

## 20-year Study Examines How Personal Genomics Affects Behavior

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With initiative and a few bucks, consumers nowadays can send tubes of saliva to a company that will analyze their DNA and offer personalized risk assessments for a host of common conditions including diabetes, heart attack, and Alzheimer disease (AD). But how useful is this information, and what do people do with it? Do those who learn they are prone to cardiovascular disease slash fat from their diets and exercise more regularly to improve their health outcomes? What about people carrying genes associated with higher risk for AD, which currently has no cure and for which lifestyle and dietary changes offer, at best, modest benefit for delaying or preventing disease?

Such matters have attracted attention in the literature (see, e.g., [Hunter et al., 2008](#); [Janssens et al., 2008](#)) and will be addressed directly in a first-of-its-kind longitudinal study recently launched by the [Scripps Translational Science Institute](#) in La Jolla, California. Using personal genomics services provided by co-sponsor [Navigenics Inc.](#), a company in Foster City, California, Scripps hopes to enroll 10,000 people in a 20-year study looking at the behavioral impact of predictive information gleaned from personal genomics data. Affymetrix and the Microsoft Corporation also co-sponsor the research.

Study sponsors said that they invite readers of the Alzheimer Research Forum, as well as their families and friends, to participate, and that they will grant a discount on the cost of the genetic testing. The study aims to enroll participants coming through this forum on May 15 and encourages them to sign up for a [wait list](#) in the interim. Navigenics will then e-mail signup information to registrants on May 15, according to Katie Kihorany from Navigenics. Enrollment for the AD block of this large study will close in mid-June.

Participants will complete a health assessment questionnaire and provide two tablespoons of saliva at the start of the study. DNA extracted from the saliva sample is analyzed on a gene scan, and data from 1.8 million genetic markers are used to estimate lifetime risk for some 24 conditions. Participants view these risk reports on a secure Web portal. The study requires no in-person clinic visits. Instead, it tracks self-reported lifestyle changes in response to the genetic susceptibility data through follow-up questionnaires completed three months, 12 months, and periodically up to 20 years after receiving the information. The personal genomics service includes round-the-clock access to genetic counseling. This service normally costs \$2,499, but is offered to study participants at \$470.

The concept of seeing how individuals respond to disease susceptibility information attracted Meryl Comer, leading AD activist and president of the [Geoffrey Beene Foundation Alzheimer's Initiative](#). Comer approached the study sponsors about creating an awareness campaign to run in parallel with the longitudinal study, but with particular focus on AD since the genetic testing is so controversial.

“My goal is to break through a stigma induced by the medical community in the late 1990s around a test that will in five to 10 years be common and pave the way for the future of personalized medicine. Well-meaning paternalism is passé,” Comer wrote in an e-mail to Alzforum (see also [Comer, 2008](#)). “The public can understand the probability of risk, and in a case like Alzheimer's, replacing the terror of the unknown—even with a sobering, imperfect estimate of percent risk—has its own comfort and supports life planning.” Comer, whose husband and mother have AD, had her own DNA analyzed as part of the longitudinal study and revealed the sobering results in a recent ABC Nightline segment (see [Part 1](#) and [Part 2](#)).

AD clinician-researcher Sam Gandy of Mount Sinai School of Medicine, New York, agrees that the medical establishment should not “take a parental stance and deny genotype information to people who want it, as though ‘we know better,’” he wrote in an e-mail to ARF. However, he and Amy Duross, vice president of policy and business affairs at Navigenics, stressed the importance of understanding what sort of information these tests do and do not provide. Unlike prenatal tests or others that screen for single gene variants that are potentially diagnostic in nature, “our test is predictive, not deterministic,” Duross told ARF. This means that the test predicts the odds of getting a disease, rather than determines with certainty whether a person will get a disease.

Fewer than 5 percent of AD cases—mostly though not exclusively those in the early-onset category—are linked to deterministic mutations in known genes. The vast majority of AD patients have a late-onset form of disease with no definitive genetic determinant. Even among people with two copies of [ApoE4](#), the most robust susceptibility gene for late-onset AD, many will not develop the disease. On the flip side, many AD patients carry no ApoE4 alleles. “ApoE4 is a risk factor, not a disease gene, not a death sentence. People ‘escape’ from ApoE4’s grip,” Gandy wrote.

Nevertheless, those with genetic variants that put them at higher risk for AD may be legally denied long-term insurance coverage—one of the areas left unprotected by the Genetic Information Nondiscrimination Act (GINA). Passed in 2008, GINA prevents denial of jobs or coverage to individuals based on genetic information (see [ARF related news story](#)).

An ongoing, federally funded study exploring how people respond to AD genetic risk information suggests that individuals place a high premium on such data. Preliminary analyses of REVEAL (Risk Evaluation and Education for Alzheimer's Disease) data found that study participants who knew they were ApoE4-negative reported less worry about their disease risk even when family and other health factors deemed their total AD risk equivalent to that of other people who had not received information about their ApoE gene status (see [ARF Live Discussion](#)).

Esther Landhuis