Hebrew University researchers find mechanism underlying depression

Study offers hope of more efficient anti-depressant drugs

By JUDY SIEGEL

Clinical depression is the most significant cause of disability around the world, yet scientists still don't understand the biological mechanisms behind it well enough to prevent or treat it adequately – partly because most research focuses on neurons in the brain and not other cells in the cerebellum.

A study by researchers at the Hebrew University of Jerusalem have found that changes in one type of non-neuronal brain cells – microglia – underlie the depressive symptoms brought on by exposure to chronic stress. Their findings, published in the prestigious scientific journal Molecular Psychiatry, showed that in experiments with animals, compounds that alter the functioning of microglia can serve as efficient anti-depressant drugs.

Yissum, the university's technology transfer company, has applied for a patent for the treatment of some forms of depression by several specific microglia-stimulating drugs.

Prof. Raz Yirmiya, director of the Hebrew University's psychoneuroimmunology lab, and doctoral student Tirzah Kreisel, together with researchers at Yirmiya's laboratory and at the University of Colorado in Boulder conducted the research.

The researchers examined in mice the involvement of microglia brain cells in the development of depression, following chronic exposure to stress. Comprising a 10th of brain cells, microglia are the representatives of the immune system in the brain; but recent studies have shown that these cells are also involved in physiological processes not directly related to infection and injury, including the response to stress.

The team found that during the first week of stress exposure, microglia cells undergo a phase of proliferation and activation, reflected by increased size and production of specific inflammatory molecules, after which some microglia begin to die. Following five weeks of stress exposure, this phenomenon led to a reduction in the number of microglia and to a degenerated appearance of some microglia cells, particularly in a specific region of the brain involved in responding to stress.

Yirmiya explained: “We were able to demonstrate that such microglia-stimulating drugs served as effective and fast-acting antidepressants, producing complete recovery of the depressive-like behavioral symptoms, as well as increasing the neurogenesis to normal levels within a few days of treatment. In addition to the clinical importance of these results, our findings provide the first direct evidence that in addition to neurons, disturbances in the functioning of brain microglia cells have a role in causing psychopathology in general, and depression in particular. This suggests new avenues for drug research, in which microglia stimulators could serve as fast-acting anti-depressants in some forms of depressive and stress-related conditions.”