

## **CRH Receptor Variant Predicts Response to Antidepressants**

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From [Reuters Health](#)

NEW YORK (Reuters Health) Dec 16

Individuals with high levels of depression and anxiety respond better to antidepressant medication if they carry a specific variation in the corticotropin-releasing hormone receptor type 1 (CRHR1) gene, results of a study indicate.

This finding is "very relevant," Dr. Julio Licinio told Reuters Health, "because the next generation of antidepressants is targeted exactly at this gene. They are CRH receptor-antagonists. Our study puts even more of an emphasis on this target for antidepressant development," he said.

Several lines of evidence support a role for CRH in the pathophysiology of depression and CRHR1 has been implicated in the treatment of depression and anxiety. For example, "if you activate this receptor in an animal, they become both stressed and anxious and if you treat animals with antidepressants the levels of CRH go down," Dr. Licinio explained.

Dr. Licinio, at the David Geffen School of Medicine, UCLA, and associates looked for associations between CRHR1 genotypes and response to fluoxetine and desipramine in 80 depressed Mexican-Americans. Both of these drugs similarly downregulate CRH expression in the central nervous system, they note in the December issue of *Molecular Psychiatry*.

They found that homozygosity for the GAG haplotype of CRHR1 was associated with a 70% greater reduction in anxiety and a 31% greater reduction in depression after treatment with either fluoxetine or desipramine in a subgroup of patients with both high anxiety and high depression scores.

There were no associations between CRHR1 genotype and response to treatment in patients with lower levels of anxiety at baseline.

If these findings can be validated and replicated, they would support the theory that "response to antidepressant treatment is heterogeneous" and that the CRHR1 gene and possibly other genes in stress-inflammatory pathways are involved, the investigators say.

This could have major implications for patients with anxiety and depression, Dr. Licinio told Reuters Health, explaining that "right now, depression treatment is basically trial and error -- you try one drug for about 6 to 8 weeks and if it doesn't work you try another. It is a very tedious process and many patients drop out of treatment if the first drug doesn't work."

The current work holds the promise of tailored antidepressant therapy based on a patient's individual genetic makeup, he added.

*Study: Licinio J, O'kirwan F, Irizarry K, et al. Association of a corticotropin-releasing hormone receptor 1 haplotype and antidepressant treatment response in Mexican-Americans. Mol Psychiatry 2004 Dec;9(12):1075-1082.*