

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel in the order listed for Form Page 2.
Follow the sample format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME		POSITION TITLE	
Fernández-Checa, José Carlos		Principal Investigator	
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
University Complutense of Madrid, Spain	MS	1975-1980	Biochemistry
University Complutense of Madrid, Spain	BS	1980-1982	Biochemistry
University Complutense of Madrid, Spain	Ph.D	1980-1985	Biochemistry

A- Positions and Honors

- 1985-1988 Postdoctoral Fellow, UCLA, Los Angeles, CA
- 1988- 1990 Assistant Research Professor, UCLA, Los Angeles, CA
- 1990-1992 Assistant Research Professor, USC, Los Angeles, CA
- 1992-1997 Investigator, University of Barcelona
- 1997-Present Investigator, Spanish Council for Research Research, Instituto Investigaciones Biomedicas, Barcelona.

Member of the following American and International Societies:

- American Society for the Study of Liver Diseases (AASLD) 1991- present
- American Association for the Advancement of Science (AAAS) 1992-present
- American Society for Research in Vision and Ophthalmology (ARVO) 1992-present
- Asociación Española para el Estudio del Hígado (AEEH), 1993-present
- American Society of Biochemistry and Molecular Biology (2002- present)

EDITORIAL BOARD

- Member of the "American Journal of Physiology: Gastrointestinal and Liver Physiology" Editorial Board (June 1996- June 1997).
- Member of the "Hepatology" Editorial Board (1997-2004).
- Member Editorial Board, Annals of Hepatology (2003- present)

B. Selected peer-reviewed publications (from 1997-present).

1. Fernández-Checa J. C., García-Ruiz C., and Kaplowitz N. GSH transport in mitochondria: defense against TNF-induced oxidative stress and alcohol-induced defect. *Am. J. Physiol.* 273:G7G-17, 1997.
2. Kannan R., Fernández-Checa J.C, García-Ruiz C., Mackic M.J., Zlokovic B.V: Lens and hepatic glutathione and cysteine regulation in galactose-fed guinea-pigs. *Curr. Eye Res.* 16: 365-371, 1997.
3. Goldin E., Ardite E., Elizalde J I., Odriozola A., Panés J., Pique J. M., and Fernández-Checa J.C.: Gastric mucosal damage in experimental diabetes in rats: role of endogenous glutathione. *Gastroenterology* 112, 855-863, 1997.
4. C. García-Ruiz, A. Colell., M. Marí, and Fernández-Checa J.C. Direct effect of ceramide on the mitochondrial electron transport chain leads to generation of reactive oxygen species: Role of mitochondrial glutathione. *J. Biol. Chem.*, 272:11369-11377, 1997.
5. A. Colell, C. García-Ruiz, Morales A., Ballesta A., Ookhtens M., Rodés J., Kaplowitz N. and Fernández-Checa J.C.: Transport of reduced glutathione in hepatic mitochondria and mitoplasts from ethanol-induced treated rats: effect of membrane physical properties and S-adenosyl-L-methionine. *Hepatology*, 26:699-708, 1997.

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6. Morales A., García-Ruiz C., Miranda M., Marí M., Colell A., Ardite E. and Fernández-Checa J.C. Tumor necrosis factor increases hepatocellular GSH levels by transcriptional regulation of the heavy subunit chain of g-glutamylcysteine synthetase. *J. Biol. Chem.*, 272:30371-30379, 1997.
7. A. Barrientos, J. Casademont, F. Cardellach, E. Ardite, X. Estivill, A. Urbano-marquez, J.C. Fernández-Checa and V. Nunes. Qualitative and quantitative changes in skeletal muscle mtDNA and expression of mitochondrial-encoded genes in the human aging process. *Biochem. Mol. Med.* 62: 165-171, 1997.
8. A. Morales, Miranda M., Sánchez-Reyes A., Colell A., Biete and Fernández-Checa J.C. Transcriptional regulation of the heavy subunit chain of g-glutamylcysteine synthetase by ionizing radiation. *FEBS Letts*, 427:15-21, 1998.
9. A. Morales, Sánchez-Reyes A., Ferrer F., A. Biete, and Fernández-Checa J.C. Oxidative damage of mitochondrial and nuclear DNA by ionizing radiation. *Int. J. Rad. Oncol. Biol. Phys.*, 42: 191-203, 1998.
10. F. Bosch-Morell, Colell A., J. C. Fernández-Checa and F. J. Romero. Chronic ethanol feeding induces cellular antioxidants decrease and oxidative stress in rat peripheral nerves. Effect of antioxidants. *Free Rad. Biol. Med.*, 25:365-368, 1998.
11. Ardite E., Panés J., Miranda M., A. Salas, Elizalde J., M. Sans, Y Arce, JM Bordas, Fernández-Checa J. C. and Piqué J.: Activation of transcription factor NF-kB in patients with inflammatory bowel disease: effects of steroid treatment. *Br. J. Pharmacol.*, 124:431-434, 1998.
12. Colell A., García-Ruiz C., Miranda M., Ardite E., Marí M., Morales A., Kaplowitz N. and Fernández-Checa J.C. Selective glutathione depletion of mitochondria by ethanol sensitizes hepatocytes to tumor necrosis factor. *Gastroenterology*, 115: 1541-1551, 1998.
13. Ardite E., Ramos C., L. Rimola A., Grande and Fernández-Checa J.C: Hepatocellular oxidative stress and initial graft injury in human liver transplantation. *J. Hepatology*, 31,921-927, 1999.
14. Román J., Colell A., Blasco C., Caballeria J., Parés A., Rodés J and Fernández-Checa J.C. Differential role of ethanol and acetaldehyde in the induction of oxidative stress in HepG2 cells: effect on transcription factors AP-1 and NF-kB. *Hepatology.*, 30: 1473-1480, 1999.
15. Román J., Gimenez M., Lluís J.M., Gassó M., Rubio M., Caballeria J., Parés A., Rodés J. and Fernández-Checa J.C. Enhanced DNA binding and activation of transcription factors Rel/NF-kB and AP-1 by acetaldehyde in HepG2 cells . *J. Biol. Chem.*, 275:14684-14690, 2000.
16. Ardite E., M. Sans., J. Panés, Romero F.J., J. M. Piqué and Fernández-Checa J.C.: Replenishment of glutathione levels improves mucosal function in experimental acute colitis. *Lab. Invest.*, 80:735-744, 2000.
17. García-Ruiz C., Colell A., París A and Fernández-Checa J. C. Direct interaction of GD3 ganglioside with mitochondria generates reactive oxygen species followed by mitochondrial permeability transition, cytochrome c release and caspase activation. *FASEB J.*, 14:847-858, 2000.
18. García-Ruiz C., Marí M., Morales A., Colell A., Ardite E., and Fernández-Checa J.C. Human placenta sphingomyelinase, an exogenous acid pH-optimum sphingomyelinase, induces oxidative stress, glutathione depletion and apoptosis in rat hepatocytes. *Hepatology*, 32, 56-65, 2000.
19. Colell A., García-Ruiz C., Román J., Ballesta A. and Fernández-Checa J. C. : Ganglioside GD3 enhances apoptosis by suppressing the nuclear factor-kB-dependent survival pathway. *FASEB J.*, 15:689-691, 2001.
20. Colell A., Coll O, García-Ruiz C., Paris R., Tiribelli C., Kaplowitz N. and Fernández-Checa J. C.. Tauroursodeoxycholate acid protects hepatocytes from ethanol-fed rats against tumor necrosis factor-induced cell death by replenishing mitochondrial glutathione. *Hepatology*, 2001; 34(5):964-71
21. Colell A., García-Ruiz C., Román J., Ballesta A. and Fernández-Checa J. C. : Ganglioside GD3 enhances apoptosis by suppressing the nuclear factor-kB-dependent survival pathway. *FASEB J.* 2001, 15:1068-1070.
22. Colell A., Morales A., Fernández-Checa J.C. and Garcia-Ruiz C. Acidic sphingomyelinase contributes to tumor necrosis factor-a-mediated cell death in human HT-29 cells through glycosphingolipids generation. Role of ganglioside GD3. *FEBS Lett* 526, 137-142, 2002.
23. Garcia-Ruiz C, Colell A, Mari M, Morales A, Calvo M, Enrich C, Fernandez-Checa JC. Defective TNF-alpha-mediated hepatocellular apoptosis and liver damage in acidic sphingomyelinase knockout mice. *J Clin Invest.* 111:197-208, 2003.

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24. Mari M, Colell A, Morales A, Paneda C, Varela-Nieto I, Garcia-Ruiz C, Fernandez-Checa JC. Acidic sphingomyelinase downregulates the liver-specific methionine adenosyltransferase 1A, contributing to tumor necrosis factor-induced lethal hepatitis. *J Clin Invest.* 113:895-904, 2004.
25. Lluís JM, Morales A, Blasco C, Colell A, Mari M, Garcia-Ruiz C, Fernandez-Checa JC. Critical role of mitochondrial glutathione in the survival of hepatocytes during hypoxia. *J Biol Chem.* 280:3224-3232, 2005.
26. Fernandez-Checa JC, Kaplowitz N. Hepatic mitochondrial glutathione: transport and role in disease and toxicity. *Toxicol Appl Pharmacol.* 204:263-273, 2005.

C. Research support

Ongoing research support:

1. Principal Investigator: "Apoptosis y expresión génica por hipoxia y glicoesfingolípidos: Relevancia en la hepatopatía alcohólica y terapia del cáncer." SAF 2001-2118. Plan Nacional I+D. 28-12-01-28-12-04. Total proyecto 28.000.000 pts.
2. Principal Investigator : " S-adenosyl-L-methionine, mitochondrial GSH and liver disease". National Institute of Alcohol Abuse and Alcoholism (NIAAA, USA). 1R21 AA014135-01. Sep/30/2002 -Aug 31/2005. \$UDS 324.000.
3. Investigador Principal: "Mitochondria, signaling lipids and alcoholic liver disease". Research Subproject 1. University of Southern California Research Center for Alcoholic Liver and Pancreatic Diseases. Funded by National Institute Alcohol Abuse and Alcoholism (NIAAA, USA). Jan 2004-Dec 2008. \$ 729.438.
4. Principal Investigator : " Caracterización del tráfico de colesterol y gangliósido GD3 a la mitocondria: papel en el daño hepatocelular por alcohol". Plan Nacional I+D. Referencia SAF2003-04974. 210.000 euros. Dec 30, 2003-Dec 29, 2006.