



UNIVERSITA' DEGLI STUDI DI CAGLIARI  
Dipartimento di Scienze Biomediche

Editor-in-Chief

*World Journal of Gastroenterology.*

Cagliari, 12/27/2016

Dear Editor,

Our publication record in English dates back several decades. The senior author of this MS (EL, see his attached CV) has earned a PhD at the University of Toronto back in 1988.

Furthermore, the reviewer of our MS agreed that the language is excellent. We strongly feel that this is sufficient to certify that our MS complies with the standards required by your distinguished *Journal*.

Sincerely,

Fabio Marongiu on behalf of all authors

# CURRICULUM VITAE

## BIOGRAPHICAL INFORMATION:

Name	Ezio Laconi
Office Address	Dept. of Biomedical Sciences Unit of Experimental Medicine Via Porcell, 4, 09125 - Cagliari, Italy
Phone No.	011-39-070-675-8342
Fax No.	011-39-070-662574
e-mail	elaconi@unica.it
Date of Birth	November 21, 1957

## DEGREES:

1982	MD (magna cum laude), University of Cagliari, Cagliari, Italy
1988	PhD, Department of Pathology, University of Toronto, Toronto, Canada
1995	Clinical Oncologist, University of Cagliari, Italy

## EMPLOYMENT:

### Present Appointment:

2002- Associate Professor, University of Cagliari School of Medicine, Cagliari, Italy

### Previous Appointments:

1992-94:	Visiting Scientist, University of Toronto, Toronto, Canada.
1994-2002:	Assistant Professor, Division of Pathology, Oncology Hospital, Cagliari, Italy.
1996:	Visiting Scientist, Albert Einstein College of Medicine, Bronx, N.Y., USA
1997:	Visiting Scientist, Albert Einstein College of Medicine, Bronx, N.Y., USA
1998:	Visiting Scientist, Academic Medical Center, Amsterdam, The Netherlands
2000:	Visiting Scientist, Dept. of Pathology, Univ of Pittsburgh, PA, USA.

## MOST RELEVANT PUBLICATIONS:

1. E.Laconi, S.Dessì, B.Batetta, P.Pani, L.Pirisi, C.Andria, A.Macciotta. *Effect of phenobarbital treatment on erythrocyte Glucose-6-Phosphate Dehydrogenase in human newborns*. Pediatric.Pharmacol. 3: 59-62, 1983.
2. S.Dessì, E.Laconi, B.Batetta, P.Pani. *Effect of 3-MC on cholesterolemia and hepatic G-6-PD*. Res.Communic.Chem.Pathol.Pharmacol. 41: 333-336, 1983.
3. P.Pani, S.Dessì, K.N.Rao, B.Batetta, E.Laconi. *Changes in serum and hepatic cholesterol in lead-induced liver hyperplasia*. Toxicol.Pathol. 12: 162-167, 1984.
4. S.Dessì, B.Batetta, E.Laconi, C.Ennas, P.Pani. *Hepatic cholesterol in lead nitrate induced liver hyperplasia*. Chem.-Biol.Inter. 48: 271-279, 1984.
5. S.Dessì, C.Chiodino, B.Batetta, E.Laconi, C.Ennas, P.Pani. *Hexose monophosphate shunt and cholesterol synthesis in the diabetic and fasting states*. Exp.Mol.Pathol. 43: 177-186, 1985.
6. E.Laconi, S.Vasudevan, P.M.Rao, S.Rajalakshmi, D.S.R.Sarma. *Complementarity between two rat liver tumor promoters*. Toxicol.Pathol. 15: 198-201, 1987.
7. P.M.Rao, E.Laconi, S.Vasudevan, A.Denda, S.Rajagopal, S.Rajalakshmi, D.S.R.Sarma. *Dietary and metabolic manipulations of the carcinogenic process: role of nucleotide pool imbalances in carcinogenesis*. Toxicol.Pathol. 15: 190-193, 1987.
8. S.Vasudevan, E.Laconi, S.E.Abanobi, P.M.Rao, S.Rajalakshmi, D.S.R.Sarma. *Effect of glycine on the induction of orotic aciduria and urinary bladder tumorigenesis in the rat*. Toxicol.Pathol. 15: 194-197, 1987.
9. D.S.R.Sarma, E.Laconi, Z.Y.Chen, E.Farber. *Metabolic adaptations and their role in carcinogenesis*. ISI Atl.Sci.Pharm. 1: 311-314, 1987.
10. A.K.Ghoshal, E.Laconi, F.Willemsen, A.Ghoshal, T.H.Rushmore, E.Farber. *Modulation by calcium of the carcinogenic process in the liver induced by a choline-deficient diet*. Can.J.Physiol.Pharmacol. 65: 478-482, 1987.
11. E.Laconi, F.Li, E.Semple, P.M.Rao, S.Rajalakshmi, D.S.R.Sarma. *Inhibition of DNA synthesis in primary cultures of hepatocytes by orotic acid*. Carcinogenesis 9: 675-677, 1988.
12. G.Pichiri-Coni, P.Coni, E.Laconi, P.E.Schwarze, P.O.Seglen, P.M.Rao, S.Rajalakshmi, D.S.R.Sarma. *Studies on the mitoinhibitory effect of orotic acid on hepatocytes in primary culture*. Carcinogenesis 11: 981-984, 1990.
13. E.Laconi, S.Vasudevan, C.S.Rao, P.M.Rao, S.Rajalakshmi, D.S.R.Sarma. *Studies on the effect of dietary orotic acid on mouse liver carcinogenesis induced by diethylnitrosamine*. Cancer Lett. 49: 67-71, 1990.
14. P.E.Schwarze, G.Saeter, D.Armstrong, R.G.Cameron, E.Laconi, D.S.R.Sarma, V.Préat, P.O.Seglen. *Diploid growth pattern of hepatocellular tumours induced by various carcinogenic treatments*. Carcinogenesis 12: 325-327, 1991.
15. E.Laconi, P.M.Rao, S.Rajalakshmi, P.Pani, D.S.R.Sarma. *Chronic mitoinhibition during promotion of hepatocarcinogenesis*. Digest.Dis.Sci. 36: 1294-1298, 1991.
16. E.Laconi, D.S.R.Sarma, P.Pani. *Rat hepatocyte nodules are resistant to the necrogenic effect of D-galactosamine*. Carcinogenesis 13: 2459-2461, 1992.
17. E.Laconi, S.Vasudevan, P.M.Rao, S.Rajalakshmi, P.Pani, D.S.R.Sarma. *Increasing the interval between initiation and the onset of exposure to orotic acid decreases its promoting effect on rat liver carcinogenesis*. Carcinogenesis 14: 1701-1704, 1993.
18. E.Laconi, A.Denda, P.M.Rao, S.Rajalakshmi, P.Pani, D.S.R.Sarma. *Studies on liver tumor promotion in the rat by orotic acid: dose and minimum exposure time required for dietary orotic acid to promote hepatocarcinogenesis*. Carcinogenesis 14: 1771-1775, 1993.

19. E.Laconi, S.Vasudevan, P.M.Rao, S.Rajalakshmi, P.Pani, D.S.R.Sarma. *The effect of long-term feeding of orotic acid on the incidence of foci of enzyme-altered hepatocytes and hepatic nodules in Fischer 344 rats*. Carcinogenesis 14: 1901-1905, 1993.
20. E.Laconi, S.Vasudevan, P.M.Rao, S.Rajalakshmi, P.Pani, D.S.R.Sarma. *The development of hepatocellular carcinoma in initiated rat liver after a brief exposure to orotic acid coupled with partial hepatectomy*. Carcinogenesis 14: 2527-2530, 1993.
21. A.Sheikh, A.Yusuf, E.Laconi, P.M.Rao, S.Rajalakshmi, D.S.R.Sarma. *Effect of orotic acid on in vivo DNA synthesis in hepatocytes of normal rat liver and in hepatic foci/nodules*. Carcinogenesis 14: 907-912, 1993.
22. S.Manjeshwar, E.Laconi, P.M.Rao, S.Rajalakshmi, D.S.R.Sarma. *Influence of orotic acid on multistage hepatocarcinogenesis in the rat: Resistance of hepatocytes from nodules to the mito-inhibitory effects of orotic acid*. Proc.Soc.Expt.Biol.Med. 202: 25-29, 1993.
23. M.R.Rossiello, E.Laconi, P.M.Rao, S.Rajalakshmi, D.S.R.Sarma. *Induction of hepatic nodules in the rat by aristolochic acid*. Cancer Letts.71: 83-87, 1993.
24. E.Laconi, S.Vasudevan, P.M.Rao, S.Rajalakshmi, P.Pani, D.S.R.Sarma. *An earlier proliferative response of hepatocytes in  $\gamma$ -glutamyl transferase positive foci to partial hepatectomy*. Cancer Letters 81: 229-235, 1994.
25. A.Denda, E.Laconi, P.M.Rao, S.Rajalakshmi, D.S.R.Sarma. *Sequential histopathological analysis of hepatocarcinogenesis in rats during promotion with orotic acid*. Cancer Letters 82: 55-64, 1994.
26. K.L.Backway, E.Laconi, S.Manjeshwar, P.M.Rao, S.Rajalakshmi, D.S.R.Sarma. *Resistance of hepatic nodules to orotic acid-induced accumulation of uridine nucleotides*. Carcinogenesis 15: 403-406, 1994.
27. S.Manjeshwar, E.Laconi, A.Sheikh, P.M.Rao, S.Rajalakshmi, D.S.R.Sarma. *In vitro and in vivo response of hepatocytes from hepatic nodules to the mitoinhibitory effects of phenobarbital*. Carcinogenesis 15: 1963-1968, 1994.
28. S.Vasudevan, E.Laconi, P.M.Rao, S.Rajalakshmi, D.S.R.Sarma. *Perturbations of endogenous levels of orotic acid and carcinogenesis: effect of an arginine-deficient diet and carbamyl aspartate on hepatocarcinogenesis in the rat and the mouse*. Carcinogenesis 15: 2497-2500, 1994.
29. E.Laconi, D.S.R.Sarma, P.Pani. *Transplantation of normal hepatocytes modulates the development of chronic liver lesions induced by a pyrrolizidine alkaloid, lasiocarpine*. Carcinogenesis 16: 139-142, 1995.
30. L.Tessitore, E.Sesca, C.Tomasi, M.Greco, E.Laconi, P.Pani, M.U.Dianzani. *Refeeding following starvation sustains the induction of liver preneoplastic lesions by a subnecrogenic dose of DENA*. Cell Proliferation 28: 166, 1995.
31. E.Laconi, L.Tessitore, G.Milia, A.Yusuf, D.S.R.Sarma, P.Todde, P.Pani. *The enhancing effect of fasting/refeeding on the growth of nodules selectable by the resistant hepatocyte model in rat liver*. Carcinogenesis 16: 1865-1869, 1995.
32. L.Tessitore, C.Tomasi, M. Greco, E.Sesca, E.Laconi, O.Maccioni, R.Ramo and P.Pani. *A subnecrogenic dose of diethylnitrosamine is able to initiate hepatocarcinogenesis in the rat when coupled with fasting/refeeding*. Carcinogenesis 17: 289-292, 1996.
33. E.Laconi, A.Yusuf, A.R.Jahangir, P.M.Rao, S.Rajalakshmi, F.Sanna, P.Pani, D.S.R.Sarma. *Transient inhibition by orotic acid does not abolish the in vivo response of rat hepatocytes to a direct mitogen, lead nitrate*. J. Hepatol. 26: 203-208, 1997.
34. S.Vasudevan, E.Laconi, G.La Piana, E.Fransvea, D.Marzulli, N.E.Lofrumento, P.M.Rao, S.Rajalakshmi and D.S.R.Sarma. *Cycloheximide sensitivity of orotic acid biosynthesis induced by ammonia and glycine administration*. Eur. J. Biochem. 251: 597-604, 1998.

35. E.Laconi, R.Oren, D.K.Mukhopadhyay, E.Hurston, S.Laconi, P.Pani, M.D.Dabeva, and D.A.Shafritz. *Long term, near total liver replacement by transplantation of isolated hepatocytes in rats treated with retrorsine*. Am. J. Pathol. 153: 319-329, 1998.
36. M.D.Dabeva, E.Laconi, R.Oren, P.M.Petkov, E.Hurston and D.A.Shafritz. *Liver regeneration and  $\alpha$ -fetoprotein mRNA expression in the retrorsine model for hepatocyte transplantation*. Cancer Res. 58: 5825-5834, 1998.
37. R.Oren, M.D.Dabeva, P.M.Petkov, E.Hurston, E.Laconi and D.A.Shafritz. *Restoration of normal serum albumin levels in Nagase analbuminemic rats by hepatocyte transplantation*. Hepatology, 29: 75-81, 1999.
38. M.Grompe, E.Laconi and D.A.Shafritz. *Principles of therapeutic liver repopulation*. Sem. Liver Dis. 19: 7-14, 1999.
39. A.Yusuf, E.Laconi, P.M.Rao, S.Rajalakshmi and D.S.R.Sarma. *The effect of 1/3 versus 2/3 partial hepatectomy on the growth of glutathione-S-transferase positive foci*. Carcinogenesis, 20: 1143-1145, 1999.
40. C.Tomasi, E.Laconi, S.Laconi, M.Greco, D.S.R.Sarma and P.Pani. *Effect of fasting/refeeding on the incidence of chemically-induced hepatocellular carcinoma in the rat*. Carcinogenesis, 20: 1979-1983, 1999.
41. P.Pani, S.Laconi, S.Pillai, F.Scintu, F.Curreli, D.A.Shafritz and E.Laconi. *Direct hyperplasia does not enhance kinetics of liver repopulation in a new model of hepatocyte transplantation in the rat*. J. Hepatol. 31: 354-359, 1999.
42. R.Oren, M.D.Dabeva, A.N. Karnezis, P.M.Petkov, R. Rosencrantz, J.P. Sandhu, S.F. Moss, S. Wang, E.Hurston, E.Laconi, P.R. Holt, S.N. Thung, L. Zhu and D.A.Shafritz. *Role of thyroid hormone in stimulating liver repopulation by transplanted hepatocytes*. Hepatology, 30: 903-913, 1999.
43. S.Laconi, F.Curreli, S. Diana, D. Pasciu, G. De Filippo, D.S.R. Sarma, P.Pani and E.Laconi. *Liver regeneration in response to partial hepatectomy in rats treated with retrorsine: a kinetic study*. J.Hepatol., 31:1069-1074, 1999.
44. E.Laconi. *Differential growth: from carcinogenesis to liver repopulation*. Am. J. Pathol. 156: 389-392, 2000.
45. M.D.Dabeva, P.M. Petkov, J. Sandhu, R. Oren, E. Laconi, E. Hurston, and D.A. Shafritz. *Proliferation and differentiation of fetal liver epithelial progenitor cells after transplantation into adult rat liver*. Am.J.Pathol., 156:2017-2031, 2000.
46. E.Laconi, C.Tomasi, F.Curreli, S.Diana, S.Laconi, G.Serra, M.Collu and P.Pani. *Early exposure to restraint stress enhances chemical carcinogenesis in rat liver*.Cancer Lett. 161:215-220, 2000.
47. S. Laconi, M. Greco, P. Pellegrini-Bettoli, M. Rais, E. Laconi and P. Pani. *One-step detection and genotyping of human papillomavirus in cervical samples by reverse-hybridization*. Diagn. Mol. Pathol. 10: 200-206, 2001.
48. E. Laconi, P. Pani and E. Farber. *The resistance phenotype in the development of cancer: a perspective*. Lancet Oncol. 1:235-241, 2000.
49. S. Laconi, S. Pillai, P.P.Porcu, D.A. Shafritz, P. Pani and E. Laconi. *Massive liver replacement by transplanted hepatocytes in the absence of exogenous growth stimuli in rats treated with retrorsine*. Am. J. Pathol. 158: 771-777, 2001.
50. S. Laconi, P.Pani, S. Pillai, D. Pasciu, DSR Sarma and E. Laconi. *A growth constrained environment drives tumor progression in vivo*. Proc. Natl. Acad. Sci. USA, 98: 7806-7811, 2001.

51. Laconi S. and Laconi E. Principles of hepatocyte transplantation. *Sem. Cell Dev Biol.* 13: 433-438, 2002
52. Kankesan J, Yusuf A, Laconi E, Vanama R, Bradley G, Tiessen JJ, Ling V, Rao PM, Rajalakshmi S and Sarma DSR. Effect of PSC 833, an inhibitor of P-glycoprotein, on 1,2-dimethylhydrazine-induced liver carcinogenesis in rats. *Carcinogenesis*. 2003 Dec;24:1977-84..
53. Pitzalis S, Doratiotto S, Greco M, Montisci S, Pasciu D, Porcu G, Pani P, Laconi S and Laconi E. Cyclin D1 is up-regulated in hepatocytes *in vivo* following cell-cycle block induced by retrorsine, *J. Hepatol.* 43: 485-490, 2005
54. Kankesan J, Laconi E, Medline A, Thiessen JJ, Ling V, Rao PM, Rajalakshmi S and Sarma DSR. PSC 833, an inhibitor of P-glycoprotein inhibits 1,2-dimethylhydrazine induced colorectal carcinogenesis in male Fischer F344 rats. *Anticancer Res.* 26: 995-1000; 2006.
55. Pasciu D, Montisci S, Greco M, Doratiotto S, Pitzalis S, Pani P, Laconi S and Laconi E. Aging is associated with increased clonogenic potential in rat liver *in vivo*. *Aging Cell*, 5: 373-377, 2006
56. Laconi S, Montisci S, Doratiotto S, Greco M, Pasciu D, Pillai S, Pani P. Laconi E. Liver repopulation by transplanted hepatocytes and risk of hepatocellular carcinoma. *Transplantation*, 82: 1319-1323, 2006.
57. Laconi E. Past, present and future of xeno-derived liver cells. *Curr Opin Organ Transpl*, 11: 654-658, 2006.
58. Laconi E. The evolving concept of tumor microenvironments. *BioEssays* 29:738-744, 2007.
59. Marongiu F, Doratiotto S, Montisci S, Pani P, Laconi E. Liver repopulation and carcinogenesis: two sides of the same coin? *Am J Pathol.* 172: 857-864, 2008. (Cover figure from this article).
60. Laconi E. Doratiotto S. Vineis P. The microenvironments of multistage carcinogenesis. *Sem Cancer Biol*, 18, 322-329, 2008.
61. Laconi E. Sonnenschein C. Cancer development at tissue level. *Sem Cancer Biol* 18, 303-304, 2008.
62. Doratiotto S, Marongiu F, Faedda S, Pani P. and Laconi E. Altered growth pattern, not altered growth *per se*, is the hallmark of early lesions preceding cancer development. *Histol Histopathol* 24, 101-106, 2009.
63. Laconi S, Doratiotto S, Montisci S, Pani P. and Laconi E. Repopulation by endogenous hepatocytes does not reconstitute liver mass in rats treated with retrorsine. *Cell Transpl.* 2008;17:1415-21.
64. Doratiotto S, Krause P, Serra MP, Marongiu F, Sini M, Koenig S, Laconi E. The growth pattern of transplanted normal and nodular hepatocytes. *Histochem Cell Biol.* 2011; 135: 581-91
65. Marongiu F, Gramignoli R, Dorko K, Miki T, Ranade AR, Paola Serra M, Doratiotto S, Sini M, Sharma S, Mitamura K, Sellaro TL, Tahan V, Skvorak KJ, Ellis EC, Badylak SF, Davila JC, Hines R, Laconi E, Strom SC. Hepatic differentiation of amniotic epithelial cells. *Hepatology*. 2011; 53(5):1719-29.
66. Alison MR, Marongiu F, Laconi E. Transplanted hepatocytes: Wiped out or washed out? *J Hepatol.* 2012; 56: 996-7
67. Serra MP, Doratiotto S, Marongiu F, Laconi E. Normal hepatocyte transplantation delays the emergence of chemically-induced pre-neoplastic nodules in rat liver. *Cell Transplant.* 2012; 21: 671-7

68. Serra MP, Marongiu F, Sini M and Laconi E. Hepatocyte senescence in vivo following preconditioning for liver repopulation. *Hepatology*. 2012; 56: 760-8
69. Marongiu F, Doratiotto S, Sini M, Serra MP and Laconi E. Cancer as a disease of tissue pattern formation. *Progr. Histochem. Cytochem*. 2012; 47:175-207
70. Marongiu F, Serra MP, Sini M, Angius F, Laconi E. Clearance of senescent hepatocytes in a neoplastic-prone microenvironment delays the emergence of hepatocellular carcinoma. *Aging (Albany NY)*. 2014; 6: 26-34
71. Fabio Marongiu\*, Maria Paola Serra\*, Marcella Sini, Michela Marongiu, Antonella Contini and Ezio Laconi. Cell turnover in the repopulated rat liver: distinct lineages for hepatocytes and the biliary epithelium. *Cell Tissue Res*. 2014; 356: 333-40
72. Serra MP, Marongiu F, Sini M, Marongiu M, Contini A, Wolff H, Rave-Fraenk M, Krause P, Laconi E and Koenig S. Radiation-induced hepatocyte senescence following priming for liver repopulation. *Int J Rad Biol*, 2014; 90: 876-83
73. Jahouh F, Marongiu F, Serra MP, Laconi E, Banoub J. as-phase fragmentation of the N-oxide and N-hydroxylated derivatives of retrorsine using liquid chromatography/electrospray ionization quadrupole time-of-flight tandem mass spectrometry. *Rapid Commun Mass Spectrom*. 2015; 29:1733-48.
74. Goodson WH 3rd, et al. Assessing the carcinogenic potential of low-dose exposures to chemical mixtures in the environment: the challenge ahead. *Carcinogenesis*. 2015; 36 Suppl 1: S254-96.
75. Casey SC, Vaccari M, Al-Mulla F, Al-Temaimi R, Amedei A, Barcellos-Hoff MH, Brown DG, Chapellier M, Christopher J, Curran CS, Forte S, Hamid RA, Heneberg P, Koch DC, Krishnakumar PK, Laconi E, Maguer-Satta V, Marongiu F, Memeo L, Mondello C, Raju J, Roman J, Roy R, Ryan EP, Ryeom S, Salem HK, Scovassi AI, Singh N, Soucek L, Vermeulen L, Whitfield JR, Woodrick J, Colacci A, Bisson WH, Felsher DW. The effect of environmental chemicals on the tumor microenvironment. *Carcinogenesis*. 2015; 36 Suppl 1: S160-83.
76. Marongiu M, Serra MP, Contini A, Sini M, Strom SC, Laconi E, Marongiu F. Rat-derived amniotic epithelial cells differentiate into mature hepatocytes in vivo with no evidence of cell fusion. *Stem Cells Dev*. 2015; 24: 1429-35.
77. Serra MP, Marongiu F, Marongiu M, Contini A, Laconi E. Cell-autonomous decrease in proliferative competitiveness of the aged hepatocyte. *J Hepatol*. 2015; 62: 1341-8.
78. Liu D, Yovchev MI, Zhang J, Alfieri AA, Tchaikovskaya T, Laconi E, Dabeva MD. Identification and characterization of mesenchymal-epithelial progenitor-like cells in normal and injured rat liver. *Am J Pathol* 2015; 185: 110-28.
79. Marongiu F, Serra MP, Doratiotto S, Sini M, Fanti M, Cadoni E, Serra M, Laconi E. Aging promotes neoplastic disease through effects on the tissue microenvironment. *Aging (Albany NY)*. 2016 Dec 6. doi: 10.18632/aging.101128.