

Hunting for the Prozac gene

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Prozac works wonders for some depressed people, but not for others. In some cases, patients derive little benefit and at worst, it can lead to bizarre hallucinations and fits of rage. Researchers and doctors remain puzzled as to what causes the wide range of reaction to Prozac and similar antidepressants.

The answer, Tel Aviv University researchers believe, can be found in a patient's [genes](#). And if their research is successful, these scientists may be able to provide psychiatrists with a simple genetic test to revolutionize the treatment of depression.

Hunting for "the Prozac gene" — its response biomarker, in science-speak — is the foundation of a new Tel Aviv University project established by a unique biobank in TAU's Sackler School of Medicine. Initiated by the biobank's director Dr. David Gurwitz, and his student Ayelet Morag, the researchers are attempting to discover reliable pharmacogenic markers for [antidepressants](#) such as Prozac.

"Many drugs for treating depression are on the market," says Dr. Gurwitz. "The most popular ones — including Prozac — are the selective serotonin reuptake inhibitors (SSRIs). But they only work for about 60% of people with depression. A drug from other families of antidepressants could be effective for the other 40%," he says. "We are working to move the treatment of depression from a trial-and-error approach to a best-fit, personalized regimen."

A genetic basis for psychiatric treatment

Dr. Gurwitz says the key is in our genes, and the first step to unlocking the puzzle lies in discovering relevant biomarkers, the biological elements in blood or DNA that provide clues for disease or conditions such as blood glucose in diabetes, blood pressure in heart disease, and hormones released in pregnancy. Clinicians already base treatments for cancer patients on genetic tests. This has proven especially useful for breast-cancer, where drugs such as Tamoxifen or Herceptin are prescribed only after genetic tests show that they would benefit the patient.

"Why not embrace the same approach for treating depression?" he asks. "We've designed an experiment to search for elements that can determine who will — and who won't — benefit from drugs such as Prozac," says Dr. Gurwitz.

An effective response to "extreme responders"

The researchers will explore "whole-genome gene expression profiles" in cell lines from healthy people. Since Prozac and similar antidepressants are known to inhibit the growth of blood cells, they are now screening a large collection of cell lines to determine which have the strongest and weakest growth-inhibition responses to SSRIs like Prozac. Those cells that exhibit extreme responses will then be screened across the entire human genome, to find out which genetic make-up works best with SSRIs.

Dr. Gurwitz believes that among our 25,000 human genes, only a few hundred will show a difference between the two types of "extreme responder" cells. In the next phase of their study, they will explore which of those "hits" can be valuable clinical biomarkers for the response to Prozac, a study that can subsequently be done by psychiatrists.

"Ours is a unique model because it does not make presumptions," says Dr. Gurwitz. "Research on Prozac response biomarkers over the past 20 years has focused on genes related to the brain metabolism of serotonin, long suspected as the cause of depression," he adds. "However, after many years of research with this focus, it is now obvious that the approach has failed. We realize that we must look at the entire repertoire of human genes."

"Psychiatric pharmacology remains a black box," says Dr. Gurwitz. "Nobody knows why some people respond to Prozac-type SSRI antidepressants, while others are helped by other kinds of antidepressants. The World Health Organization predicts by the year 2020, costs and lost productivity from [depression](#) will exceed those of cardiovascular disease as the leading cause of health expenditure in developed countries. We hope to produce a clear test for antidepressant drug responses to improve the odds for successful treatment."

Source: Tel Aviv University ([news](#) : [web](#))

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