

Roberto Ciccocioppo

Date of birth: 22.12.1965

Positions and Honors.

- 1991 Degree in Chemistry and Pharmaceutical Technology
- 1993 Spent 1 year research and study at the School of Psychology, University of Birmingham.
- 1995 Spent 6 months at the Department of Pharmacology University of Birmingham,
- 1996 PhD in Pharmaceutical Sciences, University of Camerino, Italy
- 1997-1998 Research Fellow at the Dept. Pharmacology, University of Camerino, Italy
- 1998-1999 Research fellow at the Department of Neuropharmacology, The Scripps Research Institute, La Jolla California, USA.
- 1999 Assistant professor in pharmacology at the University of Camerino, Faculty of Pharmacy
- 2004-2015 Appointed as "Adjunct Researcher" at the Dept of Molecular and Cellular Neuroscience The Scripps Research Institute, La Jolla, California.
- From 2017 Visiting professor with "Faculty position" at Chang Chun University of Technology, Chang Chung Cina
- 2005-2010 Associate Professor in pharmacology, School of Pharmacy, University of Camerino
- From 2010 Full Professor in pharmacology School of Pharmacy, University of Camerino
- From 2014 Head of the International School of Advanced Study, University of Camerino

Research Focus

The research is mainly focused on the study of the neurobiological basis of abnormal behavioral and brain functions relevant to human psychopathology with emphasis on drug addiction and eating disorders. The majority of this work is directed at the understanding the neurological mechanisms responsible for these aberrant behaviours and at identifying innovative pharmacological targets to aid the development of new more effective

treatments. Attention is also dedicated to the study of neurocircuitry and molecular mechanisms controlling emotional and cognitive disturbances associated with protracted exposure to drugs of abuse or chronic stress.

Awards

2000 Axis-shield ISBRA Junior Investigator Award of the International Society for Biomedical Research on Alcoholism, for his studies on the neurobiology of alcohol relapse

2000 SIMS Award, Pisa for his research activity in the field of drug addiction

2004 SIF (Societa' Italiana di Farmacologia)-Farindustria Award for the study of the role of Nociceptin in the mechanisms of anorexia nervosa (published in *J. Neuroscience* 23: 9445-9451. 2003)

Editorial Activities

Senior editor *Frontiers Psychiatry*, section –Psychopharmacology-

Board member of *Addiction Biology*

Guest Editor for the special issue "The genetics of alcoholism" for *Addiction Biology*

Frequent ad-hoc reviewer for several international Journals including:

Journal of Neuroscience, TINS, Biological Psychiatry, Neuropsychopharmacology, European Journal Neuroscience, European Journal Neuropsychopharmacology Psychopharmacology, Brain Research, Journal Neuroendocrinology, British Journal of Pharmacology, Behavioral Brain Research, Pharmacology Biochemistry and Behavior, Alcohol and Alcoholism, Alcohol, Life Sciences, Naunyn Schmiedeberg's Archives of Pharmacology, Peptides, Neuropharmacology, , Alcoholism Clinical Experimental Research, European Journal of Pharmacology.

Main Research Support

Principal investigator in the EU research project TARGALC (EU-FP5)

Coordinator of the EU project INFONOMIC (EU-FP6)

Co-Principal Investigator of the NIH/NIAAA (RO1) research programs. The nociceptin ORL-1 system treatment target for relapse (2005-2027)

Co-Principal Investigator of the NIH/NIAAA (RO1) research program. Gene-Environment Interaction: Focus on the Brain CRF System in Alcohol Preferring msP rats (2010-2026)

Co-Principal Investigator U01-DA045300-01A1 The genetic Basis of Opioid Dependence Vulnerability in a Rat Model (2018-2023)

Coordinator of the Project IMPACT I Dip. delle Politiche Antidroga (2009-2011)

Coordinator of the Project IMPACT II Dip. delle Politiche Antidroga (2012-2014)

He has been also PI in the national project PRIN 2006 and PRIN 2017 as well as participant to several other national programs (PRIN 2002, 2004, FIRB 2003)

Over the years the research activities of Dr Ciccocioppo have been supported by several Pharmaceutical Industries and private foundations.

Membership

Society for Neuroscience
European Behavioural Pharmacology Society
Italian Society of Pharmacology
Italian Society of Neuroscience
International Narcotic Research Conference
International Drug Abuse Research Society

Publications

Roberto Ciccocioppo has published over 220 scientific articles in prestigious peer reviewed international journals including:
Nature Neuroscience, Neuron, Journal of Neuroscience, PNAS, Biological Psychiatry, Neuropsychopharmacology, Science Advances, American Journal of Psychiatry, JAMA Psychiatry

Bibliometric parameters from Scopus:

H-index 54. Number of total citations 8355

35 publications in peer reviewed international journals in the last 3 years

Bibliometric parameters from Google Scholar:

H-index 61 Number of total citations 11360

List of selected publications

Curley DE, Vasaturo-Kolodner TR, Cannella N, Ciccocioppo R, Haass-Koffler CL. Yohimbine as a pharmacological probe for alcohol research: a systematic review of rodent and human studies Neuropsychopharmacology. 2022 Nov;47(12):2111-2122.

Domi A, Lunerti V, Petrella M, Domi E, Borruto AM, Ubaldi M, Weiss F, Ciccocioppo R. Genetic deletion or pharmacological blockade of nociceptin/orphanin FQ receptors in the ventral tegmental area attenuates nicotine-motivated behaviour. *Br J Pharmacol*. 2022 Jun;179(11):2647-2658.

Pérez-Ramírez Ú, López-Madrona VJ, Pérez-Segura A, Pallarés V, Moreno A, Ciccocioppo R, Hyytiä P, Sommer WH, Moratal D, Canals S. Brain Network Allostasis after Chronic Alcohol Drinking Is Characterized by Functional Dedifferentiation and Narrowing. *J Neurosci*. 2022 May 25;42(21):4401-4413.

De Santis S, Cosa-Linan A, Garcia-Hernandez R, Dmytrenko L, Vargova L, Vorisek I, Stopponi S, Bach P, Kirsch P, Kiefer F, Ciccocioppo R, Sykova E, Moratal D, Sommer WH, Canals S. Chronic alcohol consumption alters extracellular space geometry and transmitter diffusion in the brain. *Sci Adv*. 2020 Jun 24;6(26):eaba0154.

De Santis S, Bach P, Pérez-Cervera L, Cosa-Linan A, Weil G, Vollstädt-Klein S, Hermann D, Kiefer F, Kirsch P, Ciccocioppo R, Sommer WH, Canals S. Microstructural White Matter Alterations in Men With Alcohol Use Disorder and Rats With Excessive Alcohol Consumption During Early Abstinence. *JAMA Psychiatry*. 2019 Jul 1;76(7):749-758.

Narendran R, Tollefson S, Himes ML, Paris J, Lopresti B, Ciccocioppo R, Mason NS. Nociceptin Receptors Upregulated in Cocaine Use Disorder: A Positron Emission Tomography Imaging Study Using [¹¹C]NOP-1A. *Am J Psychiatry*. 2019 Jun 1;176(6):468-476

Domi A, Stopponi S, Domi E, Ciccocioppo R, Cannella N. Sub-dimensions of Alcohol Use Disorder in Alcohol Preferring and Non-preferring Rats, a Comparative Study. *Front Behav Neurosci*. 2019 Jan 30;13:3

Narendran R, Ciccocioppo R, Lopresti B, Paris J, Himes ML, Mason NS. Nociceptin Receptors in Alcohol Use Disorders: A Positron Emission Tomography Study Using [¹¹C]NOP-1A. *Biol Psychiatry*. 2018 Nov 15;84(10):708-714

Bifone A, Gozzi A, Cippitelli A, Matzeu A, Domi E, Li H, Scuppa G, Cannella N, Ubaldi M, Weiss F, Ciccocioppo R. pHMRI, neurochemical and behavioral responses to psychostimulants distinguishing genetically selected alcohol-preferring from genetically heterogenous rats. *Addict Biol*. 2018.

Natividad LA, Buczynski MW, Herman MA, Kirson D, Oleata CS, Irimia C, Polis I, Ciccocioppo R, Roberto M, Parsons LH. Constitutive Increases in Amygdalar Corticotropin-Releasing Factor and Fatty Acid Amide Hydrolase Drive an Anxious Phenotype. *Biol Psychiatry*. 2017

Cippitelli A, Domi E, Ubaldi M, Douglas JC, Li HW, Demopoulos G, Gaitanaris G, Roberto M, Drew PD, Kane CJ, Ciccocioppo R. Protection against alcohol-induced neuronal and cognitive damage by the PPAR γ receptor agonist pioglitazone. *Brain Behav Immun*. 2017

Kallupi M, Scuppa G, de Guglielmo G, Calò G, Weiss F, Statnick MA, Rorick-Kehn LM, Ciccocioppo R. Genetic Deletion of the Nociceptin/Orphanin FQ Receptor in the Rat Confers Resilience to the Development of Drug Addiction.

Neuropsychopharmacology. 2017 Feb;42(3):695-706

Domi E, Uhrig S, Soverchia L, Spanagel R, Hansson AC, Barbier E, Heilig M, Ciccocioppo R, Ubaldi M. Genetic Deletion of Neuronal PPAR γ Enhances the Emotional Response to Acute Stress and Exacerbates Anxiety: An Effect Reversed by Rescue of Amygdala PPAR γ Function.

J Neurosci. 2016 Dec 14;36(50):12611-12623

de Guglielmo G, Melis M, De Luca MA, Kallupi M, Li HW, Niswender K, Giordano A, Senzacqua M, Somaini L, Cippitelli A, Gaitanaris G, Demopulos G, Damadzic R, Tapocik J, Heilig M, Ciccocioppo R. PPAR γ Activation Attenuates Opioid Consumption and Modulates Mesolimbic Dopamine Transmission. **Neuropsychopharmacology.** 2015;40:927-37

Micioni Di Bonaventura MV, Ciccocioppo R, Romano A, Bossert JM, Rice KC, Ubaldi M, St Laurent R, Gaetani S, Massi M, Shaham Y, Cifani C. Role of bed nucleus of the stria terminalis corticotrophin-releasing factor receptors in frustration stress-induced binge-like palatable food consumption in female rats with a history of food restriction. **J Neurosci.** 2014;34(34):11316-24.

de Guglielmo G, Kallupi M, Scuppa G, Stopponi S, Demopulos G, Gaitanaris G, Ciccocioppo R. Analgesic tolerance to morphine is regulated by PPAR γ . **Br J Pharmacol.** 2014;171:5407-16

Ciccocioppo R, Stopponi S, Economidou D, Kuriyama M, Kinoshita H, Heilig M, Roberto M, Weiss F, Teshima K. Chronic treatment with novel brain-penetrating selective NOP receptor agonist MT-7716 reduces alcohol drinking and seeking in the rat. **Neuropsychopharmacology.** 2014;39:2601-10.

Ciccocioppo R, de Guglielmo G, Hansson AC, Ubaldi M, Kallupi M, Cruz MT, Oleata CS, Heilig M, Roberto M. Restraint stress alters nociceptin/orphanin FQ and CRF systems in the rat central amygdala: significance for anxiety-like behaviors. **J Neurosci.** 2014;34:363-72

Thorsell A, Tapocik JD, Liu K, Zook M, Bell L, Flanigan M, Patnaik S, Marugan J, Damadzic R, Dehdashti SJ, Schwandt ML, Southall N, Austin CP, Eskay R, Ciccocioppo R, Zheng W, Heilig M. A novel brain penetrant NPS receptor antagonist, NCGC00185684, blocks alcohol-induced ERK-phosphorylation in the central amygdala and decreases operant alcohol self-administration in rats. **J Neurosci.** 2013 Jun 12;33(24):10132-42

Cannella N, Kallupi M, Ruggeri B, Ciccocioppo R, Ubaldi M The role of the neuropeptide S system in addiction: Focus on its interaction with the CRF and hypocretin/orexin neurotransmission. **Prog Neurobiol.** 2013 Jan;100:48-59

Schank JR, Ryabinin AE, Giardino WJ, Ciccocioppo R, Heilig M Stress-related neuropeptides and addictive behaviors: beyond the usual suspects. **Neuron.** 2012 Oct 4;76(1):192-208.

Gozzi A, Agosta F, Massi M, Ciccocioppo R, Bifone A Reduced limbic metabolism and fronto-cortical volume in rats vulnerable to alcohol addiction. **Neuroimage.** 2012 Dec 20;69C:112-119.

Stopponi S, Somaini L, Cippitelli A, Cannella N, Braconi S, Kallupi M, Ruggeri B, Heilig M, Demopulos G, Gaitanaris G, Massi M, Ciccocioppo R. Activation of

Nuclear PPAR γ Receptors by the Antidiabetic Agent Pioglitazone Suppresses Alcohol Drinking and Relapse to Alcohol Seeking. **Biol Psychiatry**. 2011;69:642-9.

Kallupi M, Cannella N, Ruggeri B, Ubaldi M, Economidou D, Weiss F, Massi M, Marugan J, Heilig M, de Lecea L, Ciccocioppo R. Role for the Neuropeptide S system in the physiopathology of cue-induced cocaine relapse: A mechanism mediated by the hypothalamic hypocretin system. **Proc Natl Acad Sci** 2010;107:19567-72.

Fedeli A, Braconi S, Economidou D, Cannella N, Kallupi M, Guerrini R, Calò G, Cifani C, Massi M, Ciccocioppo R. The paraventricular nucleus of the hypothalamus is a neuroanatomical substrate for the inhibition of palatable food intake by neuropeptide S. **Eur J Neurosci**. 2009 Oct;30(8):1594-602.

Cifani C, Zanoncelli A, Tessari M, Righetti C, Di Francesco C, Ciccocioppo R, Massi M, Melotto S Pre-exposure to environmental cues predictive of food availability elicits hypothalamic-pituitary-adrenal axis activation and increases operant responding for food in female rats. **Addict Biol**. 2009 Sep;14(4):397-407

Cannella N, Economidou D, Kallupi M, Stopponi S, Heilig M, Massi M, Ciccocioppo R. Persistent increase of alcohol-seeking evoked by neuropeptide s: an effect mediated by the hypothalamic hypocretin system. **Neuropsychopharmacology**. 2009 Aug;34(9):2125-34.

Economidou D, Hansson AC, Weiss F, Terasmaa A, Sommer WH, Cippitelli A, Fedeli A, Martin-Fardon R, Massi M, Ciccocioppo R, Heilig M. Dysregulation of nociceptin/orphanin FQ activity in the amygdala is linked to excessive alcohol drinking in the rat. **Biol Psychiatry**. 2008;64:211-8.

Hansson AC, Cippitelli A, Sommer WH, Fedeli A, Bjork K, Soverchia L, Terasmaa A, Massi M, Heilig M, Ciccocioppo R. Variation at the rat Crhr1 locus and sensitivity to relapse into alcohol seeking induced by environmental stress. **Proc Natl Acad Sci U S A**. 2006 Oct 10;103(41):15236-41.

Ciccocioppo R, Economidou D, Cippitelli A, Cucculelli M, Ubaldi M, Soverchia L, Lourdasamy A, Massi M. Genetically selected Marchigian Sardinian alcohol-preferring (msP) rats: an animal model to study the neurobiology of alcoholism. **Addict Biol**. 2006 Sep;11(3-4):339-55.

Ciccocioppo R, Economidou D, Rimondini R, Sommer W, Massi M, Heilig M. Buprenorphine Reduces Alcohol Drinking Through Activation of the Nociceptin/Orphanin FQ-NOP Receptor System. **Biol Psychiatry**. 2006 Mar 11

Bachteler D, Economidou D, Danysz W, Ciccocioppo R, Spanagel R. The effects of acamprosate and neramexane on cue-induced reinstatement of ethanol-seeking behavior in rat. **Neuropsychopharmacology**. 2005 Jun;30(6):1104-10.

Ciccocioppo R, Martin-Fardon R, Weiss F. Stimuli associated with a single cocaine experience elicit long-lasting cocaine-seeking. **Nat Neurosci**. 2004 May;7(5):495-6. Epub 2004 Mar 28.

Ciccocioppo R, Fedeli A, Economidou D, Policani F, Weiss F, Massi M. The bed nucleus is a neuroanatomical substrate for the anorectic effect of corticotropin-releasing factor and for its reversal by nociceptin/orphanin FQ. **J Neurosci**. 2003 Oct 15;23(28):9445-51.

Ciccocioppo R, Martin-Fardon R, Weiss F. Effect of selective blockade of mu(1) or delta opioid receptors on reinstatement of alcohol-seeking behavior by drug-associated stimuli in rats. **Neuropsychopharmacology**. 2002 Sep;27(3):391-9.

Weiss F, Martin-Fardon R, Ciccocioppo R, Kerr TM, Smith DL, Ben-Shahar O. Enduring resistance to extinction of cocaine-seeking behavior induced by drug-related cues. **Neuropsychopharmacology**. 2001 Sep;25(3):361-72.

Ciccocioppo R, Sanna PP, Weiss F. Cocaine-predictive stimulus induces drug-seeking behavior and neural activation in limbic brain regions after multiple months of abstinence: reversal by D(1) antagonists. **Proc Natl Acad Sci U S A**. 2001 Feb 13;98(4):1976-81

Patents

Dr Ciccocioppo is inventor for the following patents:

Andrographis Paniculata Compositions and Methods for Treatment of Addictions

Application number: 20140072662

Type: Application

Filed: July 3, 2013

Issued: March 13, 2014

Inventor: Roberto Ciccocioppo

Compositions and Methods for Prophylaxis and Treatment of Addictions

Application number: 20130296347

Type: Application

Filed: March 29, 2013

Issued: November 7, 2013

Inventor: Roberto Ciccocioppo

Treatment of Addiction and Impulse-Control Disorders Using PDE7 Inhibitors

Application number: 20130267502

Type: Application

Filed: March 15, 2013

Issued: October 10, 2013

Inventors: Gregory A. Demopoulos, George A. Gaitanaris, Roberto Ciccocioppo

Compositions and methods for prophylaxis and treatment of addictions

Patent number: 8426439

Type: Grant

Filed: April 11, 2008

Issued: April 23, 2013

Assignee: Omeros Corporation

Inventor: Roberto Ciccocioppo

Agent for prophylaxis or treatment of alcohol dependence or drug dependence

Patent number: 820720

Type: Grant

Filed: October 16, 2007

Issued: June 26, 2012

Assignee: Mitsubishi Tanabe Pharma Corporation

Inventors: Koji Teshima, Roberto Ciccocioppo, Maurizio Massi

COMPOSITIONS AND METHODS FOR PROPHYLAXIS AND TREATMENT OF ADDICTIONS

Application number: 20100234413

Type: Application

Filed: March 11, 2010

Issued: September 16, 2010

Assignee: OMEROS CORPORATION

Inventor: Roberto Ciccocioppo

Agent for prophylaxis or treatment of alcohol dependence or drug dependence

Application number: 20100069382

Type: Application

Filed: October 16, 2007

Issued: March 18, 2010

Inventors: Koji Teshima, Roberto Ciccocioppo, Maurizio Massi

COMPOSITIONS AND METHODS FOR PROPHYLAXIS AND TREATMENT OF ADDICTIONS

Application number: 20090048232

Type: Application

Filed: April 11, 2008

Issued: February 19, 2009

Inventor: Roberto Ciccocioppo

Scientific communications

Dr. Ciccocioppo presented more than 300 works as scientific conferences. On numerous occasions he has served as "Invited Speaker".