

CURRICULUM VITAE ET STUDIORUM GRAZIA GRAZIANI

BIOGRAPHICAL AND PERSONAL INFORMATION

Date of birth December 9th, 1956
Place of birth Piacenza, Italy
Home Address Angelo Brelich, 6, 00133 Rome, Italy
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EDUCATION

1982: Graduated in Medicine at the University of Perugia, Italy
1986: Specialist in Oncology at the University of Rome “Tor Vergata”, Italy

POSITION HELD AND SCIENTIFIC CAREER:

2015 to present: Component of the Italian National University Council
2014 to present: National Scientific Qualification as full professor of Pharmacology
2001 to present: Associate Professor of Pharmacology at the Department of Systems Medicine, School of Medicine of the University of Rome “Tor Vergata”;
1984-2000: Research Associate at the Department of Neuroscience University of Rome “Tor Vergata”;
1986-1990: Visiting Fogarty Fellow at the laboratory of Cellular and Molecular Biology, National Cancer Institute, National Institutes of Health, Bethesda, Maryland, U.S.A.
1983: Guest Scientist at the laboratory of Tumor Cell Biology, National Cancer Institute, National Institutes of Health, Bethesda, Maryland, U.S.A.

TEACHING

2015-present: Course of Chemotherapy, School of Medicine at the University of Rome “Tor Vergata” (English course)
2011-present: Course of Chemotherapy, School of Pharmacy, University of Rome “Tor Vergata” (English course)
2009-present: Course of Pharmaceutical Biology, School of Pharmacy, University of Rome “Tor Vergata” (English course)
2007-present: Course of Chemotherapy, School of Dentistry, University of “Nostra Signora del Buon Consiglio”, Tirana, Albany
2006-present: Course of Chemotherapy, School of Medicine, University of “Nostra Signora del Buon Consiglio”, Tirana, Albany
2006-present: Course of Pharmacology and Toxicology, Biomedical Laboratory Technician degree, University of Rome “Tor Vergata”
1998-present: Course of Chemotherapy, School of Medicine at the University of Rome “Tor Vergata”
1995-present: Course of Chemotherapy, Specialty School of Oncology, Faculty of Medicine. University of Rome “Tor Vergata”
1993-present: Course of Pharmacology, Orthoptist degree, University of Rome “Tor Vergata”
1993-1999: Course of Pharmacology, Nursing degree, University of Rome “Tor Vergata”
1992-1998: Course of Oncology, Biomedical Laboratory Technician degree, University of Rome “Tor Vergata”

MAIN RESEARCH INTERESTS

Studies on chemotherapy, immunopharmacology, mechanisms involved in the cytotoxic activity of antitumor agents, resistance to anticancer drugs, pharmacological modulation of tumor chemoresistance through the use of DNA repair inhibitors, anti-angiogenic agents.

PUBLICATIONS

Co-author of 123 full papers in Medline-based journals, of which 72 as first or last author, and 10 book chapters. H-index 33 (Scopus and Web of Science); mean citations: 99.

Full papers

1. Riccardi C., Migliorati G., Giuliani-Bonmassar A., **Graziani G.** Adriamycin: Mechanisms of modulation of natural antitumor reactivity. *Drugs under Experimental and Clinical Research* 9: 365-368, 1983.
2. Giuliani-Bonmassar A., **Graziani G.**, Frati L., Bonmassar E. Interferon-induced changes of the susceptibility of murine and human lymphoma cells to natural cytotoxic lymphocytes. *International Journal of Tissue Reaction* 6: 35-41, 1984.
3. De Vecchis L., **Graziani G.**, Macchi B., Grandori C., Pastore S., Popovic M., Gallo R. C., Bonmassar E. Decline of natural cytotoxicity of human lymphocytes following infection with human T cell leukemia/lymphoma virus (HTLV). *Leukemia Research* 9: 349-355, 1985.
4. **Graziani G.**, Pasqualetti D., Lopez E., D'Onofrio C., Testi A.M., Mandelli F., Gallo R.C., Bonmassar E. Increased susceptibility of peripheral mononuclear cells of leukemic patients to HTLV-I infection *in vitro*. *Blood* 69: 1175-1181, 1987.
5. D'Onofrio C., Perno C.F., Mazzetti P., **Graziani G.**, Caliò R., Bonmassar E. Depression of early phase of HTLV-I infection *in vitro* mediated by human Beta-interferon. *British Journal of Cancer* 57: 481-488, 1988.
6. Fuggetta M.P., **Graziani G.**, Aquino A., D'Atri S., Bonmassar E. Effect of hydrocortisone on human natural killer activity and its modulation by beta interferon. *International Journal of Immunopharmacology* 10: 687-694, 1988.
7. **Graziani G.**, Ron D., Eva A., Srivastava S.K. The human *dbl*-proto-oncogene product is a cytoplasmic phosphoprotein which is associated with the cytoskeletal matrix. *Oncogene* 4: 823-829, 1989.
8. Ron D., **Graziani G.**, Aaronson S.A., Eva A. The N-terminal region of proto-*dbl* down regulates its transforming activity. *Oncogene* 4: 1067-1072, 1989.
9. Eva A., **Graziani G.**, Zannini M., Merin L.M., Khillan J.S., Overbeek P.A. Dominant dysplasia of the lens in transgenic mice expressing the *dbl* oncogene. *The New Biologist* 3: 158-168, 1991.
10. Garcia de Herreros A., Dominguez I., Diaz-Meco M.T., **Graziani G.**, M.E. Cornet, Guddal P.H., Johansen T., Moscat J. Requirement of phospholipase C-catalyzed hydrolysis of *Xenopus laevis* oocytes in response to insulin and ras *p21*. *Journal of Biological Chemistry* 266:6825-6829, 1991.
11. Ron D., Zannini M., Lewis M., Wichner R.B., Hunt L.T., **Graziani G.**, Tronick S.R., Aaronson S.A., Eva. A. A region of proto-*dbl* essential for its transforming activity shows a sequence similarity to a yeast cell cycle gene, CDC 24, and the human breakpoint cluster gene, bcr. *The*

new Biologist 3: 372-379, 1991.

12. Eisemann A., Ahn J.A., **Graziani G.**, Tronick S.R., Ron D. Alternative splicing generates at least five different isoforms of the human basic-FGF receptor. *Oncogene* 6: 1195-1202, 1991.
13. Dominguez I., Marshall M.S., Gibbs J.B., De Herreros A.G., Cornet M.E., **Graziani G.**, Diaz-Meco M.T., Johansen T., McCormick F., Moscat J. Role of GTPase activating protein in mitogenic signalling through phosphatidylcholine-hydrolysing phospholipase C. *EMBO Journal* 10: 3215-3220, 1991.
14. **Graziani G.**, Nebreda A.R., Srivastava S., Santos E., Eva A. Induction of *Xenopus* oocyte meiotic maturation by the *dbl* oncogene product. *Oncogene* 7: 229-235, 1992.
15. **Graziani G.**, Faraoni I., Zhang J., Caronti B., Lauro G., Bonmassar E., Macchi B. Transient HTLV-I infection of a human glioma cell line following cell-free exposure. *Virology* 197: 767-769, 1993.
16. Fuggetta M.P., Aquino A., Pepponi R., D'Atri S., Lanzilli G., Bonmassar E., **Graziani G.** In vitro combined effects of human interferons and interleukin-2 on natural cell-mediated cytotoxicity. *International Journal of Immunopharmacology* 15: 1-10, 1993.
17. Macchi B., **Graziani G.**, Zhang J., Mastino A. Emergence of double-positive CD4/CD8 cells from adult peripheral blood mononuclear cells infected with Human T Cell Leukemia Virus Type I (HTLV-I). *Cellular Immunology* 149: 376-389, 1993.
18. Piccioni D., D'Atri S., Papa G., Caravita T., Franchi A., Bonmassar E., **Graziani G.** Cisplatin increases sensitivity of human leukemic blasts to triazene compounds. *Journal of Chemotherapy* 7: 224-228, 1995.
19. Tentori L., **Graziani G.**, Gilberti S., Lacal P.M., Bonmassar E., D'Atri E. Triazene compounds induce apoptosis in O⁶-alkylguanine-DNA alkyltransferase deficient leukemia cell lines. *Leukemia* 9: 1888-1895, 1995.
20. Giuliani A., Vernole P., D'Atri S., Del Poeta G., D'Onofrio C., Faraoni I., Greiner J.W., Bonmassar E., **Graziani G.** In vitro infection of leukemic bone-marrow with HTLV-I generates immortalized cell lines expressing T or myeloid cell phenotype. *Leukemia* 9: 2071-2081, 1995.
21. **Graziani G.**, Faraoni I., Grohmann U., Bianchi R., Binaglia L., Margison G. P., Watson A.J., Orlando L., Bonmassar E., D'Atri S. O⁶-alkylguanine-DNA alkyltransferase attenuates triazene-induced cytotoxicity and tumor cell immunogenicity in murine L1210 leukemia. *Cancer Research* 55: 6231-6236, 1995.
22. Reich-Slotky R., Shaoul E., Berman B., **Graziani G.**, Ron D. Chimeric molecules between keratinocyte growth factor and basic fibroblast growth factor define domains that confer receptor binding specificities. *Journal of Biological Chemistry* 270: 29813-8, 1995.
23. Lacal P.M., D'Atri S., Orlando L., Bonmassar E., **Graziani G.** In vitro inactivation of human O⁶-alkylguanine-DNA alkyltransferase by antitumor triazene compounds. *The Journal of Pharmacology and Experimental Therapeutics* 279: 416-422, 1996.
24. Prete S.P., Aquino A., Masci G., Orlando L., Giuliani A., De Santis S., De Vecchis L., De Filippi R., Greiner J.W., Bonmassar E., **Graziani G.** Drug-induced changes of carcinoembryonic antigen expression in human cancer cells: effect of 5-fluoracil. *The Journal of Pharmacology and Experimental Therapeutics* 279: 1574-1581, 1996.
25. Faraoni I., Turriziani M., Bonmassar E., De Vecchis L., **Graziani G.** Development of a novel in vitro chemosensitivity assay: telomerase as a possible marker of tumor cell survival. *Journal of Chemotherapy* 8: 394-398, 1996.

26. Faraoni I., Turriziani M., **Graziani G.**, De Vecchis L., Bonmassar E. Telomerase as a marker of tumor cell viability: a new approach for in vitro chemosensitivity assays. *Journal of Experimental and Clinical Cancer Research* 15: 311-312, 1996.
27. Giuliani A., Tentori L., Pepponi R., Porcelli S.A., Aquino A., Orlando L., Sugita M., Brenner M.B., Bonmassar E., **Graziani G.** Cytokine-induced expression of CD1b molecules by peripheral blood monocytes: influence of 3'-Azido-3'-deoxythymidine. *Pharmacological Research* 35: 135-140, 1997.
28. Tentori L., Orlando L., Lacial P.M., Benincasa E., Faraoni I., Bonmassar E., D'Atri S., **Graziani G.** Inhibition of O⁶-alkylguanine-DNA alkyltransferase or poly(ADP-ribose) polymerase increases susceptibility of leukemic cells to apoptosis induced by temozolomide. *Molecular Pharmacology* 52: 249-258, 1997.
29. Tricarico M., **Graziani G.**, Franzese O., Giuliani A., Starace G., Fuggetta M.P. CD1b expression in Molt-4 clones exposed to IL-4 and GM-CSF. *European Journal of Histochemistry* 41: 119-120, 1997.
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31. Faraoni I., Turriziani M., Masci G., De Vecchis L., Shay J.S., Bonmassar E., **Graziani G.** Decline in telomerase activity as a measure of tumor cell killing by antineoplastic agents *in vitro*. *Clinical Cancer Research* 3: 579-585, 1997.
32. Tentori L., **Graziani G.**, Porcelli S.A., Sugita M., Brenner M.B., Madaio R. Bonmassar E., Giuliani A., Aquino A. Rifampin increases cytokine-induced expression of CD1b molecule in human peripheral blood monocytes. *Antimicrobial Agents and Chemotherapy* 42: 550-554, 1998.
33. Tentori L., Lacial P.M., Benincasa E., Franco D., Faraoni I., Bonmassar E., **Graziani G.** Role of wild-type p53 on the antineoplastic activity of temozolomide alone or combined with an inhibitor of poly(ADP-ribose) polymerase. *The Journal of Pharmacology and Experimental Therapeutics* 285: 884-893, 1998.
34. D'Atri S., Tentori L., Lacial P.M., **Graziani G.**, Pagani E., Benincasa E., Zambruno G., Bonmassar E., Jiricny J. (1998) Involvement of the mismatch repair system in temozolomide-induced apoptosis. *Molecular Pharmacology* 54: 334-341, 1998.
35. Giuliani A., Porcelli S.A., Tentori L., **Graziani G.**, Testorelli C., Prete S.P., Brenner M.B., Bonmassar E., Bussini S., Cappelletti D., Aquino A. Effect of rifampin on CD1b molecule induction in peripheral blood monocytes and on mycobacteria recognition by double-negative T cells. *Life Science* 63: 985-994, 1998.
36. Bonmassar E., Aquino A., Giuliani A., Porcelli S.A., Tentori L., Testorelli C., Prete S.P., Brenner M.B., Cirello I., Cappelletti D., **Graziani G.** New aspects of immune responses against mycobacteria: immunopharmacology studies. *Haematologica* 83: 58-59, 1998.
37. Levati L., Marra G., Lettieri T., D'Atri S., Vernole P., Tentori L., Lacial P.M., Pagani E., Bonmassar E., Jiricny J., **Graziani G.** Mutation of the mismatch repair gene hMSH2 in a human T-cell leukemia line tolerant to methylating agents. *Gene Chromosome & Cancer* 23: 159-166, 1998.
38. Franzese O., Comandini A., Cannavò E., **Graziani G.**, Bonmassar E. Effect of prostaglandin on proliferation and telomerase activity of human melanoma cells in vitro. *Melanoma Research* 8: 323-328, 1998.

39. Aquino A., Prete S.P., Giuliani A., **Graziani G.**, Turriziani M., de Filippi R., Masci G., Greiner J.W., Bonmassar E., De Vecchis L. Effect of the combined treatment with 5-fluorouracil, β -interferon or folinic acid in carcinoembryonic antigen expression in colon cancer cells. *Clinical Cancer Research* 4: 2473-2481, 1998.
40. Tonini G., Nunziata C., Prete S.P., Pepponi R., Turriziani M., Masci G., **Graziani G.**, Bonmassar E., De Vecchis L. Adjuvant treatment of breast cancer: a pilot immunochemotherapy study with CMF, interleukin-2 and interferon-alpha. *Cancer Immunology and Immunotherapy* 47: 157-176, 1998.
41. Tricarico M., Macchi B., Morrone S., Bonmassar E., Fuggetta M.P., **Graziani G.** In vitro infection of CD4+ T lymphocytes with HTLV-I generates immortalized cell line coexpressing lymphoid and myeloid markers. *Leukemia* 13: 222-229, 1999.
42. Tentori L., Turriziani M., Franco D., Serafino A., Levati L., Roy R., Bonmassar E., **Graziani G.** Treatment with temozolomide and poly(ADP-ribose) polymerase inhibitors induces early apoptosis and increases base excision repair gene transcripts in leukemic cells resistant to triazene compounds. *Leukemia* 13: 901-909, 1999.
43. Faraoni I., **Graziani G.**, Turriziani M., Masci G., Mezzetti M., Testori A., Veronesi U., Bonmassar E. Suppression of telomerase activity as an indicator of drug-induced cytotoxicity against cancer cells: in vitro studies with fresh human tumor samples. *Laboratory Investigation* 79: 993-1005, 1999.
44. Faraoni I., **Graziani G.** Telomerase as a potential anticancer target: growth inhibition and genomic instability. *Drug Resistance Updates* 3: 3-6, 2000.
45. Aquino A., Prete S.P., Baier S., Cappelletti D., Greiner J.W., De Vecchis L., **Graziani G.**, Bonmassar E. Staurosporine increases carcinoembryonic antigen expression in a human colon cancer cell line. *Journal of Chemotherapy* 12: 167-172, 2000.
46. Faraoni I., Bonmassar E., **Graziani G.** Clinical applications of telomerase in cancer treatment. *Drug Resistance Updates* 3: 161-170, 2000.
47. D'Atri S., **Graziani G.**, Lacal P.M., Nisticò V., Gilberti S., Faraoni I., Watson A.J., Bonmassar E., Margison G.P. Attenuation of O⁶-Methylguanine-DNA Methyltransferase Activity and mRNA levels by Cisplatin and Temozolomide in Jurkat Cells. *The Journal of Pharmacology and Experimental Therapeutics* 294: 664-671, 2000.
48. Tentori L., Vernole P., Lacal P.M., Madaio R., Portarena I., Levati L., Balduzzi A., Turriziani M., Dande P., Gold B., Bonmassar E., **Graziani G.** Cytotoxic and clastogenic effects of a DNA minor groove binding methyl sulfonate ester in mismatch repair deficient leukemia cells. *Leukemia* 14: 1451-1459, 2000.
49. Aquino A., Prete P.S., Guadagni F., Greiner J.W., Giuliani A., Orlando L., Masci G., De Santis S., Bonmassar E., **Graziani G.** Effect of 5-fluorouracil on carcinoembryonic antigen expression and shedding at clonal level in colon cancer cells. *Anticancer Research* 20: 3475--3484, 2000.
50. Prete S.P., Giuliani A., Iona E., Fattorini L., Orefici G., Franzese O., Bonmassar E., **Graziani G.** Bacillus calmette-guerin down-regulates CD1b induction by granulocyte-macrophage colony stimulating factor in human peripheral blood monocytes. *Journal of Chemotherapy* 13: 52-58, 2001.
51. Tentori L., Portarena I., Vernole P., De Fabritiis P., Madaio R., Balduzzi A., Roy R., Bonmassar E., **Graziani G.** Effects of single or split exposure of leukemic cells to temozolomide, combined with poly(ADP-ribose) polymerase inhibitors on cell growth, chromosomal aberrations and base excision repair components. *Cancer Chemotherapy and*

Pharmacology 47: 361-369, 2001.

52. Tentori L., Portarena I., Bonmassar E., **Graziani G.** Combined effects of adenovirus-mediated wild-type p53 transduction, temozolomide and poly (ADP-ribose) polymerase inhibitor in mismatch repair deficient and non-proliferating tumor cells. *Cell Death & Differentiation* 8: 457-469, 2001.
53. Tentori L., Balduzzi A., Portarena I., Levati L., Vernole P., Gold B., Bonmassar E., **Graziani G.** Poly (ADP-ribose) polymerase inhibitor increases apoptosis and reduces necrosis induced by a DNA minor groove binding methyl sulfonate ester. *Cell Death & Differentiation*, 8: 817-828, 2001.
54. Pepponi R., **Graziani G.**, Falcinelli S., Vernole P., Levati L., Lacial P.M., Pagani E., Bonmassar E., Jiricny J., D'Atri S. hMSH3 overexpression and cellular response to cytotoxic anticancer agents. *Carcinogenesis* 22: 1131-1137, 2001.
55. Giuliani A., Prete S.P., **Graziani G.**, Aquino A., Balduzzi A., Sugita M., Brenner M.B., Iona E., Fattorini L., Orefici G., Porcelli S.A., Bonmassar E. Influence of Mycobacterium bovis bacillus Calmette Guerin on in vitro induction of CD1 molecules in human adherent mononuclear cells. *Infection Immunity* 69: 7461-70, 2001.
56. Tentori L., Portarena I., **Graziani G.** Potential clinical applications of poly(ADP-ribose) polymerase (PARP) inhibitors. *Pharmacological Research* 45: 73-85, 2002.
57. Tentori L., Portarena I., Vernole P., Gold B., **Graziani G.** Apoptotic and genotoxic effects of a methyl sulfonate ester that selectively generates N3-methyladenine and poly (ADP-ribose) polymerase inhibitors in normal peripheral blood lymphocytes *Cancer Chemotherapy and Pharmacology* 49: 217-224, 2002.
58. Tentori L., Leonetti C., Scarsella M., d'Amati G., Portarena I., Zupi G., Bonmassar E., **Graziani G.** Combined treatment with temozolomide and poly(ADP-ribose) polymerase inhibitor enhances survival of mice bearing hematologic malignancy at the central nervous system site. *Blood* 99: 2241-2244, 2002.
59. **Graziani G.**, Tentori L., Portarena I., Barbarino M., Tringali G., Pozzoli G., Navarra P. Corticotropin-releasing hormone inhibits cell growth of human endometrial adenocarcinoma cells via CRH-R1 mediated activation of cAMP-protein kinase A pathway. *Endocrinology* 43: 807-13, 2002.
60. Dolci S., Levati L., Pellegrini M., Faraoni I., **Graziani G.**, Di Carlo A., Geremia R. Stem cell factor activates telomerase in mouse mitotic spermatogonia and in primordial germ cells. *Journal of Cell Science*; 115: 1643-9, 2002.
61. Prete S.P., Cappelletti D., Baier S., Nasuti P., Guadagni F., De Vecchis L., Greiner J.W., Bonmassar E., **Graziani G.**, Aquino A. Pharmacological modulation of carcinoembryonic antigen in human cancer cells: studies with staurosporine. *International Immunopharmacology* 2: 641-51, 2002.
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64. Tentori L., Portarena I., Torino F., Scerrati M., Navarra P., **Graziani G.** Poly(ADP-ribose)

polymerase inhibitor increases growth inhibition and reduces G₂/M cell accumulation induced by temozolomide in malignant glioma cells. *Glia* 40: 44-54, 2002.

65. Tentori L., **Graziani G.** Pharmacological strategies to increase the antitumor activity of methylating agents. *Current Medicinal Chemistry* 9: 1285-1301, 2002.
66. Tentori L., Leonetti C., Scarsella M., D'Amati G., Vergati M., Portarena I., Xu W., Kalish V., Zupi G., Zhang J., **Graziani G.** Systemic administration of GPI 15427, a novel poly(ADP-ribose) polymerase-1 inhibitor, increases the antitumor activity of temozolomide against intracranial melanoma, glioma, lymphoma. *Clinical Cancer Research* 9:5370-5379, 2003.
67. **Graziani G.**, Tentori L., Portarena I., Vergati M., Navarra P. Valproic acid increases the stimulatory effect of estrogens on proliferation of human endometrial adenocarcinoma cells. *Endocrinology* 144: 2822-2828, 2003.
68. Tentori L., Portarena I., Barbarino M., Balduzzi A., Levati L., Vergati M., Biroccio A., Gold B., Lombardi M.L., **Graziani G.** Inhibition of telomerase increases resistance of melanoma cells to temozolomide, but not to temozolomide combined with poly (ADP-ribose) polymerase inhibitor. *Molecular Pharmacology* 63: 192-202, 2003.
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72. Tentori L., Leonetti C., Scarsella M., Vergati M., Xu W., Calvin D., Morgan L., Tang Z., Wozniak K., Alemu C., Hoover R., Lapidus R., Zhang J., **Graziani G.** Brain distribution and efficacy as chemosensitizer of an oral formulation of PARP-1 inhibitor GPI 15427 in experimental models of CNS tumors. *International Journal of Oncology* 2005; 26:415-422.
73. Tentori L., Forini O., Fossile E., Muzi A., Vergati M., Portarena I., Amici C., Gold B., **Graziani G.** N3-methyladenine induces early poly (ADP-ribosylation), reduction of NF-kB DNA binding ability and nuclear up-regulation of telomerase activity. *Molecular Pharmacology* 2005; 67:572-81.
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