participants. In 1971, BU, which now owns about 20% of FGM, took over its administration, adding 5,135 additional participants (the children of the original participants and their spouses), and expanding the scope of the research to include conditions related to aging, such as stroke, hearing loss, and arthritis. Over the years, the study has recorded an increasing range of physical measurements such as blood pressure, cognitive function, and bone density. Clinical data were collected every 2 years for the original group and every 4 years for the second generation, along with data on environment, family histories, and lifestyle habits such as diet, smoking, and exercise. Ten years ago, the study began collecting blood and tissue samples as well (immortal cell lines have been created from 4000 study participants), and a 300-marker map has been completed already.

The heart study has obtained informed consent from all participants since its inception and Ledley says FGM will continue to do so. He adds that study participants are also aware that pharmaceutical companies already have been using the data for years to develop products. According to Ledley, an undisclosed percentage of FGM's stock will be set aside in a trust for participants to fund community efforts and to retain ethicists to act as community advocates. In addition, NHLBI has told BU that neither the university nor FGM can profit directly from data collected with public funds, and that no BU researcher involved in the study can have a financial stake in FGM.

Meanwhile, the first step for FGM, says Ledley, is to transfer the 52 years worth of clinical measurements into digital format and to combine it with patients' other information. He expects to have a prototype of the data-mining software up and running in about 9 months.

Because the searchable data are prospective and longitudinal (meaning the same patients were studied for a long period of time), they could allow researchers to go back and look for disease predictors in a patient after that disease occurs, providing insight not only into genes that cause disease, but genes that protect against disease or contribute to disease progression. Richard Lifton, a professor of genetics and medicine at Yale University School of Medicine (New Haven, CT), says the Framingham study is "one of the best repositories of longitudinal phenotype data."

In addition, the Framingham data have, from the start, been collected specifically for the purpose of research—something Ledley says is crucial to the value of the data now. He says their resulting reliability have great advantages over retrospective studies (such as the one being conducted by deCODE in Iceland (*Nat. Biotechnol.* **16**, 1017, 1998) where medical records can often be incomplete or contain errors.

Moreover, Ledley says the Framingham data, which contain records on families from a diverse population, are likely to be more applicable to a wider range of people than studies focussing on homogeneous populations; such studies include that being carried out by Gemini in Newfoundland, Canada (*Nat. Biotechnol.*, **18**, 366, 2000).

However, several researchers say the Framingham data are lacking in some areas. For instance, Zahed Subhan, chief business officer of Gemini, questions the diversity of the data, noting that the Framingham study has drawn participants from a small geographic area. Pointing out that Gemini has studied twins in normal populations from such diverse geographic regions as UK, Sweden, Australia, and China, he says it is important to look at different populations because natural genetic variations can occur in different founder groups.

In addition, Kari Stefansson, president and CEO of deCODE, has criticized the plan to market the Framingham database in the Icelandic press, saying the lack of genealogical data beyond two generations will make it difficult to study familial patterns.

Others say the relatively small number of participants will make it hard to find markers for many diseases in a normal population. Tom Meade, director of the MRC Epidemiology and Medical Care Unit, Wolfson Institute (London), is chairing a working group that is currently setting up the UK Population Biomedical Collection sponsored by the Wellcome Trust. He says the intended prospective UK study, which will look at many variables and focus on cardiovascular disease and cancer, aims to study as many as 500,000 participants from a normal population.

However, Ledley, Subhan, and others involved with the groups conducting such linkage studies agree that the efforts should be seen as complementary, not competitive, and that pharmaceutical companies will want access to as many sources of data as possible when looking for genes.

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