

Format: Abstract

Send to

J Exp Med. 2012 Jun 4;209(6):1121-34. doi: 10.1084/jem.20120242. Epub 2012 May 14.

# Cannabinoids suppress inflammatory and neuropathic pain by targeting $\alpha 3$ glycine receptors.

Xiong W<sup>1</sup>, Cui T, Cheng K, Yang F, Chen SR, Willenbring D, Guan Y, Pan HL, Ren K, Xu Y, Zhang L.

## Author information

### Abstract

Certain types of nonpsychoactive cannabinoids can potentiate glycine receptors (GlyRs), an important target for nociceptive regulation at the spinal level. However, little is known about the potential and mechanism of glycinergic cannabinoids for chronic pain treatment. We report that systemic and intrathecal administration of cannabidiol (CBD), a major nonpsychoactive component of marijuana, and its modified derivatives significantly suppress chronic inflammatory and neuropathic pain without causing apparent analgesic tolerance in rodents. The cannabinoids significantly potentiate glycine currents in dorsal horn neurons in rat spinal cord slices. The analgesic potency of 11 structurally similar cannabinoids is positively correlated with cannabinoid potentiation of the  $\alpha 3$  GlyRs. In contrast, the cannabinoid analgesia is neither correlated with their binding affinity for CB1 and CB2 receptors nor with their psychoactive side effects. NMR analysis reveals a direct interaction between CBD and S296 in the third transmembrane domain of purified  $\alpha 3$  GlyR. The cannabinoid-induced analgesic effect is absent in mice lacking the  $\alpha 3$  GlyRs. Our findings suggest that the  $\alpha 3$  GlyRs mediate glycinergic cannabinoid-induced suppression of chronic pain. These cannabinoids may represent a novel class of therapeutic agents for the treatment of chronic pain and other diseases involving GlyR dysfunction.

PMID: 22585736 PMCID: PMC3371734 DOI: 10.1084/jem.20120242

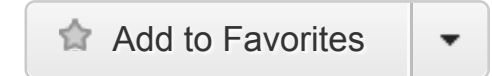
[Indexed for MEDLINE] **Free PMC Article**



### Full text links



### Save items



### Similar articles

Involvement of glycine receptor  $\alpha 1$  subunits in c [Neuropharmacology. 2018]

Cannabinoid potentiation of glycine receptors contribu [Nat Chem Biol. 2011]

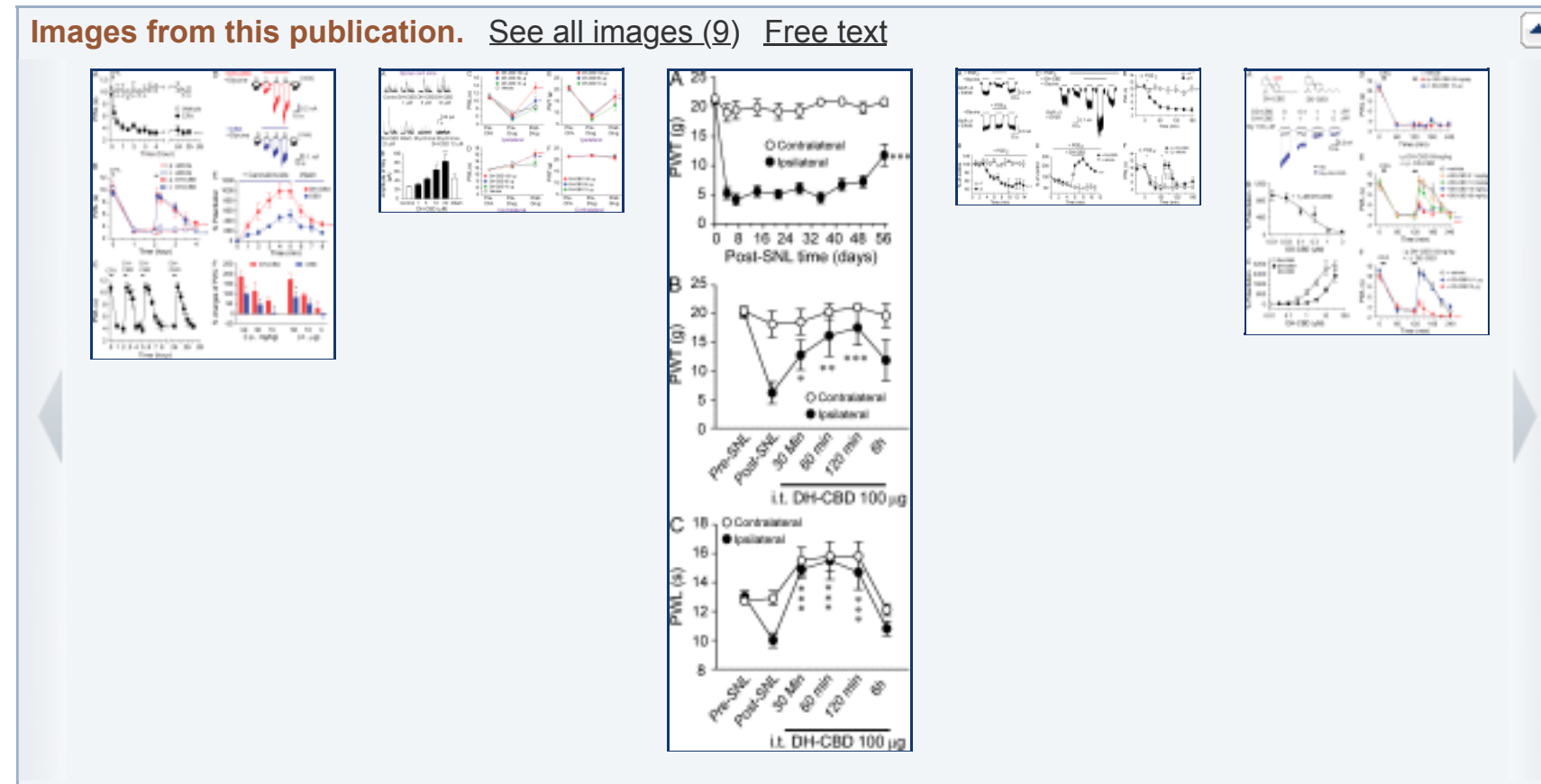
A common molecular basis for exogenous and endoc [J Neurosci. 2012]

**Review** Glycine receptors: a new therape [Curr Opin Investig Drugs. 2006]

**Review** Current evidence of cannabinoid-based an [Eur J Pain. 2018]

See reviews...

See all...



Publication type, MeSH terms, Substances, Grant support

LinkOut - more resources

### Cited by 33 PubMed Central articles

**Review** Cannabinoids and Pain: New Insights From O [Front Pharmacol. 2018]

Identification of Glycine Receptor  $\alpha 3$  as a Colchicine-Bin [Front Pharmacol. 2018]

Cannabidiol enhances morphine antinociception, diminis [Mol Brain. 2018]

See all...

### Related information

### Recent Activity

Turn Off Clear

Cannabinoids suppress inflammatory and neuropathic PubMed

Antihyperalgesic effect of a Cannabis sativa extract in a r. PubMed

Cannabidiol inhibits paclitaxel-induced neuropathic pain thrc PubMed

Vanilloid TRPV1 receptor mediates the antihyperalgesic effect of PubMed

The non-psychoactive cannabis constituent cannabidiol is an PubMed

See more...

You are here: NCBI > Literature > PubMed

Support Center

### GETTING STARTED

- NCBI Education
- NCBI Help Manual
- NCBI Handbook
- Training & Tutorials
- Submit Data

### RESOURCES

- Chemicals & Bioassays
- Data & Software
- DNA & RNA
- Domains & Structures
- Genes & Expression
- Genetics & Medicine
- Genomes & Maps
- Homology
- Literature
- Proteins
- Sequence Analysis
- Taxonomy
- Variation

### POPULAR

- PubMed
- Bookshelf
- PubMed Central
- BLAST
- Nucleotide
- Genome
- SNP
- Gene
- Protein
- PubChem

### FEATURED

- Genetic Testing Registry
- GenBank
- Reference Sequences
- Gene Expression Omnibus
- Genome Data Viewer
- Human Genome
- Mouse Genome
- Influenza Virus
- Primer-BLAST
- Sequence Read Archive

### NCBI INFORMATION

- About NCBI
- Research at NCBI
- NCBI News & Blog
- NCBI FTP Site
- NCBI on Facebook
- NCBI on Twitter
- NCBI on YouTube
- Privacy Policy