

Rafael MALDONADO, Full Professor of Pharmacology (*Catedrático de Universidad*).

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H-index = 84 (411 scientific articles in peer-reviewed journals, 25,065 citations, 61 cit/art)

Number of doctoral thesis supervised in the last 10 years: 33.

Total publications in first quartile (Q1): 322. During the last 5 years in first quartile (Q1): 64 (out of a total of 78).

Rafael Maldonado, MD, PhD, received his **Medical Degree** in 1985 from the School of Medicine of the University of Cadiz (Spain), where he also obtained a **PhD in Neuropsychopharmacology** in 1988 on the effects of benzodiazepines and antidepressants on opioid dependence. In 1990, he obtained a **PhD in Molecular Pharmacology** (INSERM U 266) at the School of Pharmacy (University René Descartes Paris V, France) on the participation of the endogenous opioid system on dependence and emotional disorders. Then, he was a postdoctoral fellow (1990-1991) at The **Scripps** Research Institute (La Jolla, USA), directed by Prof. G.F. Koob, where he studied the neuroanatomical substrate of opioid dependence and cocaine self-administration. Thereafter, he returned to the laboratory of Molecular Pharmacology (**INSERM U266**), directed by Prof. B.P. Roques in Paris, he obtained permanent position as Scientific Researcher (CR-1) in the INSERM (1992) and lead a pharmacological team devoted to the study of the cannabinoid and opioid systems by using pharmacological and molecular approaches. In 2000, he obtained a permanent position as Professor at the **University Pompeu Fabra** in Barcelona, where he is director of the Laboratory of Neuropharmacology, and studies the physiological role of the **endogenous cannabinoid and opioid systems** in pain, addiction, eating, affective and cognitive disorders, with a particular focus in the development of **behavioural models** and **novel treatments** for those disorders. He has 12 **patents** (4 licensed/commercialised) and 2 **models of utility** (licensed), and has obtained contracts with industry exceeding 2.000.000 € in the last 5 years. He has been **external advisor** to several public bodies including the World Health Organization, EMCDDA, European Commission DGs SANCO & RTD and NIH-NIDA, among others. His research has focused on the neurobiological basis of chronic pain, drug dependence, affective disorders and food intake, using pharmacological and genetic strategies. His most outstanding scientific contributions have been:

1) The identification of key neurobiological mechanisms in the development of addiction. Of particular impact has been the work identifying the crucial role of the transcription factor CREB (Science, 1996), mu (Nature, 1996; Biol Psych, 2017) and delta opioid receptors (Biol Psych, 2011;2015), dopaminergic (Nature, 1997; PNAS, 2008), orphanin receptors (Nat Neurosci, 2005; Biol Psych, 2018), cannabinoid CB1 (Biol Psych, 2008; 2008; Science, 2014; Trends Neurosci, 2006, Nat Commun, 2020; Nat Med, 2023), ERK1 signaling pathways (Neuron, 2002), serotonergic (Biol Psych, 2007) and hypocretinergic (Biol Psych, 2012, Biol Psych 2013) systems and epigenetic factors (Nat Commun, 2023). These findings may facilitate new drugs development for the treatment of addiction (drug identified in Science 2024 in Phase IIb clinical trial) and to improve the management of these disorders.

2) The identification of certain key neurobiological mechanisms in the development of emotional disturbances: identification of the role of the transcription factor CREM (PNAS, 1999), delta opioid receptor (Nat Gen, 2000), cannabinoid CB1 (Nat Rev Neurosci, 2015) in such disorders.

3) The identification of mechanisms explaining cognitive alterations related to the endocannabinoid system (Nat Neurosci, 2009; Biol Psych, 2011; Nat Met, 2013; PNAS 2016) and motor disorders produced by cannabis (J Clin Inv, 2013).

4) The identification of new therapeutic targets for the treatment of osteoarthritic, neuropathic and endometrial pain such as cannabinoid receptors CB1 (eLife, 2020; Pain, 2016) and CB2 (J Neurosci, 2008a, 2008b; Pain, 2013; eLife, 2020), 5HT7 serotonergic (Pain, 2010), sigma (Brit J Pharmacol, 2019), delta opioid (Pain, 2011; Brit J Pharmacol, 2020) and enkephalin degradation system (Brit J Pharmacol, 1995; 1996; 2018; 2021), which have led to a better understanding of the pathophysiological mechanisms to facilitate new and more efficient therapeutic strategies while minimizing undesirable effects.

5) The identification of specific microbiota profiles associated with memory (Cell Metab, 2020; Sci Adv, 2023), obesity (Microbiome 2020a; Gut, 2021) and food addiction (Gut 2024, Nat Metab 2024) through particular metabolic pathways and/or metabolic profiles, the role of specific Caudoviral bacteriophages in executive function and memory (Cell Host Microbe, 2022), the impact on depression of microbiota alterations in proline metabolism via GABA and extracellular matrix homeostasis (Cell Metab, 2022), as well as sexual dimorphism in the microbiota implicated in obesity and menopausal status (Microbiome, 2020b).

10 relevant publications in the last 5 years as corresponding author

1. Castells-Nobau, A.; Puig I.; Motger-Albertí, A.; et al; Maldonado, R.*(AC), Fernández-Real*, JM.; Mayneris-Perxachs*, J.; (20/22, AC). 2024. Microviridae bacteriophages influence behavioral hallmarks of food addiction via tryptophan and tyrosine signaling pathways. **Nature Metabolism** (Under second revision with minor comments). NATMETAB-A23038558D. IF: 18.9.

2. Samulénaité, S.; García-Blanco, A.; Mayneris-Perxachs, J.; et al; Maldonado, R*(AC), Martin-Garcia*, E.; (18/19, AC). 2024. Gut microbiota signatures of vulnerability to food addiction in mice and humans. *Gut*. 2024 Jun 26:gutjn1-2023-331445. IF: 24.5.
3. Grau, S; Vela, J-M; Gurt, A; et al; Maldonado, R*(AC), Monfort*, J.; (10/11, AC). 2024. Efficacy of SIGMAR1-based therapy in the early treatment of confirmed mild symptomatic COVID-19 patients. *Journal of Infection*. 88:187-190. IF: 38,6.
4. Cheron J, Beccari L, Hagué P; et al; Maldonado R. (AC), de Kerchove d'Exaerde A; (11/14, AC). 2023. USP7/Maged1-mediated H2A monoubiquitination in the paraventricular thalamus: an epigenetic mechanism involved in cocaine use disorder. *Nature Communications*. 14; 8481. IF: 14.9.
5. Mayneris-Perxachs, J.; Castells-Nobau, A.; Arnoriaga-Rodríguez, M.; et al; Maldonado, R.*(AC), Fernández-Real*, JM.; (18/19, AC). 2022. Caudovirales bacteriophages are associated with improved executive function and memory in flies, mice, and humans. *Cell Host and Microbe*. 30-3, pp.340-356. IF: 30.3.
6. García-Blanco, A.; Domingo-Rodríguez, L.; Cabana-Domínguez, J.; et al; Maldonado, R. (AC) (15/15,AC). 2022. MicroRNAs signatures associated with vulnerability to food addiction in mice and humans. *Journal Clinical Investigation*. e156281. IF: 15.9.
7. Mayneris-Perxachs, J.; Arnoriaga-Rodríguez, M.; Martin, M.; et al; Maldonado R.*(AC), Fernández-Real*, JM.; (27/28, AC). 2022. Microbiota alterations in proline metabolism impact depression. *Cell Metabolism*. 34-5, pp.681-701. IF: 29.1.
8. Arnoriaga-Rodríguez, M.; Mayneris-Perxachs, J.; Contreras-Rodríguez, O.; et al; Maldonado, R.*(AC), Fernández-Real*, J.M.; (28/29, AC). 2021. Obesity-Associated Deficits in Inhibitory Control Are Phenocopied to Mice through Gut Microbiota Changes in One-Carbon and Aromatic Amino Acids Metabolic Pathways. *Gut*. 70-12, pp.2283-2296. IF: 31.7.
9. Domingo-Rodríguez, L.; Ruiz de Azua, I.; Dominguez, E.; et al; (16/16) Maldonado, R. (AC). 2020. A specific prelimbic-nucleus accumbens pathway controls resilience versus vulnerability to food addiction. *Nature Communications*. 11-1. IF: 14.9.
10. Arnoriaga-Rodríguez, M.; Mayneris-Perxachs, J.; Burokas, A.; et al; Maldonado, R.*(AC), Fernández-Real*, J.M.; (26/27, AC). 2020. Obesity Impairs Short-Term and Working Memory through Gut Microbial Metabolism of Aromatic Amino Acids. *Cell Metabolism*. 32-4, pp.548-560.e7. IF: 27.2.

10 relevant research project in the last 5 years as principal investigator

1. Study of the vulnerability to cocaine use disorder after alcohol consumption. Fundació La Marató. **Coordinator:** Rafael Maldonado. 2023-2026. Overall budget: 400.000 €. Group's budget: 155.000 €.
2. LCF/PR/HR22/52420017, Involvement of the gut microbiota-brain cross talk in the loss of eating control. Caixa Research Health. **Coordinator:** Rafael Maldonado. 2022-2025. 1.000.000 €. Group's budget: 400.000 €.
3. PNSD 2021I076, Estudio de las alteraciones conductuales y de la conectividad neural producidas por la exposición a cannabis durante la adolescencia. Plan Nacional sobre Drogas. Principal Investigator: Rafael Maldonado. 2022- 2024. 70.131 €.
4. PID2020-120029GB-I00, New approaches to clarify the biological substrate underlying food addiction. Principal Investigator: Rafael Maldonado. 2021-2024. 447.700 €.
5. H2020-SC1-2019-2-RTD-848068, Effective combinational treatment of chronic pain in individual patients, by an innovative quantitative systems pharmacology pain relief approach (QSPain Relief). European Commission H2020. Principal Investigator: Rafael Maldonado. 2020-2024. 6.239.538,75 €. Group's budget: 845.000 €.
6. H2020-SC1-2019-2-RTD-848099, Molecular Mechanisms Associating Chronic Pain with Fatigue, Affective Disorders, Cardiovascular Disease and Total Comorbidity (PainFACT). European Commission H2020. Principal Investigator: Rafael Maldonado. 2020-2024. 6.000.000 €. Group's budget: 655.000 €.
7. PDC2021-121434-I00, Co-adjuvant peptides to avoid side effects associated to cannabis use to treat chronic pain. Ministerio de Ciencia e Innovación. Principal Investigator: Rafael Maldonado. 2021-2023. 149.500 €.
8. RTC-2017-6689-1, Identification of novel therapeutic targets for neuropathic pain in neurons and glial cells (RIBOPAIN). Ministerio de Ciencia e Innovación. Universidades. Principal Investigator: Rafael Maldonado. (Universitat Pompeu Fabra). 2018- 2021. 400,000 €.
9. RD16/0017/0020, Redes temáticas de investigación cooperativa en salud (RETICS) del Instituto de Salud Carlos III. Red de trastornos adictivos (RTA). Instituto de Salud Carlos III. Principal Investigator: Rafael Maldonado. 2017-2021. 253.808,5 €.
10. CI18-00045, Fighting pain with cannabis avoiding side-effects. La Caixa Banking Foundation Call CaixaImpulse. Principal Investigator: Rafael Maldonado. 2018- 2019. 70.000 €.