

# Inflammation and Depression



An international research team in the U of I Department of Animal Sciences is pursuing the role of inflammation in clinical depression and how it may interfere with the treatment of individuals receiving immunotherapy for cancer and other diseases. Led by professors Robert Dantzer and Keith Kelley, the work is supported by a \$1.7 million, five-year grant from the National Institute of Mental Health.

Dantzer is an adjunct professor in the Department and Director of the Laboratory of Integrative Neurobiology at the National Institute for Scientific Research in Bordeaux, France. Kelley has been collaborating with Dantzer for 25 years.

"Dantzer made a basic breakthrough several years ago when his research showed that inflammation in the brain is really a major factor in a number of diseases and conditions," said Kelley. He added that there is increasing focus on the role inflammation plays in obesity, Type 2 diabetes, and coronary heart disease.

The current project continues to focus on the effects of inflammation on the brain, but the current target is its role in depression.

"Depression is still considered as a condition that is independent of the somatic disease patients are afflicted with, and depression can worsen the somatic disease. Dantzer's research is providing the first lead that this mood disorder can actually be another facet of the disease that relates to mechanisms of inflammation. This research is important for understanding the mechanics of depression, how they work, and the potential for treatments," said Kelley.

Part of the current project is looking at how depression develops in patients undergoing treatment for hepatitis C and for a deadly cancer known as malignant melanoma.

Immunotherapy, which is also used to treat patients with AIDS and hepatitis C, involves the injections of cytokines,

which are chemicals normally made by immune cells that boost the immune system to fight infectious pathogens and kill cancer cells. However, the cytokine treatment depletes serotonin and leads to the symptoms of depression.

"Since depression is a severe side effect of immunotherapy that can lead to suicide in these patients," said Kelley, "the immunotherapy treatments are often discontinued, leaving the patient with the disease. This is a huge problem."

Rozenn Mingam, one of the French graduate students involved in the research, pointed out that the project also has important applications in livestock because inflammation leads to a reduction in food consumption, which is one of the most important economic traits in many types of livestock.

Dantzer and Kelley are trying understand how cytokines work in the brain. The project also involves evaluation of potential treatments to ease cytokine-caused depression. In addition to standard antidepressants, one possibility involves antioxidants and will be tested in mice.

Kelley explains that scientists have always known that behavioral changes accompany sickness. The work Dantzer and he are doing, however, explores why sickness causes those changes.

"If we can better understand depression and devise better therapies for treating it, this would not only benefit patients on immunotherapy but millions of people worldwide who suffer from clinical depression," said Kelley.



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