# Depression research on a big scale: UCLA's Depression Grand Challenge

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Jonathan Flint is one of four directions of the Depression Grand Challenge

UCLA is embarking on a depression research project, the likes of which are unprecedented among those currently studying medicine on campus. It involves 25 departments, 100,000 patients and a host of ambitious goals to ease the disease's effect as much as 50 percent by 2050.

#### **Genetics and depression**

"The idea is to tackle the common cause of the most common disease in the world — depression," says Jonathan Flint, MD, professor in residence at the Department of Psychiatry and Biobehavioral Sciences for the David Geffen School of Medicine at UCLA. The depression research study is the Depression Grand Challenge.



Researchers expect this to be a 35-year project. It includes a genetic component to understand the causes of depression, which Dr. Flint hopes will inspire new treatments. But they'll look environment interplay as well. "As is true for many complex conditions," he says, "genetics and environment are deeply confounded."

The genetic component is one factor that drew him to the project. He recently published the largest genetics study to date, as detailed by *Nature*, recruiting about 5,300 women with depression and 5,300 controls subjects in China. They were the first to identify genetic markers contributing to depression.

#### What sets this one apart

As one of four directors of the study, Dr. Flint came to California from Oxford University in January for a unique opportunity. This depression research study is different than others because of its multidisciplinary approach. "One of the things that make depression so difficult to deal with is that it affects so many parts of our lives," he says, noting its social stigma and economic impact.

In tandem with Dr. Flint's team, the engineering department is helping to develop ways to monitor the participants over the long term. This potentially includes using wearable devices to monitor daily activity, which Dr. Flint considers useful when examining depression because it affects your sleep, appetite and how much you move around. But "we want to be more ambitious," he states. "Maybe [we can] monitor their biochemistry and, in the future, possibly monitor brain activity and do it in a remote fashion."

### Preparing the project

The depression research study starts in the next six weeks, collecting information on several thousand subjects to make sure the protocols work. They'll initially draw from UCLA Health, which has around two million enrollees and can identify qualified people from this pool. Eventually they'll recruit from other areas.

One of the innovations is study funding — important as it could cost \$525 million for the first decade. "We're trying to think out of the box here," he says. Standard study funding involves applying for the National Institutes of Health (NIH) and federal grants, as well as philanthropic funding. This will be a form of public-private partnership, as they expect to develop drug therapies that present commercial opportunity.

### A commitment by (and to) the people

But this study is different in that they also anticipate having subjects pay to enroll as participants. "We see it as stakeholder science. We're asking people to contribute their time and follow them for maybe 10 years. It's an investment on their part," he admits. It's a two-way process. And while researchers want to sequence the genetics of their participants, the participants will receive the results and health information that go with it. If they screen the subject for something and notice there's a health concern, for example, they'll reach out to him or her to make sure they're getting the proper treatment.

Dr. Flint hopes that eventually, participants will benefit directly from any new therapies.

Dr. Flint stresses the magnitude of what UCLA is doing with the Depression Grand Challenge. "In the developed world, this really is the leading cause of morbidity in society. That puts it above cancer, diabetes, and at the moment it's second only to heart disease," he says. "UCLA is unique in devoting all its energy to this."

## By Deborah Abrams Kaplan