

## Prof.ssa Gabriella LEONARDUZZI

- **Curriculum scientifico** - Settori di indagine: Patologie umane e sperimentali caratterizzate da fenomeni di infiammazione e/o fibrosi correlabili a stress ossidativo e ad eventi radicalici, quali steatosi, fibrosi, cirrosi epatica, carcinomi epatici e aterosclerosi. Meccanismi molecolari di modulazione della risposta cellulare da parte di prodotti di ossidazione lipidica. I risultati ottenuti nel corso della sua attività scientifica sono stati oggetto di: 48 pubblicazioni su riviste internazionali con revisore e Impact Factor; 14 su libri o monografie; numerosi atti e partecipazioni a congressi internazionali e nazionali.

Pubblicazioni su riviste con revisori

1. Carini R, Chiarpotto E, Biasi F, Leonarduzzi G, Comoglio A, Carpi C, Poli G. Relation between liver necrosis and intrahepatic cholestasis in rats poisoned with CCl<sub>4</sub>. *Boll Soc Ital Biol Sper.*,
2. Comoglio A, Leonarduzzi G, Carini R, Busolin D, Basaga H, Albano E, Tomasi A, Poli G, Morazzoni P, Magistretti MJ. Studies on the antioxidant and free radical scavenging properties of IdB 1016 a new flavanolignan complex. *Free Radic Res Commun*, 11:109-115, 1990.
3. Chiarpotto E, Biasi F, Comoglio A, Leonarduzzi G, Poli G, Dianzani MU. CCl<sub>4</sub>-induced increase of hepatocyte free arachidonate level: pathogenesis and contribution to cell death. *Chem Biol Interact*, 74:195-206, 1990.
4. Parola M, Muraca R, Dianzani I, Barrera G, Leonarduzzi G, Bendinelli P, Piccoletti R, Poli G. Vitamin E dietary supplementation inhibits transforming growth factor beta 1 gene expression in the rat liver. *FEBS Lett*, 308:267-270, 1992.
5. Parola M, Leonarduzzi G, Biasi F, Albano E, Biocca ME, Poli G, Dianzani MU. Vitamin E dietary supplementation protects against carbon tetrachloride-induced chronic liver damage and cirrhosis. *Hepatology*, 16:1014-1021, 1992.
6. Poli G, Parola M, Leonarduzzi G, Pinzani M. Modulation of hepatic fibrogenesis by antioxidants. *Mol Aspects Med*, 14:259-264, 1993.
7. Canuto RA, Ferro M, Muzio G, Bassi AM, Leonarduzzi G, Maggiora M, Adamo D, Poli G, Lindahl R. Effects of aldehyde products of lipid peroxidation on the activity of aldehyde metabolizing enzymes in hepatomas. *Adv Exp Med Biol*, 328:17-25, 1993
8. Parola M, Biocca ME, Leonarduzzi G, Albano E, Dianzani MU, Gilmore KS, Meyer DJ, Ketterer B, Slater TF, Cheeseman KH. Constitutive and inducible profile of glutathione S-transferase subunits in biliary epithelial cells and hepatocytes isolated from rat liver. *Biochem J*, 291:641-647, 1993.
9. Canuto RA, Ferro M, Muzio G, Bassi AM, Leonarduzzi G, Maggiora M, Adamo D, Poli G, Lindahl R. Role of aldehyde metabolizing enzymes in mediating effects of aldehyde products of lipid peroxidation in liver cells. *Carcinogenesis*, 15:1359-1364, 1994.
10. Canuto RA, Muzio G, Bassi AM, Maggiora M, Leonarduzzi G, Lindahl R, Dianzani MU, Ferro M. Enrichment with arachidonic acid increases the sensitivity of hepatoma cells to the cytotoxic effects of oxidative stress. *Free Radic Biol Med*, 18:287-293, 1995.
11. Leonarduzzi G, Parola M, Muzio G, Garramone A, Maggiora M, Robino G, Poli G, Dianzani MU, Canuto RA. Hepatocellular metabolism of 4-hydroxy-2,3-nonenal is impaired in conditions of chronic cholestasis. *Biochem Biophys Res Commun*, 214:669-675, 1995.
12. Parola M, Leonarduzzi G, Robino G, Albano E, Poli G, Dianzani MU. On the role of lipid peroxidation in the pathogenesis of liver damage induced by long-standing cholestasis. *Free Radic Biol Med*, 20:351-359, 1996.
13. Parola M, Pinzani M, Casini A, Leonarduzzi G, Marra F, Caligiuri A, Ceni E, Biondi P, Poli G, Dianzani MU. Induction of procollagen type I gene expression and synthesis in human hepatic stellate cells by 4-hydroxy-2,3-nonenal and other 4-hydroxy-2,3-alkenals is related to their molecular structure. *Biochem Biophys Res Commun*, 222:261-264, 1996.

14. Camandola S, Leonarduzzi G, Musso T, Varesio L, Carini R, Scavazza A, Chiarpotto E, Baeuerle PA, Poli G. Nuclear factor kB is activated by arachidonic acid but not by eicosapentaenoic acid. *Biochem Biophys Res Commun*, 229:643-647, 1996.
15. Carini R, Leonarduzzi G, Camandola S, Musso T, Varesio L, Baeuerle PA, Poli G. Activation of human immunodeficiency virus long terminal repeat by arachidonic acid. *Free Radic Biol Med*, 22:195-199, 1997.
16. Chiarpotto E, Scavazza A, Leonarduzzi G, Camandola S, Biasi F, Teggia PM, Garavoglia M, Robecchi A, Roncari A, Poli G. Oxidative damage and transforming growth factor beta 1 expression in pretumoral and tumoral lesions of human intestine. *Free Radic Biol Med*, 22:889-894, 1997.
17. Camandola S, Scavazza A, Leonarduzzi G, Biasi F, Chiarpotto E, Azzi A, Poli G. Biogenic 4-hydroxy-2-nonenal activates transcription factor AP-1 but not NF-kappa B in cells of the macrophage lineage. *BioFactors*, 6:173-179, 1997.
18. Leonarduzzi G, Scavazza A, Biasi F, Chiarpotto E, Camandola S, Vogel S, Dargel R, Poli G. The lipid peroxidation end product 4-hydroxy-2,3-nonenal up-regulates transforming growth factor beta1 expression in the macrophage lineage: a link between oxidative injury and fibrosclerosis. *FASEB J*, 11:851-857, 1997.
19. Parola M, Robino G, Bordone R, Leonarduzzi G, Casini A, Pinzani M, Neve E, Bellomo G, Dianzani MU, Ingelman-Sundberg M, Albano E. Detection of cytochrome P4503A (CYP3A) in human hepatic stellate cells. *Biochem Biophys Res Commun*, 238:420-424, 1997.
20. Parola M, Robino G, Marra F, Pinzani M, Bellomo G, Leonarduzzi G, Chiarugi P, Camandola S, Poli G, Waeg G, Gentilini P, Dianzani MU. HNE interacts directly with JNK isoforms in human hepatic stellate cells. *J Clin Invest*, 102:1942-1950, 1998.
21. Marra F, DeFranco R, Grappone C, Parola M, Milani S, Leonarduzzi G, Pastacaldi S, Wenzel UO, Pinzani M, Dianzani MU, Laffi G, Gentilini P. Expression of monocyte chemoattractant protein-1 precedes monocyte recruitment in a rat model of acute liver injury, and is modulated by vitamin E. *J Invest Med*, 47:66-75, 1999.
22. Camandola S, Aragno M, Cutrin JC, Tamagno E, Danni O, Chiarpotto E, Parola M, Leonarduzzi G, Biasi F, Poli G. Liver AP-1 activation due to carbon tetrachloride is potentiated by 1,2-dibromoethane but is inhibited by alpha-tocopherol or gadolinium chloride. *Free Radic Biol Med*, 26:1108-1116, 1999.
23. Leonarduzzi G, Arkan MC, Basaga H, Chiarpotto E, Sevanian A, Poli G. Lipid oxidation products in cell signaling. *Free Radic Biol Med*, 28:1370-1378, 2000.
24. Leonarduzzi G, Sevanian A, Sottero B, Arkan MC, Biasi F, Chiarpotto E, Basaga H, Poli G. Up-regulation of the fibrogenic cytokine TGF-beta1 by oxysterols: a mechanistic link between cholesterol and atherosclerosis. *FASEB J*, 15:1619-1621, 2001.
25. Arkan MC, Leonarduzzi G, Biasi F, Basaga H, Poli G. Physiological amounts of ascorbate potentiate phorbol ester-induced nuclear-binding of AP-1 transcription factor in cells of macrophagic lineage. *Free Radic Biol Med*, 31:374-382, 2001.
26. Leonarduzzi G, Sevanian A, Poli G. Cholesterol oxidation products and fibrogenesis. *BioFactors*, 15:117-119, 2001.
27. Chiarpotto E, Allasia C, Biasi F, Leonarduzzi G, Ghezzi F, Berta G, Bellomo G, Waeg G, Poli G. Down-modulation of nuclear localisation and pro-fibrogenic effect of 4-hydroxy-2,3-nonenal by thiol- and carbonyl-reagents. *Biochim Biophys Acta*, 1584:1-8, 2002.
28. Leonarduzzi G, Sottero B, Poli G. Oxidized products of cholesterol: dietary and metabolic origin, and proatherosclerotic effects *J Nutr Biochem*, 13:700-710, 2002.
29. Massarenti P, Biasi F, De Francesco A, Pauletto D, Rocca G, Silli B, Vizio B, Serviddio G, Leonarduzzi G, Poli G, Palmo A. 4-Hydroxynonenal is markedly higher in patients on a standard long-term home parenteral nutrition. *Free Radic Res*, 38:73-80, 2004.
30. Leonarduzzi G, Biasi F, Chiarpotto E, Poli G. Trojan horse-like behavior of a biologically representative mixture of oxysterols. *Mol Aspects Med*, 25:155-167, 2004.

31. Biasi F, Leonarduzzi G, Vizio B, Zanetti D, Sevanian A, Sottero B, Verde V, Zingaro B, Chiarpotto E, Poli G. Oxysterol mixtures prevent proapoptotic effects of 7-ketocholesterol in macrophages: implications for proatherogenic gene modulation. *FASEB J*, 18:693-695, 2004.
32. Poli G, Leonarduzzi G, Biasi F, Chiarpotto E. Oxidative stress and cell signalling. *Curr Med Chem*, 11:1163-1182, 2004.
33. Leonarduzzi G, Robbesyn F, Poli G. Signaling kinases modulated by 4-hydroxynonenal. *Free Radic Biol Med*, 37:1694-1702, 2004.
34. Sottero B, Gamba P, Longhi M, Robbesyn F, Abuja PM, Schaur RJ, Poli G, Leonarduzzi G. Expression and synthesis of TGF- $\beta$ 1 is induced in macrophages by 9-oxononanoyl cholesterol, a major cholesteryl ester oxidation product. *BioFactors*, 24:209-216, 2005.
35. Leonarduzzi G, Gamba P, Sottero B, Kadl A, Robbesyn F, Calogero RA, Biasi F, Chiarpotto E, Leitinger N, Sevanian A, Poli G. Oxysterol-induced up-regulation of MCP-1 expression and synthesis in macrophage cells. *Free Radic Biol Med*, 39:1152-1161, 2005.
36. Castello L, Froio T, Cavallini G, Biasi F, Sapino A, Leonarduzzi G, Bergamini E, Poli G, Chiarpotto E. Calorie restriction protects against age-related rat aorta sclerosis. *FASEB J*, 19:1863-1865, 2005.
37. Leonarduzzi G, Chiarpotto E, Biasi F, Poli G. 4-Hydroxynonenal and cholesterol oxidation products in atherosclerosis. *Mol Nutr Food Res*, 49:1044-1049, 2005.
38. Chiarpotto E, Castello L, Leonarduzzi G, Biasi F, Poli G. Role of 4-hydroxy-2,3-nonenal in the pathogenesis of fibrosis. *BioFactors*, 24:229-236, 2005.
39. Castello L, Marengo B, Nitti M, Froio T, Domenicotti C, Biasi F, Leonarduzzi G, Pronzato MA, Marinari UM, Poli G, Chiarpotto E. 4-Hydroxynonenal signalling to apoptosis in isolated rat hepatocytes: the role of PKC- $\delta$ . *Biochim Biophys Acta*, 1737:83-93, 2005.
40. Leonarduzzi G, Vizio B, Sottero B, Verde V, Gamba P, Mascia C, Chiarpotto E, Poli G, Biasi F. Early involvement of ROS overproduction in apoptosis induced by 7-ketocholesterol. *Antioxidant & Redox Signaling*, 8:375-380, 2006.
41. Biasi F, Vizio B, Mascia C, Gaia E, Zarkovic N, Chiarpotto E, Leonarduzzi G, Poli G. JNK up-regulation as a key event in the pro-apoptotic interaction between TGF- $\beta$ 1 and 4-hydroxynonenal in colon cancer. *Free Radic Biol Med*, 41:443-454, 2006.
42. Leonarduzzi G, Poli G, Sottero B, Biasi F. Activation of the mitochondrial pathway of apoptosis by oxysterols. *Frontiers in Biosciences*, 12:791-799, 2007.
43. [Sottero B, Pozzi R, Leonarduzzi G, Aroasio E, Gamba P, Gargiulo S, Rabajoli F, Ferrari F, Greco Lucchina P, Poli G.](#) Lipid peroxidation and inflammatory molecules as markers of coronary artery disease. *Redox Rep.*, 12:81-85, 2007.
44. [Poli G, Schaur RJ, Siems WG, Leonarduzzi G.](#) 4-hydroxynonenal: a membrane lipid oxidation product of medicinal interest. *Med. Res. Rev.*, 28:569-631, 2008.
45. [Poli G, Biasi F, Leonarduzzi G.](#) 4-Hydroxynonenal-protein adducts: 4-Hydroxynonenal-protein adducts: A reliable biomarker of lipid oxidation in liver diseases. *Mol. Aspects Med.*, 29:67-71, 2008.
46. [Leonarduzzi G, Gamba P, Gargiulo S, Sottero B, Kadl A, Biasi F, Chiarpotto E, Leitinger N, Vendemiale G, Serviddio G, Poli G.](#) Oxidation as a crucial reaction for cholesterol to induce tissue degeneration: CD36 overexpression in human promonocytic cells treated with a biologically relevant oxysterol mixture. *Aging Cell*, 7:375-382, 2008.
47. [Sottero B, Gamba P, Gargiulo S, Leonarduzzi G, Poli G.](#) Cholesterol oxidation products and disease: an emerging topic of interest in medicinal chemistry. *Curr Med Chem*, 2009, in via di pubblicazione.

#### **Pubblicazioni su libri o monografie**

1. Poli G, Chiarpotto E, Biasi F, Leonarduzzi G, Comoglio A, Albano E, Dianzani MU. Role of aldehydes in the propagation of lipid peroxidation-induced liver toxicity. In: *Free Radicals in*

- the Pathogenesis of Liver Injury Advances in the Biosciences (G Poli, KH Cheeseman, MU Dianzani, TF Slater, Eds.), Pergamon Press, Oxford, vol. 76, pp. 73-81, 1989.
2. Danni O, Chiarpotto E, Aragno M, Biasi F, Comoglio A, Leonarduzzi G, Poli G. Carbon tetrachloride and 1,2-dibromoethane: synergistic effect on lipid peroxidation and cell damage in isolated rat hepatocytes. In: *Advances in Free Radicals in Disease* (A Tomasi, F Ursini, V Vannini, Eds.), Cleup Editrice, Padova, pp. 115-121, 1990.
  3. Canuto RA, Muzio G, Leonarduzzi G, Bassi AM, Maggiora M, Biocca ME, Poli G, Ferro M. Induction of 4-hydroxynonenal metabolizing enzymes. In: *Carcinogenesis as Process* (D Kanduc, P Pani, Eds.), Supertecnica, Bari, Italy, pp. 155-160, 1992.
  4. Canuto RA, Ferro M, Muzio G, Bassi AM, Leonarduzzi G, Maggiora M, Adamo D, Poli G, Lindahl R. Effects of aldehyde products of lipid peroxidation on the activity of aldehyde metabolizing enzymes in hepatomas. In: *Enzymology and molecular Biology of Carbonyl Metabolism 4* (H Weiner, Ed.), Plenum Press, New York, pp. 17-25, 1993.
  5. Parola M, Albano E, Leonarduzzi G, Muraca R, Dianzani I, Poli G, Dianzani MU. Evidence for a possible role of lipid peroxidation in experimental liver fibrosis. In: *Free Radicals: from Basic Science to Medicine* (G Poli, E Albano, MU Dianzani, Eds.) Birkhauser Verlag, Basel, pp. 274-287, 1993.
  6. Parola M, Albano E, Biocca ME, Leonarduzzi G, Dianzani MU, Gilmore K, Meyer DJ, Ketterer B, Slater TF, Cheeseman KH. Induction of cytosolic GSH transferases by ethoxyquin in rat hepatocytes and biliary epithelial cells. In: *Free Radicals and Antioxidants in Nutrition* (FP Corongiu, C Rice-Evans, Eds.), Free Radical Series, Richelieu Press, London, pp. 303-319, 1993.
  7. Parola M, Leonarduzzi G, Albano E, Biasi F, Biocca ME, Poli G, Dianzani MU. Experimental liver cirrhosis induced by carbon tetrachloride: a role for lipid peroxidation. In: *Role of Free Radicals in Biological Systems* (J Feher, A Blazovits, B Matkovics, M Mezes, Eds.) Akademiai Kiado, Budapest, Hungary, pp. 115-121, 1993.
  8. Parola M, Leonarduzzi G, Albano E, Poli G, Dianzani MU. Oxidative damage in the pathogenesis of liver cirrhosis. In: *Liver Pathophysiology* (MU Dianzani, P Gentilini, Eds.) Elsevier Science B.V, Amsterdam, pp. 3-12, 1994.
  9. Camandola S, Musso T, Leonarduzzi G, Carini R, Varesio L, Baeuerle PA, Poli G. Modulation of HIV-1 long terminal repeat by arachidonic acid. In: *Oxidative Stress in Cancer, AIDS, and Neurodegenerative Disease* (L Montagnier, R Olivier, C Pasquier, Eds.) Marcel Dekker, Inc., New York, 37, pp. 389-397, 1997.
  10. Scavazza A, Leonarduzzi G, Camandola S, Parola M, Poli G. Oxidative damage and fibrosclerosis in various tissue. In: *Free Radicals, Oxidative Stress, and Antioxidants* (T Ozben, Ed.) Plenum Press, New York, 14, pp. 145-149, 1998.
  11. Chiarpotto E, Biasi F, Leonarduzzi G, Parola M, Bellomo G, Poli G. Effect of 4-hydroxy-2,3-nonenal on transforming growth factor- $\beta$ 1 gene expression in a macrophage cell line. In *Advances in Free Radicals in Disease*. (R Pizzala, A Tomasi, V Vannini, Eds.), La Goliardica Pavese, Pavia, Italy, vol. IV, pp. 37-48, 1999.
  12. Biasi F, Tessitore L, Zanetti D, Allasia C, Leonarduzzi G, Chiarpotto E, Poli G. Lipid peroxidation and transforming growth factor- $\beta$  expression. In *Free Radicals in Chemistry Biology and Medicine* (T Yoshikawa, S Toyokuni, Y Yamamoto, Y Naito, Eds.), OICA International (UK) Ltd, London, England, pp.182-190, 2000.
  13. Poli G, Leonarduzzi G, Chiarpotto E. 4-Hydroxynonenal signaling. In: *Signal Transduction by Reactive Oxygen and Nitrogen Species: Pathways and Chemical Principles*. (HJ Forman, J Fukuto, M Torres, Eds.). Kluwer Academic Publishers, pp. 180-193, 2003.
  14. Leonarduzzi G, Sottero B, Verde V, Poli G. Oxidized products of cholesterol: toxic effects. In: *Reviews in food and nutrition toxicity* (VR Preedy, RR Watson, Eds.), CRC Press, 3, pp. 129-164, 2005.