

<b>Parte A. PERSONAL INFORMATION</b>		<b>Fecha del CVA</b>		<b>01-11-2020</b>
Nombre y apellidos	Consuelo Guerri Sirera			
DNI/NIE/pasaporte		Edad		
Núm. identificación del investigador	Researcher ID	B-5181-2014		
	Código Orcid	0000-0002-0330-7556		

**A.1. Current professional status**

Organismo	Fundacion Valenciana Centro de Investigación Príncipe Felipe			
Dpto./Centro	Centro de Investigación Príncipe Felipe			
Dirección	Eduardo Primo Yufera 3, 46012-Valencia			
Teléfono	96 3289680	correo electrónico	<a href="mailto:cguerri@cipf.es">cguerri@cipf.es</a>	
Categoría profesional	Investigador senior	Fecha inicio	1979	
Espec. cód. UNESCO	2302,2402,,3214			
Palabras clave	Alcohol, desarrollo de cerebro, neuroinmunología, TLR4, células gliales, neurodegeneración, neuropatologías, adolescencia, síndrome alcohólico fetal			

**A.2. Academic background**

**A.1. (título, institución, fecha)**

Licenciatura/Grado/Doctorado	Universidad	Año
Lda. Biología y Bioquímica	Universidad de Valencia	1974
-Dra Bioquímica	University of Valencia	1978
-Fellow in Biochemistry and Research Associate	University of Kansas City, Medical School	1974-1976
- Dra en Bioquímica,	University of Valencia	1978
Profesor	Pharmacology Dept. University of Kansas City, Medical School	1983-2000
Researcher	Instituto de Investigaciones Citológicas	1978-2005
Head of Cell and Molecular Pathology	Centro de Investigación Príncipe Felipe	2005-2020

**A.2. A.3. indicators of scientific production**

**Directed Theses: total 26+3 in progress**  
**Number of publications: 173 (Pub-MED)**  
**Publications in first quartile: 110**  
**Total citations: 11.700; Index H: 59**

**Parte B. SHORT SUMMARY OF THE CV**

My scientific career began in 1974, where after finishing my Bachelor's degree and Biology and Thesis, I went to work with Professor Santiago Grisolia to the Department of Biochemistry of the Faculty of Medicine at the University of Kansas City, where I formed in Biochemistry and Molecular Biology and do my Doctoral Thesis. My first my first scientific works were in enzymology, and one of my first scientific contribution was to demonstrate that acetaldehyde and formaldehyde, products derive from ethanol and methanol metabolism, respectively, exert significant toxic effects by reducing the anti-oxidants levels, triggering oxidative stress. These findings introduced me to the field of ethanol and methanol toxicity. Upon returning from the USA I joined one of the few biomedical research centers in Valencia in those years, Institute of Cytological Research. At this stage my studies and findings were pioneers in developing an experimental model of fetal alcohol syndrome (FAS), confirming that ethanol is a teratogen. We also investigated the mechanisms involved in the effects of ethanol on the developing brain, including the participation of radial glia dysfunction and astrocytes in the neuroteratogenesis of alcohol and in FAS, being the only European group working on this issue. In 2005, I was incorporated as head of Cell Molecular Laboratory at the Principe Felipe Research. At this time based on the first studies tin humans showing that adolescence is a stage of brain maturation, in which certain brain regions ( e.g. prefrontal cortex and limbic system) are still in the maturation stage, we develop an experimental model of intermittent

binge-drinking in adolescent animals, demonstrating for the first time, that alcohol by activating the innate immune system can cause neuro-inflammation and brain damage associated with cognitive and behavioral dysfunctions that are permanent in adulthood, effects that have been corroborated in humans. The scientific contributions of our group about the molecular mechanisms of alcohol neurotoxicity, alterations in synapses and myelin during adolescence, and specifically the involvement of the response of the neuroimmune system and TLR4 receptors activation, have been pioneers with a great international scientific relevance. In fact, I believe that one of the main scientific contributions I have made in the last 20 years has been to demonstrate how ethanol through its interaction with membrane microdomains (lipid rafts) activates the immune system receptors TLR4 in macrophages and glial cells (J. Immunol, 2005,2009), causing neuroinflammation and brain damage (J. Neurosci, 2010, Glia 2012). The elimination of TLR4 receptors, prevents brain damage and cognitive alterations in both adults and adolescents, indicating their participation in the effects of ethanol on the brain. Recently we have demonstrated the participation of the TLR4 response in the damage caused by alcohol during the embryo-fetal phase and that could cause fetal alcohol syndrome. The relevance of our work and the mechanisms of neuroinflammation in neurodegenerative and in mental diseases, led to the initiative of the National Institute of Health Abuse and Alcoholism (NIAAA) to prioritize projects on this topic, where I was invited to evaluate research projects. During the last years, our interest has focused on the molecular mechanisms of the actions of alcohol on TLR4 response within the brain, and using TLR4-KO mice with or without alcohol consumption as controls, since the ethanol-induced neurotoxic and behavioral dysfunction are not observed in TLR4-KO mice. The significance of the findings in the field of ethanol actions on the adult and developing brain (adolescence and fetal period) is shown by the increase in citations of our published manuscripts during the recent years (see Citation Report, Web of Science ).(<https://scholar.google.com/citations?user=5lqyEmsAAAAJ&hl=es>)

### C.1. Publications (including books)

- 1-**Pascual M**, López-Hidalgo R, Montagud-Romero S, Ureña-Peralta JR, Rodríguez-Arias M, and **Guerrero C**. Role of mTOR-regulated autophagy in spine pruning and memory impairments induced by Binge-like ethanol treatment in adolescent mice, *Brain Pathol* 2020 ( in press)
- 2 -**Ibáñez F**, **Ureña-Peralta J**, **Costa-Alba P**, **Torres JL**, **Laso FJ**, **Marcos M**, **Guerrero C**, **Pascual M**. Circulating MicroRNAs in Extracellular Vesicles as Potential Biomarkers of Alcohol-Induced Neuroinflammation in Adolescence: Gender Differences. *Int J Mol Sci* 21: 6130, 2020.
- 3- **Ureña-Peralta JR**, **Pérez-Moraga R**, **García-García F**, **Guerrero C**. Lack of TLR4 modifies the miRNAs profile and attenuates inflammatory signaling pathways, *Plos One* 15(8):e0237066, 2020.
- 4- **Casanova-Ferrer F**, **Pascual M**, **Hidalgo MR**, **Malmierca-Merlo P**, **Guerrero C**, **García-García F**. Unveiling Sex-Based Differences in the Effects of Alcohol Abuse: A Comprehensive Functional Meta-Analysis of Transcriptomic Studies *Genes* 21;11(9):E1106. 2020: 10.3390.
- 5- **Pascual M**, **Ibáñez F**, **Guerrero C**. Exosomes as mediators of neuron-glia communication in neuroinflammation. *Neural Regen Res.* 15(5):796-80, 2020
- 6- **Pascual M**, **Ureña-Peralta J** and **Guerrero C**. The Regulatory Role of miRNAs in Ethanol-induced TLR4 Activation and Neuroinflammation. *Current, Pathobiology Reports* vol, 8, 37–45( 2020) .
- 7- **Ibáñez F**, **Montesinos J**, **Ureña-Peralta JR**, **Guerrero C**, **Pascual M**, TLR4 participates in the transmission of ethanol-induced neuroinflammation via extracellular vesicles *J. Neuroinflammation*16(1):136, 2019
- 8- **Guerrero C** and **Pascual M** , Role of neuroinflammation in ethanol neurotoxicity, In :*Advances in Neurotoxicology*. Vol 3, pg 359-394, 2019.
- 9- **Ureña-Peralta JR**, **Alfonso-Loeches S**, **Cuesta-Diaz CM**<sup>1</sup>, **García-García F**<sup>2</sup>, **Guerrero C**. Deep sequencing and miRNA profiles in alcohol-induced neuroinflammation and the TLR4 response in mice cerebral cortex. *Sci Rep.* 8 : 15913 , 2018
- 10- **Marco EM**, **Peñasco S**, **Hernández MD**, **Gil A**, **Borcel E**, **Moya M**, **Giné E**, **López-Moreno JA**, **Guerrero C**, **López-Gallardo M**, **Rodríguez de Fonseca F**. Long-Term Effects of Intermittent Adolescent Alcohol Exposure in Male and Female Rats. *Front Behav Neurosci.*;11:233, 2017
- 11- **Pascual M**, **Montesinos J**, **Montagud-Romero S**, **Forteza J**, **Rodríguez-Arias M**, **Miñarro J**, **Guerrero C**. TLR4 response mediates ethanol-induced neurodevelopment alterations in a model of fetal alcohol spectrum disorders. *J.Neuroinflammation*, 4(1):145, 2017.
- 12- **C Guerrero and M,Pascual**, Effects of alcohol on embryo/fetal development. In **REPRODUCTIVE**

TOXICOLOGY ( Ed Ramesh C Gupta) pp 431-445. Academic Press , ISBN; 978-0-12-804239-7, 2017

### Relevant publications

- Montesinos J, Alfonso-Loeches S, **Guerri C**. Impact of the Innate Immune Response in the Actions of Ethanol on the Central Nervous System, Alcohol Clin Exp Res, 40(11):2260-2270, 2016 (Citations 110)
- Montesinos J, **Pascual M**. Pla A, Maldonado C, Rodríguez-Arias M, Miñarro J and **Guerri C**, TLR4 elimination prevents synaptic and myelin alterations and long-term cognitive dysfunctions in adolescent mice with intermittent ethanol treatment. Brain Behav. Immunol 45:233-44, 2015
- Montesinos J, **Pascual M**, Pla A, Maldonado C, Rodríguez-Arias M, Miñarro J, **Guerri C**. Involvement of TLR4 in the long-term epigenetic changes, rewarding and anxiety effects induced by intermittent ethanol treatment in adolescence. Brain Behav Immun. 53:159-171, 2016
- Alfonso-Loeches S, Pascual M, Gómez-Pinedo U, Pascual-Lucas M, Renau-Piqueras J, **Guerri C**. Toll-like receptor 4 participates in the myelin disruptions associated with chronic alcohol abuse. Glia. 60(6):948-64, 2012
- Alfonso-Loeches S, Pascual-Lucas M, Blanco AM, Sanchez-Vera I, **Guerri C**. Pivotal role of TLR4 receptors in alcohol-induced neuroinflammation and brain damage J Neurosci. 30(24):8285-95, 2010
- Fernández-Lizarbe S, Pascual M, **Guerri C**. Critical role of TLR4 response in the activation of microglia induced by ethanol. J. Immunol. 183(7): 4733- 4744, 2009 (IF:6.1)
- Blanco AM, Vallés SL, **Pascual M**, **Guerri C**. Involvement of TLR4/IL-1RI signalling in the induction of inflammatory mediators and cell death induced by ethanol in cultured astrocytes. J. Immunol. 175: 6893-6899, 2005

### D1 Projects Granted.

During the last 40 years, my research has been continuously funded by different National and International ( EU, NIH-NIAAA) Research Agencies( EEUU) ( 40 Research Grants). Current and Grants are included

**Title;** *Neuroinflamacion and alterations in brain plasticity in adolescent mice with alcohol abuse: Gender differences biomarkers and treatments*

**Research agency** Ministerio de Sanidad y Política Social. Delegación del Gobierno para el Plan Nacional sobre Drogas (2018 I003), 01-01 -2019 to 1-2021, 98,99.850 ,00€,

**PI** :C. Guerri

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**Título :** *MicroRNAs as biomarkers of the neuroinflammation associated with alcohol abuse: Diagnostic and therapeutic implications*

**Research Agency:** Ministerio de Economía y Competitividad (SAF2015-SAF2015-.69187R) 1-02-2016 , hasta: 30-12-2020, 160,000 €

**PI; C, Guerri;**

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**Title.** Retics, Red- de Transtornos Adictivos,

**Reserach Agency:** Carlos III, RD16 0017 0004 (2016-2021)

**From** 1-08-2016., 01-08-2021,

**PI:** C. Guerri, 150.302,00€

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**Título.:** Biomarkers of neuroinflammation associated with alcohol abuse and treatment

**Research Agency:** Ministerio de Sanidad y Política Social. Delegación del Gobierno para el Plan Nacional sobre Drogas.

**Duración, from** 02 -2016 **to:** 02-2019, 99.850 ,00€,

**PI : C. Guerri**

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### D1- Awards and recognition

-Silver Medal of the *Orden al Mérito del Plan Nacional Sobre Drogas*, Ministerio

- de Sanidad (BOE, 13 de mayo 2016).
- *Scientific recognition to the scientific career, Valencian Health Ministry (Conselleria de Sanitat) (2015)*
  - *Manfred Lautenschlaeger Award (ESBRA, 2011) (25.000 €),*
  - Isabel de Villena Award (Valencia, 2012).
  - Research Society for Alcohol Research (USA), "Recognition of contribution to the alcohol Research field", 2001.
  - Fetal alcohol Study Group (RSA) (USA), "Recognition of outstanding research advancing the understanding of the mechanisms underlying FAS and alcohol-related Birth defects", 2002.

## **D2- Participation in National and International Committees**

- Member of the Publication Committee of Federations of European Biochemical Societies (FEBS, 2019-2022).
- Member of the Board of the Valencian Innovation Agency (2018-2022)
- ANEP, from 1995-2020
- Member of the Jury of the JAIME I PRIZE, (2016-2019)
- Advisory member of the WHO, in an international project on Fetal Alcohol Syndrome (2010-2014).
- Member of advisers to the Ministry of Health "Alcohol consumption in Adolescents (2012-2013).
  
- Member of the Board of Directors of the International Society for Biomedical -Research on Alcohol (ISBRA) ((1981-1985, 1998-2002, 2002-2006, 2006-2010).
- .- Chairman of the Publication Committee of ISBRA (2006-2012) and member of the Board of Directors de la European Society for Biomedical - Research on Alcoholism (ESBRA) (1985-1989; 1990- 1994, 2000-2004, 2004- 2008, 2009-2012).
- President of the ESBRA AWARD (1990, 1992, 1994, 1996, 1998, 2000, 2004-2010).
- Member of the committee of experts of INSERN (Institut National de la Santé et de la Recherche Médicale, France (2006-2017).
- Member of the Committee of experts of AERES (Assises Nationales de l'enseignement Supérieur et la Recherche) for the evaluation of research groups and research projects (2010- 2020)

## **D3 Participación in International Reserach Gant Committees**

- NIAAA (National Institute of Alcohol Abuse and Alcoholism) USA , 2009, 2010, 2011,2012
- French National Research Agency (ANR, 2010-2011-,2014-2015),
- Israel Science Foundation, 2010-2011, 2013-2014
- US-Israel Binational Science Fountation, 2015-2016
- European Foundation for Alcohol Research, 2011-2015
- The Netherlands Organisation for Health Research and Development, 2014-2015.
- Britain's Medical Research Council, Neuroscience, 2010, 2011, 2012
- German Research Foundation DFG, 2013-14
- Colombia Projects ( Univ Antonio Nariño), 2015-2017
- FONTCYT, Argentina, 2014-2020

## **D4 Member of Editorial Committees of Journals and Societies**

- Editorial Board member of journals
- -" Alcoholism: Clin. Exp. Res. (EEUU) 2005-2013.
- Alcohol and Alcoholism (UK) 1990-presente.
- "Editorial Board Member" de la revista Addiction Biology 1996-2005.
- Alcohol (EEUU), 1995-Presente.
- " Neurochemical Researchh"( 2010-presente)
- "Drug and alcohol Dependence (2013).
- "Adicciones" (2013-presente)

### **Student training and doctoral PH theses**

I have directed 26 Ph. D theses, 7 during the last 10 years and 4 of them were awarded with “*Premio Extraordinario*” by the University of Valencia. Likewise, three PH.D students are finishing their Ph,D research work. I have directed research work to 5 students for TFGs and 3 TFMs.