



**Gianpaolo Perletti**

 UNIVERSITY OF INSUBRIA



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## Contact data

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## Biography

Birth date and place October 22, 1962, Milan, Italy

Graduation: 1988, University of Milan, Italy (Doctor of Biological Sciences).

1989-1990, Postgraduate Research Scientist, Roswell Park Cancer Institute, Buffalo NY, USA

1990-2000, Tenure Research associate, Institute of Pharmacology, University of Milan, Italy.

1994 Visiting scientist; Department of Molecular and Cellular Toxicology, Harvard School of Public Health, Boston MA USA.

1995 Visiting scientist; Department of Molecular and Cellular Toxicology, Harvard School of Public Health, Boston MA USA.

1997 Visiting scientist; Department of Cancer Cell Biology, Harvard School of Public Health, Boston MA. USA.

1998 Visiting Scientist, Children's Hospital, Harvard Medical School, Boston, MA. USA

2000-Present, Assistant Professor, University of Insubria, Varese, Italy.

## Qualifications and awards

1994, ICRET award, International Union against Cancer (UICC), Geneva

## Research interests

1) Our current research interest is focused on the oncogenic/tumor suppressive role of specific isoforms of the Protein Kinase C family. In particular, we have demonstrated that the epsilon isoform of PKC acts as an oncogene by activating a ras-Raf signalling pathway, and that the delta isoform of PKC (PKC $\delta$ ) acts as a tumor suppressor in human colon cancer cells by inducing p21/p53-mediated growth suppression, differentiation features, and mitotic abnormalities. However, the function of PKC $\delta$  seems to be cell-specific: whereas suppression was documented in colon cancer, T-cell neoplasms and skin tumors, this isoform was shown to be a positive regulator of human breast cancer cell growth and metastasis. Our present research is aimed at characterizing the mechanisms by which PKC $\delta$  concurs to breast cancer onset in human cells.

2) In the context of an international research collaboration project, it has been demonstrated that a high percentage of breast cancer patients shows enhanced in vitro chromosomal radiosensitivity, compared to healthy individuals. These findings point to a correlation between radiosensitivity, breast cancer predisposition and defects in

DNA double strand break (dsb) repair genes/tumor suppressor genes, and suggest that enhanced radiosensitivity may be a marker for breast cancer predisposing genes of low penetrance. The goal of our current research is to investigate which DNA dsb repair pathways and genes are involved in the generation of genomic instability in human lymphoid cells, in order to unravel the underlying genetic cause of enhanced chromosomal radiosensitivity observed in breast cancer patients.

## Teaching experience and appointments

- Toxicology, Biology of Health first level degree.
- Toxicology, Biological Sciences first level degree, Environmental Contamination curriculum
- Molecular and Cellular Toxicology, Biology Applied to Biomedical Sciences second level degree.
- Applied Toxicology, Environmental Toxicology curriculum, Biological Sciences second level degree.

## Representative publications

1. La Porta C, Perletti G, Piccinini F and Comolli R (1993) Analysis of calcium dependent Protein Kinase C isoforms in the early stages of Diethylnitrosamine-induced rat hepatocarcinogenesis. *Molecular Carcinogenesis* 8,255-263
2. Perletti G and Piccinini F (1994) Differential phorbol ester growth modulation and protein kinase C isoenzyme expression in rat hepatoma cells vs. non neoplastic rat hepatocytes. *Oncology reports* 1,963-966
3. Tessitore L, Perletti G, Sesca E, Pani P, Dianzani MU, and Piccinini F (1994). Protein kinase C isozyme pattern in liver hyperplasia. *Biochemical and Biophysical Research Communications* 205, 208-214
4. Perletti G, Smeraldi C, Porro D, and Piccinini F (1994) Involvement of the alpha isoenzyme of protein kinase c in the growth inhibition induced by phorbol esters in MH1C1 hepatoma cells. *Biochemical and Biophysical Research Communications* 205,1589-1594
5. Tessitore L, Perletti G, Sesca E, Pani P, Piccinini F, and Dianzani MU (1995) Protein kinase C isozymes during liver regeneration. *Biochemical and Biophysical Research Communications* 214,354-360
6. Perletti G, Folini M, Lin H, Mischak H, Piccinini F, and Tashjian Jr, AH (1996) Overexpression of Protein Kinase C epsilon is oncogenic in rat colonic epithelial cells. *Oncogene* 12, 847-854
7. Perletti G, Tessitore, L, Sesca, E, Pani, P, Dianzani, MU, and Piccinini, F (1996).  $\epsilon$ PKC acts like a marker of progressive malignancy in rat liver, but fails to enhance tumorigenesis in rat hepatoma cells in culture. *Biochemical and Biophysical Research Communications* 221,688-691
8. Perletti G and Monti E (1996) PKCs: transducers of critical signals in cancer cells. *International Journal of Oncology* 9,171-177

9. Sesca E, Perletti G, Binasco V, Chiara M, and Tessitore L (1996) Phosphatidylethanolamine N-methyltransferase 2 and CTP-Phosphocoline cytidyltransferase expressions are related with protein kinase C isozymes in developmental liver growth. *Biochemical and Biophysical Research Communications*, 229, 158-162
  
10. Perletti G, Concari P, Brusaferrri S, Marras E, Piccinini F and Tashjian Jr AH (1998). Protein Kinase C  $\epsilon$  is oncogenic in colon epithelial cells by interaction with the *RAS* signal transduction pathway. *Oncogene* 16, 3345-3348
  
11. Perletti G, Marras, E, Concari P, Piccinini F and Tashjian Jr AH (1999). Protein Kinase C  $\delta$  acts as a growth and tumor suppressor in rat colonic epithelial cells. *Oncogene* 18:1251-1256
  
12. Perletti, G, Concari, P, Chen, L, Giardini, R, Marras E, Folkman, J, and Piccinini F (2000) Antitumor activity of Endostatin against carcinogen-induced rat mammary carcinomas. *Cancer research* 60:1793-1796, 2000
  
13. De Eguileor M, Grimaldi A, Tettamanti G, Ferrarese R, Congiu T, Protasoni M, Perletti G, Valvassori R and Lanzavecchia G. (2001) *Hirudo Medicinalis*: a new model system for testing activators and inhibitors of angiogenesis. *Angiogenesis*, 4: 299-312
  
14. Perletti G, Marras E, Concari P, Cortellezzi L, de Eguileor M and Piccinini F (2001) Involvement of PI3K in PKC $\epsilon$ -mediated oncogenic signal in rat colonic epithelial cells. *International Journal of Oncology*, 19:395-399
  
- Perletti G, Marras E, Dondi D, Grimaldi A, Tettamanti G, Valvassori R and de Eguileor M. (2003) Assessment of the biological activity of an improved naked-DNA vector for angiogenesis gene therapy on a novel non-mammalian model. *International Journal of Molecular Medicine* 11:691-696
  
- Radaelli A, Zanotto C, Perletti G, Elli V, Vicenzi E, Poli G, De Giuli Morghen C. (2003) Comparative analysis of immune responses and cytokine profiles elicited in rabbits by the combined use of recombinant fowlpox viruses, plasmids and virus-like particles in prime-boost vaccination protocols against SHIV. *Vaccine* 3648, 1-13
  
17. de Eguileor M, Tettamanti G, Grimaldi A, Perletti G, Congiu T, Rinaldi L and Valvassori R. (2004) *Hirudo Medicinalis*: Avascular Tissues for Clear-Cut Angiogenesis Studies? *Current Pharmaceutical Design* 10, 1979-1988
  
18. Perletti G, Osti D, Marras E, Tettamanti G, de Eguileor M (2004). Generation of VSV-G pseudotyped lentiviral particles in 293T cells. *Journal of Cellular and Molecular Medicine* 8, 142-144, 2004
  
19. Perletti G, Marras M, Osti D, Felici L, Zaro S and de Eguileor M. (2004) Protein Kinase C delta requires functional p53 for tumor

suppression in human colon cancer cells. *Journal of Cellular and Molecular Medicine*, 8, 563-569

20. Perletti G, Marras E, Dondi D, Osti D, Congiu T, Ferrarese R, de Eguileor M and Tashjian AH (2004) p21<sup>Waf1/Cip1</sup> and p53 are downstream effectors of Protein Kinase C delta in tumor suppression and differentiation in human colon cancer cells. *International Journal of Cancer*, 113, 42-53, 2005
21. Perletti G and Terrian, D. (2005) Distinctive cellular roles for novel protein kinase C isoenzymes. *Current Pharmaceutical Design*, *in press*
22. Osti D, Marras E and Perletti G (2005). Comparative analysis of molecular tools attenuating positional effects in lentiviral vectors carrying multiple genes. *Journal of Virological Methods*, *in press*.