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TINY MOLECULE COULD HELP DIAGNOSE AND TREAT MENTAL DISORDERS

*Weizmann Institute scientists “fingerprint” a culprit in depression, anxiety,
and other mood disorders*

REHOVOT, ISRAEL—June 19, 2014—According to the World Health Organization, mood disorders such as depression affect some 10% of the world’s population and are associated with a heavy burden of disease. That is why numerous scientists around the world have invested a great deal of effort in understanding these diseases. Yet the molecular and cellular mechanisms that underlie these problems are still only partly understood.

The existing antidepressants are not good enough: Some 60-70% of patients get no relief from them. For the other 30-40%, that relief is often incomplete, and they must take the drugs for a long period before feeling any effects. In addition, there are many side effects associated with the drugs. New and better drugs are clearly needed, an undertaking that requires, first and foremost, a better understanding of the processes and causes underlying the disorders.

The Weizmann Institute of Science’s Prof. Alon Chen, together with his then PhD student Dr. Orna Issler, investigated the molecular mechanisms of the brain’s serotonin system, which, when misregulated, is involved in depression and anxiety disorders. Prof. Chen and his colleagues researched the role of microRNA molecules (small, non-coding RNA molecules that regulate various cellular activities) in the nerve cells that produce serotonin. They succeeded in identifying, for the first time, the unique “fingerprints” of a microRNA molecule that acts on the serotonin-producing nerve cells. Combining bioinformatics methods with experiments, the researchers found a connection between this particular microRNA, called miR135, and two proteins that play a key role in serotonin production and the regulation of its activities. The findings appear June 19 in *Neuron*.

The scientists noted that in the area of the brain containing the serotonin-producing nerve cells, miR135 levels increased when antidepressant compounds were introduced. Mice that were genetically engineered to produce higher-than-average amounts of the microRNA were more resistant to constant stress: They did not develop any of the behaviors associated with chronic stress, such as anxiety or depression, which would normally appear. In contrast, mice that expressed low levels of miR135 exhibited more of these behaviors; in addition, their response to antidepressants was weaker. In other words, the brain needs the proper miR135 levels – low enough to enable a healthy stress response, but high enough to avoid depression or anxiety disorders and to respond to serotonin-boosting antidepressants. When this idea was tested on human blood samples, the researchers found that subjects who suffered from depression had unusually low miR135 levels in their blood. On closer inspection, the scientists discovered that the three genes involved in producing miR135 are located in areas of the genome that are known to be associated with risk factors for bipolar mood disorders.

These findings suggest that miR135 could be a useful therapeutic molecule – both as a blood test for depression and related disorders, and as a target whose levels might be raised in patients. Yeda Research and Development Co. Ltd., the technology transfer arm of the Weizmann Institute, has applied for a patent connected to these findings and recently licensed the rights to miCure Therapeutics to develop a drug and diagnostic method. After completing preclinical trials, the company hopes to begin clinical trials in humans.

Prof. Alon Chen is the Head of the Max Planck Society – Weizmann Institute of Science Laboratory for Experimental Neuropsychiatry and Behavioral Neurogenetics. His research is supported by the Henry Chanoch Kreuter Institute for Biomedical Imaging and Genomics; the Perlman Family Foundation, Founded by Louis L. and Anita M. Perlman; the Adelis Foundation; the Irving I. Moskowitz Foundation; the European

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