

Curriculum Vitae del Prof. Antonio Iavarone

Antonio Iavarone, M.D.

Academic Training

- Liceo Ginnasio "Pietro Giannone" Benevento Italy) (Italian equivalent of College) 1972-1976. Degree achieved: Maturita' classica (July 1981).
- Medical School, Catholic University, School of Medicine, Rome, Italy (1981-1987). Degree achieved: Medical Doctor (Summa cum Laude, July 1987).

Traineeship

Internship

- Pediatric Oncology Post-graduate Training, Division of Pediatric Oncology, Catholic University, School of Medicine, Rome, Italy (1987-1991).

Residency

- Residency in Pediatrics, Catholic University, School of Medicine, Rome, Italy (1987-1991).

Post-doctoral Fellowship

- Research Fellow, Preuss Laboratory for Molecular Neuro-oncology, Brain Tumor Research Center, UCSF, San Francisco (12/90-8/94).
- Research Fellow, Howard Hughes Medical Institute and Cell Biology and Genetics Program, Memorial Sloan-Kettering Cancer Center, New York (9/1994-8/1998).

Board qualification

- Italian Medical Board (Certification achieved in November 1987).
- Italian Board in Pediatrics (Certification achieved in July 1991).

Professional organizations and Societies

- American Association for Cancer Research (AACR).
- The Harvey Society.

Academic appointments

- Assistant Professor, Division of Pediatric Oncology, Department of Pediatrics, Catholic University, School of Medicine, Rome, Italy (3/95-9/98).
- Assistant Professor, Department of Neurology and Department of Molecular and Developmental Biology (DMB), Comprehensive Cancer Center, Albert Einstein College of Medicine, Bronx, New York (9/98-6/2001).
- Associate Professor, Department of Neurology and Department of Molecular and Developmental Biology (DMB), Comprehensive Cancer Center, Albert Einstein College of Medicine, Bronx, New York (6/2001-8/2002).
- Associate Professor, Department of Neurology and Department of Pathology, Institute for Cancer Genetics, Columbia University, New York (8/2002-present).

Past fellowships and grant support

- Recipient, Fellowship from the Italian Association for Cancer Research (AIRC) (1989-1991).
 - Recipient, Exchange Fellowship from EORTC-NCI (1991-1992).
 - Recipient, 1992 American Society of Clinical Oncology (ASCO) Award.
- Recipient, Fellowship from the Robert Steel Foundation for Pediatric Cancer Research (June 1992).
- Recipient, Fellowship for Physicians from Howard Hughes Medical Institute (January 1992-December 1995).
 - Recipient, Young investigator travel grant "Cancer and the Cell Cycle" Symposium Lausanne 17-20 January 1996.
- Recipient, Fellowship from the Charles Revson Foundation of the Clinical Scholars Training Program of Memorial Sloan-Kettering Cancer Center, New York (February 1996-February 1998).
- Principal Investigator, American Cancer Society Institutional Research Grant.

(11/1/1999-10/31/2000).

- Principal Investigator, Research Grant from L.I.L.A.C. (Long Island League to Abolish Cancer). (2000-2002).
 - Sinsheimer Scholar Award (7/1/1999 – 6/30/2002).
- Principal Investigator, Charlotte Geyer Cancer Foundation (8/1/2005-7/31/2006). Direct costs: \$100,000. This foundation provided interim funding to identify Id2 protein complexes in neuroblastoma.

Active grant support

- Principal Investigator, NIH/NCI R01-CA85628 “Id2 in cell cycle regulation and cancer”. Total funding: \$230,000/year direct costs (8/1/2006-7/30/2011; 35% efforts).
- Principal Investigator NIH/NCI R01-CA127643 “Mechanisms and regulation of post-translational modifications of Id proteins”. Requested funding: \$250,000/year direct costs (12/1/2007-11/30/2012; 25% efforts).
- Principal Investigator, Brain Tumor and Development Fellowships Program of the Welfare Ministry of Italy (1/1/2007-1/1/2012; Total costs: Euro 1,500,000).
 - Principal Investigator, The Chemotherapy Foundation grant “The N-Myc oncoprotein and its ubiquitin ligase Ureb1 as master regulators of cancer stem cells in malignant glioma” (1/1/2008-12/31/2009; Total costs: \$50,000/year).
 - Co-investigator, NIH/NCI R01-CA101644 “The Rb-Id2 pathway in mouse development and tumorigenesis”. Total funding: \$250,000/year direct costs (4/1/2003-3/31/2008; 25% efforts).
- Co-investigator for the Brain Tumor Program of the Research Infrastructure NIH grant PA-03-040 assigned in September 2003 to the Dean of the Medical School of Columbia University, P. I. Gerald Fischbach.

Patent inventor

- Method for diagnosing and treating pediatric neoplasm (filed December 2000).
- Methods for Treating Tumors Including ENH Dislocation of Id Proteins (filed May 2005).
 - Degradation Resistant Id Proteins and Uses Thereof (filed May 2006).

Departmental and University Committees

- Albert Einstein College of Medicine Senator (1999-2001).
- Organizer of the Work in Progress Friday seminars for the Department of Developmental and Molecular Biology (DMB, 1999-2001) at the Albert Einstein College of Medicine.
- Coordinator of the Seminar series at the Institute for Cancer Genetics of Columbia University, New York (June 2002-present).

Teaching experience and responsibilities

- Lecturer in 1999, 2000 and 2001 to Ph.D. students in the Gene Expression Course at AECOM.
- Journal reviews in 1999 to Ph.D. students in the Molecular Biology and Genetics course at AECOM.
- Lecturer in 2000 to Ph.D. students in the Course on Development at AECOM.
- Member of the Ph.D Thesis Examination Committee and of the Ph.D. Advisory Committee of 9 M.D, Ph.D. and Ph.D. students at AECOM and 4 Ph. D. students at Columbia University.
- Lecturer and Examiner in 2003, 2004, 2005 and 2006 to Ph.D. students in the Cancer Biology Course at Columbia University.

Other professional activities

Meeting Organizer

- 3rd International Symposium “Basic-Helix-Loop-Helix genes: Regulators of Normal Development and Indicators of Malignant Transformation”, May 9-10, 2005, Rome, Italy.

Editorial

- Editorial board member of Cell Division.
 - Reviewer for the following Journals:
 - Nature;
 - Developmental Cell;

- Nature Cell Biology;
- Genes & Development;
 - Neuron;
 - EMBO Journal;
 - EMBO Reports;
- Molecular and Cellular Biology;
 - Journal of Cell Biology;
 - Journal of Neuroscience;
 - Oncogene;
- Journal of Clinical Investigation;
 - Cancer Research;
- Cell Growth and Differentiation;
- International Journal of Cancer;
- Journal of Neuroscience Research;
 - Journal of Neurooncology;
 - Neuroscience;
 - Brain Research;
 - Molecular Brain Research;
 - Cell Death and Differentiation.

Consultative

- Permanent Member of CSRS (Cellular Signaling and Regulatory Systems) Study Section, NIH, from July 1, 2008 to June 30, 2012.
 - Ad hoc reviewer for P01 site visit for the National Cancer Institute/National Institutes of Health (NCI/NIH), June 2002, June 2003.
 - Ad hoc reviewer, NCI subcommittee C, August 2002.
- Ad hoc Member of CSD Study Section, NIH, October 12-13, 2006; February 15-16, 2007.
 - Ad hoc Member of CSRS Study Section, NIH, June 7-8, 2007; January 31-February 1, 2008.
 - Ad hoc Member of MONC (Molecular Oncogenesis) Study Section, NIH, September 24-25, 2007.
- Member of Scientific Advisory Board of the Biotechnology company Angiogenex (2001-present).

Publications

Original, peer reviewed articles

1. Masullo C., Pocchiari M., Neri G., Casaccia P., **lavarone A.**, Ladogana A., Macchi G. A retrospective study of Creutzfeldt-Jacob disease in Italy (1972-1986). *Eur. J. Epidem.* 4: 482-487, 1988.
2. **lavarone A.**, Eboli M.L., Osti M., Redler A., Pocchiari M., Russo M.A. 3-D Changes in neuroblastoma/glioma hybrid (NG108-15). Cell differentiation as studied by SEM and TEM. *Prog. Clin. Biol. Res.*, 295: 377-382, 1989.
3. **lavarone A.**, Servidei T., Riccardi R., Lasorella A., Mastrangelo R. Specific uptake of 125-I-metaiodobenzylguanidine in human neuroblastoma cell lines is associated with the neuroblastic cell type. *Prog. Clin. Biol. Res.*, 366:447-454, 1991.
4. **lavarone A.**, Lasorella A., Servidei T., Riccardi R., Troncone L., Mastrangelo R. Biology of metaiodobenzylguanidine interactions with human neuroblastoma cells. *J. Nuc. Biol. Med.*, 35(4):186-190, 1991.
5. Mastrangelo R; Lasorella A; Troncone L; Rufini V; **lavarone A**; Riccardi R. [131I]metaiodobenzylguanidine in neuroblastoma patients at diagnosis. *J. Nuc. Biol. Med.*, 35(4):252-254, 1991.
6. Mastrangelo R, Lasorella A, **lavarone A**, Troncone L. Urinary vanilmandelic acid and homovanillic acid: markers of two distinct cell populations in neuroblastoma? *Ped. Hem. Onc.*, 8(4):379-381, 1991.
7. **lavarone A.**, Matthay K.K., Steinkirchner T.M., Israel M.A. Germ-line and somatic p53 mutations in multifocal osteogenic sarcoma. *Proc. Natl. Acad. Sci. USA* 89: 4207-4209, 1992.
8. **lavarone A.**, Lasorella A., Servidei T., Riccardi R., Mastrangelo R. Uptake and storage of m-iodobenzylguanidine are frequent neuronal functions of

- human neuroblastoma cell lines. *Cancer Res.*, 53(2):304-309, 1993.
9. Mastrangelo R; Lasorella A; **lavarone A**; Rufini V; Troncone L; Danza F; Riccardi R. Critical observations on neuroblastoma treatment with 131-I-metaiodobenzylguanidine at diagnosis. *Med. Ped. Onc.*, 21(6):411-5, 1993.
10. **lavarone A.**, Garg P., Lasorella A., Hsu J., Israel M.A. The helix-loop-helix protein Id-2 enhances cell proliferation and binds to the retinoblastoma protein. *Genes & Dev.*, 8(11):1270-1284, 1994.
11. Riccardi R., Riccardi A., Lasorella A., Di Rocco C., Carelli G., Tornesello A., Servidei T., **lavarone A.**, Mastrangelo R. Clinical Pharmacokinetics of Carboplatin in Children. *Cancer Chem. Pharmacol.*, 33(6):477-483, 1994.
12. Mastrangelo R., Lasorella A., Riccardi R., Colosimo C., **lavarone A.**, Tornesello A., Ausili-Cefaro G., Di Rocco C. Carboplatin in childhood medulloblastoma/PNET: feasibility of an in vivo sensitivity test in an "up front" study. *Med. Ped. Onc.*, 24(3):188-196, 1995.
13. Chen P., **lavarone A.**, Fick J., Edwards M.S., Prados M.D., Israel M.A. Constitutional p53 mutations associated with brain tumors in young adults. *Cancer Genet. & Cytogenet.*, 82(2):106-115, 1995.
14. Jensen S., Paderanga D.C., Chen P.C., Olson K., Edwards M., **lavarone A.**, Israel M.A., Shannon K. Molecular analysis at the NF1 locus in astrocytic brain tumors. *Cancer*, 76(4):674-677, 1995.
15. Reynisdottir I., Polyak K., **lavarone A.**, Massague J. (*The first three authors contributed equally to this study*) Kip/Cip and Ink4 Cdk inhibitors cooperate to induce cell cycle arrest in response to TGF-beta. *Genes & Dev.*, 9(15):1831-1845, 1995.
16. Servidei T., **lavarone A.**, Lasorella A., Mastrangelo S., Riccardi R. Release mechanisms of [125I]meta-iodobenzylguanidine in neuroblastoma cells: evidence of a carrier-mediated efflux. *Eur. J. Cancer*, 31A(4):591-595, 1995.
17. Lasorella A., **lavarone A.**, Israel MA. Differentiation of neuroblastoma enhances Bcl-2 expression and induces alterations of apoptosis and drug resistance. *Cancer Res.*, 55(20):4711-6, 1995.
18. Lasorella A., **lavarone A.**, Israel MA. Id2 specifically alters regulation of the cell cycle by tumor suppressor proteins. *Mol. Cell. Biol.* 16 (6):2570-2578, 1996.
19. Orlow I., **lavarone A.**, Cridermiller Sj., Bonilla F., Latres E., Lee MH., Gerald WL., Massague' J., Weissman BE., Cordon-Cardo' C. Cyclin-dependent kinase inhibitor p57(Kip2) in soft tissue sarcomas and Wilms tumors. *Cancer Res.*, 56 (6):1219-1221, 1996.
20. Liu M. , **lavarone A.**, Freedman L.P. Transcriptional activation of the human p21WAF1/CIP1 gene by retinoic acid receptor. Correlation with retinoid induction of U937 cell differentiation. *J. Biol. Chem.* 271 (49): 31723-31728, 1996.
21. Hiyama H., **lavarone A.**, LaBaer J., Reeves S.A. Regulated ectopic expression of cyclin D1 induces transcriptional activation of the cdk inhibitor p21 gene without altering cell cycle progression. *Oncogene*, 14:2533-2542, 1997.
22. **lavarone A.**, Massague' J. Repression of the Cdk activator Cdc25A and cell cycle arrest by cytokine TGF- β in cells lacking the Cdk inhibitor p15. *Nature (Letter)*, 387: 417-422, 1997.
23. Mastrangelo R., Tornesello A., Lasorella A., **lavarone A.**, Mastrangelo S., Riccardi R., Diociaiuti L., Rufini V., Pession A., Troncone L. Optimal use of the 131-I-metaiodobenzylguanidine and cisplatin combination in advanced neuroblastoma. *J. Neurocol.* 31:153-158, 1997.
24. Hiyama H., **lavarone A.**, Reeves S.A. Regulation of the cdk inhibitor p21 gene during cell cycle progression is under the control of the transcription factor E2F. *Oncogene*, 16:1513-1523, 1998.
25. **lavarone A.** & Massague' J. E2F and histone deacetylase mediate TGF β

- repression of *cdc25A* during keratinocyte cell cycle arrest, *Mol. Cell. Biol.*, 19:916-922, 1999.
26. Rots N.Y., **lavarone A.**, Bromleigh V., Freedman L.P. Induced differentiation of U937 cells by 1,25-dihydroxyvitamin D3 involves cell cycle arrest in G1 that is preceded by a transient proliferative burst and an increase in cyclin expression. *Blood* 93:2721-2729, 1999.
 27. Bouzahzah B., Fu M., **lavarone A.**, Factor V.M., Thorgeirsson S.S., Pestell R.G. Transforming growth factor- α -1 recruits histone deacetylase 1 to a p130 repressor complex in transgenic mice in vivo. *Cancer Res.* 60:4531-4537, 2000.
 28. Lasorella A., Nosedà M., Beyna M., **lavarone A.** Id2 is a target of the retinoblastoma protein and mediates signalling by Myc oncoproteins. *Nature (Article)*, 407:592-598, 2000.
 29. Park D.S., Razani B., Lasorella A., Schreiber-Agus N., Pestell R.G., **lavarone A.**, Lisanti M.P. Evidence that Myc isoforms transcriptionally repress caveolin-1 gene expression via INR-dependent mechanism. *Biochemistry* 40:3354-3362, 2001.
 30. Wainwright L.J., Lasorella A., **lavarone A.** Distinct mechanisms of cell cycle arrest control the decision between differentiation and senescence in human neuroblastoma cells. *Proc Natl Acad Sci U S A* 98:9396-9400, 2001.
 31. Lasorella A., Boldrini R., Dominici C., Donfrancesco A., Yokota Y., Inserra A., **lavarone A.** Id2 is critical for cellular proliferation and is the oncogenic effector of N-myc in human neuroblastoma. *Cancer Res.* 62:301-306, 2002.
 32. Russell R.G., Lasorella A., Dettin L.E., **lavarone A.** Id2 drives differentiation and suppresses tumor formation in the intestinal epithelium. *Cancer Res.* 64:7220-5, 2004.
 33. **lavarone A.**, E. R. King, X. M. Dai, G. Leone, E. R. Stanley, and A. Lasorella. Retinoblastoma promotes definitive erythropoiesis by repressing Id2 in fetal liver macrophages. *Nature*, 432:1040-1045, 2004 (see also *News and Views*, Palis J. Developmental biology: no red cell is an island *Nature* 432:964-965, 2004).
 34. Light W, Vernon AE, Lasorella A, **lavarone A.**, Labonne C. Xenopus Id3 is required downstream of Myc for the formation of multipotent neural crest progenitor cells. *Development.* 132:1831-1841, 2005.
 35. Lasorella, A., G. Rothschild, Y. Yokota, R. G. Russell, **A. lavarone.** Id2 mediates tumor initiation, proliferation and angiogenesis in Rb mutant mice. *Mol Cell Biol* 25:3563-3574, 2005.
 36. Lasorella A., **lavarone A.** The protein ENH is a new cytoplasmic sequestration factor for Id2 in normal and tumor cells from the nervous system. *Proc. Natl. Acad. Sci. USA.*, 103:4976-4981, 2006.
 37. Rothschild G., Zhang X-D., **lavarone A.**, Lasorella, A. E proteins and Id2 converge on p57Kip2 to regulate cell cycle in neural cells. *Mol Cell Biol* 26:4351-4361, 2006.
 38. Lasorella A., Stegmüller J., Guardavaccaro D., Liu G., Carro M.S., Rothschild G., de la Torre-Ubieta L., Pagano M., Bonni A., **lavarone A.** Degradation of Id2 by the Anaphase Promoting Complex couples cell cycle exit and axonal growth. *Nature*, 442:471-474, 2006 (see also *News & Views*, Jackson P. *Nature*, 442:365-366, 2006; Research Highlights, *Degrading Id.* *Nature Reviews Neuroscience*, 7:592, 2006; *Making the Paper.* *Nature* 442(7101)xiii, 2006).
 39. Guardavaccaro D., Frescas D., Dorrello N.V., Peschiaroli A., Multani A.S., Cardozo T., Lasorella A., **lavarone A.**, Chang S., Hernando E., Pagano M. Control of chromosome stability by the α -TrCP-REST-Mad2 axis. *Nature*, 452:365-369, 2008
 40. Zhao X., Ik-Tsen Heng J., Guardavaccaro D., Jiang R., Pagano M., Guillemot F., **lavarone A.**, Lasorella A. The HECT-domain ubiquitin ligase Huwe1 controls neural differentiation and proliferation by destabilizing the N-Myc

oncoprotein. *Nature Cell Biology*, 10:643-653, 2008.

41. Carro M.S., Lim W.K., Snyder E.Y., Colman H., Lasorella A, Aldape K., Califano A, **Iavarone A.** A transcriptional module synergistically initiates and maintains mesenchymal transformation in the brain. *Nature*, in review.

Invited Review

Lasorella A, Uo T, **Iavarone A.** Id proteins at the cross-road of development and cancer. *Oncogene* 20:8326-8333, 2001.

Iavarone A., Lasorella A. Id proteins in neural cancer. *Cancer Letters* 204:189-196, 2004.

Perk J, **Iavarone A.** and Benezra R. Id family of helix-loop-helix proteins in cancer *Nature Reviews Cancer*, 5:603-614, 2005.

Iavarone A., Lasorella A. Id proteins as targets in neural cancer and tools in neurodegenerative diseases. *Trends in Molecular Medicine*, 12:588-594, 2006.

Selected Invited Seminars and Conferences

October 24, 1995 Boston. Department of Neurology, Harvard Medical School.

June 20, 1997 Bethesda. NIH, Pediatric Branch.

September 22, 1997 Boston. BASF/Mitotix Corporation.

January 26, 1998 Vienna (Austria) IMP.

February 20, 1998 Maui, Hawaii. USA/Japan meeting on Cell Cycle Regulation.

February, 1998 University of California at San Francisco (UCSF).

March 1998 MD Anderson Cancer Center, Houston, Texas.

April 1998 Department of Cell Biology, University of Cincinnati.

July 1998 Department of Biochemistry, Medical and Dental School of the University of New Jersey.

April 30, 1999 National Institutes of Health (NIH).

December 1, 2000 National Cancer Institute (NCI, Pediatric Branch).

December 29, 2000 Istituto Gaslini, Genoa, Italy.

February 15, 2001. Columbia University, Grand Round, Institute of Neurology and Institute for Cancer Genetics.

April 19, 2001. Department of Neuroscience, University of Massachusetts Medical School.

July 15, 2002. Department of Pathology and Cancer Center, New York University.

October 21, 2002 2nd International Symposium "Basic Helix-loop-Helix genes: Regulators of Normal Development and Indicators of Malignant Development",

Amsterdam, Netherlands.

March 6, 2003. Pediatric Grand Round at the Memorial Sloan Kettering Cancer Center, New York.

April 22, 2003. University of Texas Health Science Center at San Antonio.

November 16-18, 2003. "Molecular Differentiation of Benign and Malignant Pheochromocytomas and Neuroblastomas", Banbury Center, Cold Spring Harbor Laboratory.

March 5, 2004. SUNY Downstate Medical Center, Brooklyn, New York.

February 4, 2005. Hematology/Oncology Seminar. New York University, New York.

August 30, 2005. Oncology Grand Rounds. Georgetown University Medical Center, Washington, DC.

September 9, 2005. Merck Research Laboratories. Boston.

February 10, 2006. Cancer Biology and Genetics Seminar. Memorial Sloan Kettering Cancer Center, New York.

October 22-27, 2006. Ubiquitin – New insights into regulation and function in chronic diseases and cancer. The Hebrew University of Jerusalem, Israel.

May 17-18, 2007. 4th International Symposium on Basic Helix-Loop-Helix Genes: Development and Diseases. Kyoto, Japan.

August 28, 2007. Neuro-oncology Grand Round, Department of Pathology, MD Anderson Cancer Center, Houston, Texas.