

Curriculum Vitae

Domenico D'Arca

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Personal and lab Information

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Education and training

2006

February 2006: I earned the PhD degree in Experimental Medicine at the University of Modena and Reggio Emilia, Faculty of Medicine, Italy.

2004-2006

During the second stage of my PhD program, I have been a visiting researcher at the Department of Urology, Kimmel Cancer Center, Thomas Jefferson University Hospital in Philadelphia, Pennsylvania, USA (Laboratory of Prof. Baffa R. and Gomella L.); my projects were focused on the characterization and functional analysis of *MITOSTATIN*, a new tumor suppressor gene, at 12q24.1 chromosome 12, and *in vivo* study of the effect of Rofecoxib in the inhibition or slowing the development of BBN-induced urinary bladder cancers in mice lacking the *FHIT* tumour suppressor gene. The experience and the accomplishments achieved in this outstanding laboratory allowed me to publish my results in the international peer-reviewed journals.

2003-2004

I started my PhD program in 2003, Faculty of Medicine, University of Modena and Reggio Emilia, Italy; over the first stage, my project was to better define the role of Clusterin protein in prostate cancer. In particular I investigated the localization and expression of different Clusterin isoforms during prostate cancer development in a transgenic mice model (Transgenic Adenocarcinoma of the Mouse Prostate, TRAMP) and in transformed cell lines. The role of this protein in the chemoprevention of prostate cancer has been investigated as well. I contributed on the accomplishment of the above research programs, and achieved several publications in the international peer-reviewed journals.

2001

Degree in Biological Sciences, 110/110, University of Modena and Reggio Emilia, Italy. I started working on cancer research field as graduate student, and my project was focused on the role of polyamine metabolism regulatory genes and Clusterin (SGP2, TRPM-2, APO-J) during the cell cycle and neoplastic transformation. I contributed

on the accomplishment of the above research program, achieving the publication in the leading international peer-reviewed journals.

Leadership and other Professional Experiences

2008 - to present

Assistant Professor position, University of Modena e Reggio Emilia, Department of Biomedical Sciences, Italy. Started my own laboratory. The experience and accomplishments achieved, provided me with the opportunity to continue to produce the highest quality work in the Oncology field. My research interests are mostly focused on the molecular basis of human tumors with emphasis on Prostate, Ovarian and Colorectal cancers. Structural and functional characterization of the new protein TpMs, endowed with tumor suppressor activity. Based on our preliminary results, TpMs may play a critical role in guarding the fidelity of mitosis; we demonstrated that its depletion leads to incorrect chromosome segregation, followed by aneuploidy and chromosomal aberrations. I have achieved in this laboratory the possibility to publish my results on the leading international peer-reviewed journals and obtained 1 Patent approved, 2015 (102015000088249, "ANTICANCER DRUGS").

2007-2009

Postdoctoral research fellow. Since May 2007, after my PhD program, I have been a postdoctoral research fellow at the outstanding laboratory of professors Antonio Iavarone and Anna Lasorella, Columbia University, Medical Center Institute for Cancer Genetics New York, USA. Over the three years of this postdoctoral fellowship, my projects were focused on the molecular mechanisms of tumor angiogenesis (roles of Id proteins in Hif1 α -VEGF pathway). I investigated also the roles of Huwe1, E3 ubiquitin ligase, that operate upstream of a novel N-Myc-Dll3-Notch pathway to control neural stem cell activity and promote neurogenesis. We found that the deregulation of Huwe1 function is involved in tumor development.

I have achieved in this laboratory the possibility to publish my results on the leading international peer-reviewed journals as main author.

In this laboratory I had the chance to supervise a technician and graduate students, who helped me in developing my projects.

Teaching activity

2008 - to present

Course on Biochemistry and Molecular Biology, New Technologies of Molecular Biology at the Faculty of Medicine, University of Modena and Reggio Emilia, Italy.

Supervision of undergraduate students, graduate students and postdoctoral fellows.

Research grants

2016-2018

2016-2018 AIRC Grant (Associazione italiana per la ricerca sul cancro) "Protein-protein interaction inhibitors of thymidylate synthase against colorectal cancers" IG 16977. *Participant.*

2016-2018

2016-2018 "Fondazione di Vignola" Grant. "Ruolo chiave della proteina Mitostatin per la stabilità genomica del tumore prostatico: nuovo biomarcatore capace di distinguere tumori indolenti da tumori aggressivi per una terapia personalizzata". *Principal Investigator*

2014-2017

2014-2017: BHF Grant (British Heart Foundation, PhD Studentship) " Trichoplein: Role

for a novel regulator in the endothelial cell function in diabetes” *Participant*.

- 2010-2013 2010-2013 AIRC Grant (Associazione italiana per la ricerca sul cancro) “Targeting drug resistance in ovarian cancer” IG 10474. *Participant*.
- 2006 PRIN 2006: “Study of anti-tumoral activity of green tea catechins (GTCs) and the role of Clusterin (CLU) and its nuclear form (nCLU) as possible mediator of their action”. ID: 2006062247. *Participant*.
- 2004 PRIN 2004: “Expression levels of Clusterin isoforms in inflammation and cancer of the lung”. ID: 2004061839_002. *Participant*.
- 2004 PRIN 2004: “Expression profiles of Clusterin isoforms and genes involved in cell proliferation during prostate carcinoma development”. ID: 2004062571_003. *Participant*.
- 2003 PRIN 2003: “Correlation between the expression patterns of Clusterin isoforms and of the genes controlling the metabolism of aliphatic polyamines in prostate cancer initiation and progression”. ID: 2003063881_003. *Participant*.

Reviewer for funding agencies

Grant award peer reviewer Expert Evaluator of the European Commission for Horizon 2020, the Marie Skłodowska-Curie Individual Fellowship H2020-MSCA-IF (MSCA-IF-2016, MSCA-IF-2017, MSCA-IF-2018); European & Global Fellowships – Scientific Panel LIF, since 2016.

University Grant: Bando di Ateneo per la Ricerca di Base, since 2015. PRIN, since 2018.

Reviewer for scientific journals

Biochemical Journal, Brain Research, British Journal of Medicine and Medical Research, British Journal of Pharmaceutical Research, Developmental Biology, Journal of Molecular Endocrinology, Medicinal Chemistry Journal.

Member of the editorial board

Member of the Editorial Board of Scientific Journals: Oxidative Medicine and Cellular Longevity, Analytical Cellular Pathology.

Participation to clinical trial studies

I am participating to the translational research activity of the following clinical trials: i) MITO group “Multicenter Italian Trials in Ovarian cancer and gynecologic malignancies” (MITO is a member of the Gynecologic Cancer Intergroup, GCIG and part of the European Network of Gynaecological Oncological Trial Groups, ENGOT); ii) EUTROC (European Network for Translational Research in Ovarian Cancer, Jalid Sheouli), and iii) translational research activity of clinical trial of the IRCCS Istituto Scientifico Romagnolo (Dr. Ugo De Giorgi) per lo Studio e la Cura dei Tumori (I.R.S.T.) Meldola, Forlì –Italy.

Patents

2015

Patent approved: "ANTICANCER DRUGS". Inventors: Costi MP, Costantino L, Ponterini G, Marverti G, Franchini S, Tondi D, **D'Arca D**, Ferrari S, Luciani R, Venturelli A, Sammak S, Lauriola A, Gozzi G. Submitted: 29/12/2015, Patent N°: 102015000088249.

Publications

Losi L, Lauriola A, Tazzioli E, Gozzi G, Scurani L, **D'Arca D**, Benhattar J. "Involvement of epigenetic modification of TERT promoter in response to all-trans retinoic acid in ovarian cancer cell lines". *J Ovarian Res.* 2019 Jul 10;12(1):62. doi: 10.1186/s13048-019-0536-y.

Elisi GM, Santucci M, **D'Arca D**, Lauriola A, Marverti G, Losi L, Scalvini L, Bolognesi ML, Mor M, Costi MP. "Repurposing of Drugs Targeting YAP-TEAD Functions". *Cancers (Basel).* 2018 Sep 14;10(9). pii: E329. doi: 10.3390/cancers10090329.

Sacchetti F, Marverti G, **D'Arca D**, Severi L, Maretti E, Iannuccelli V, Pacifico S, Ponterini G, Costi MP, Leo E. "pH-Promoted Release of a Novel Anti-Tumour Peptide by "Stealth" Liposomes: Effect of Nanocarriers on the Drug Activity in Cis-Platinum Resistant Cancer Cells". *Pharm Res.* 2018 Sep 12;35(11):206. doi: 10.1007/s11095-018-2489-z.

Saxena P, Severi L, Santucci M, Taddia L, Ferrari S, Luciani R, Marverti G, Marraccini C, Tondi D, Mor M, Scalvini L, Vitiello S, Losi L, Fonda S, Pacifico S, Guerrini R, **D'Arca D**, Ponterini G, Costi MP. "Conformational propensity and biological studies of proline mutated LR peptides inhibiting human thymidylate synthase and ovarian cancer cell growth". *J Med Chem.* 2018 Jul 23. doi: 10.1021/acs.jmedchem.7b01699.

Leda Severi, Lorena Losi, Sergio Fonda, Laura Taddia, Gaia Gozzi, Gaetano Marverti, Fulvio Magni, Clizia Chinello, Martina Stella, Jalid Sheouli, Elena I. Braicu, Filippo Genovese, Angela Lauriola, Chiara Marraccini, Alessandra Gualandi, **Domenico D'Arca**, Stefania Ferrari and Maria P. Costi. "Proteomic and Bioinformatic Studies for the Characterization of Response to Pemetrexed in Platinum Drug Resistant Ovarian Cancer". *Front Pharmacol.* 2018 May 8;9:454. doi: 10.3389/fphar.2018.00454. eCollection 2018.

Davalli Pierpaola, Marverti Gaetano, Lauriola Angela and **D'Arca Domenico**. "Targeting Oxidatively induced DNA damage Response in Cancer: Opportunities for Novel Cancer Therapies". *Oxid Med Cell Longev.* 2018 Mar 27;2018:2389523. doi: 10.1155/2018/2389523. eCollection 2018.

Sacchetti F, **D'Arca D**, Genovese F, Pacifico S, Maretti E, Hanuskova M, Iannuccelli V, Costi MP, Leo E. "Conveying a newly designed hydrophilic anti-human thymidylate synthase peptide to cisplatin resistant cancer cells: are pH-sensitive liposomes more effective than conventional ones?". *Drug Dev Ind Pharm.* 2016 Nov 25:1-28. [Epub ahead of print].

Glauco Ponterini, Andrea Martello, Giorgia Pavesi, Angela Lauriola, Rosaria Luciani, Matteo Santucci, Michela Pelà, Gaia Gozzi, Salvatore Pacifico, Remo Guerrini, Gaetano Marverti, Maria Paola Costi, and **Domenico D'Arca**. "Intracellular quantitative detection of human thymidylate synthase engagement with an unconventional inhibitor using tetracysteine-diarsenical-probe technology". *Sci. Rep.* 2016 Jun 2;6:27198. doi: 10.1038/srep27198.

Davalli Pierpaola, Mitic Tijana, Caporali Andrea, Lauriola Angela and **D'Arca Domenico**. "Ros, cell senescence and novel molecular mechanisms in aging and age-related diseases". *Oxid Med Cell Longev.* 2016. 2016;2016:3565127. doi: 10.1155/2016/3565127. Epub 2016 May 10.

Laura Taddia, **Domenico D'Arca**, Stefania Ferrari, Chiara Marraccini, Leda Severi, Glauco Ponterini, Yahuda G. Assaraf, Gaetano Marverti, Maria Paola Costi. (2015) "Inside the biochemical pathways of thymidylate synthase perturbed by anticancer drugs: novel strategies to overcome cancer chemoresistance". *Drug Resist Updat.* 2015 Nov;23:20-54. doi: 10.1016/j.drug.2015.10.003.

Sacchetti F, Marraccini C, **D'Arca D**, Pelà M, Pinetti D, Maretti E, Hanuskova M, Iannuccelli V, Costi MP, Leo E. (2015) "Enhanced anti-hyperproliferative activity of human thymidylate synthase inhibitor peptide by solid lipid nanoparticle delivery". *Colloids Surf B Biointerfaces.* 2015 Sep 25;136:346-354. doi: 10.1016/j.colsurfb.2015.09.040.

Genovese F, Gualandi A, Taddia L, Marverti G, Pironi S, Marraccini C, Perco P, Pelà M, Guerrini R, Amoroso MR, Esposito F, Martello A, Ponterini G, **D'Arca D**, Costi MP. (2014) "Mass spectrometric/bioinformatic identification of a protein subset that characterizes the cellular activity of anticancer peptides". *J Proteome Res.* 2014 Nov 7;13(11):5250-61. doi: 10.1021/pr500510v. Epub 2014 Sep 29.

Pelà M, Saxena P, Luciani R, Santucci M, Ferrari S, Marverti G, Marraccini C, Martello A, Pironi S, Genovese F, Salvadori S, **D'Arca D**, Ponterini G, Costi MP, Guerrini R. (2014) "Optimization of peptides that target human thymidylate synthase to inhibit ovarian cancer cell growth". *J Med Chem.* 2014 Feb 27;57(4):1355-67. doi: 10.1021/jm401574p. Epub 2014 Feb 12.

Pierpaola Davalli, Federica Rizzi, Andrea Caporali, Davide Pellacani, Serena Davoli, Saverio Bettuzzi, Maurizio Brausi, **Domenico D'Arca**. (2012) "Anticancer activity of green tea polyphenols in prostate gland". *Oxid Med Cell Longev.* 2012;2012:984219. Epub 2012 May 15.

Fassan M, **D'Arca D**, Letko J, Vecchione A, Gardiman MP, McCue P, Wildemore B, Ruggie M, Shupp-Byrne D, Gomella LG, Morrione A, Iozzo RV, Baffa R. (2011) "Mitostatin is down-regulated in human prostate cancer and suppresses the invasive phenotype of prostate cancer cells". *PLoS One.* 2011 May 6;6(5):e19771.

Domenico D'Arca, Xudong Zhao, Wenming Xu, Nadya C. Ramirez-Martinez, Antonio Iavarone and Anna Lasorella. (2010) "The Huwe1 ubiquitin ligase is essential to synchronize neuronal and glial differentiation in the developing cerebellum". *Proc Natl Acad Sci U S A.* 2010 Mar 30; 107(13):5875-80. Epub 2010 Mar 15.

Xudong Zhao, **Domenico D'Arca**, Wei Keat Lim, Manisha Brahmachary, Maria Stella Carro, Thomas Ludwig, Carlos Cordon Cardo, Francois Guillemot, Ken Aldape, Andrea Califano, Antonio Iavarone and Anna Lasorella. (2009) "A novel N-Myc-DLL3 cascade is suppressed by the ubiquitin ligase Huwe1 to inhibit proliferation and promote neurogenesis in the developing brain". *Dev Cell*. 2009 Aug; 17(2):210-21.

D'Arca D, LeNoir J, Wildemore B, Gottardo F, Bragantini E, Shupp-Byrne D, Zanesi N, Fassan M, Croce CM, Gomella LG, Baffa R. (2009) "Prevention of bladder cancer in the FHIT knock-out mouse model with ROFECOXIB, a Cox-2 inhibitor". *Urol Oncology: Seminars and Original investigations*. 2010 Mar-Apr; 28(2):189-94. Epub 2009 Apr 16.

Vecchione A, Fassan M, Anesti V, Morrione A, Goldoni S, Baldassarre G, Byrne D, **D'Arca D**, Palazzo JP, Lloyd J, Scorrano L, Gomella LG, Iozzo RV, Baffa R. (2009) "MITOSTATIN, a putative tumor suppressor on chromosome 12q24.1, is downregulated in human bladder and breast cancer". *Oncogene*. 2009 Jan 15; 28(2):257-69. Epub 2008 Oct 20.

Carnevali S., Luppi F., **D'Arca D.**, Caporali A., Ruggieri M.P., Vettori M.V., Caglieri A., Astancolle S., Panico F., Davalli P., Mutti A., Fabbri L.M., Corti A. (2006) "Clusterin Decreases Oxidative Stress in Lung Fibroblasts Exposed to Cigarette Smoke". *Am J Respir Crit Care Med*. 2006 Aug 15; 174(4):393-9. Epub 2006 May 18.

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Marverti G., Monti M.G., Pegg A.E., McCloskey D.E., Bettuzzi S., Ligabue A., Caporali A., **D'Arca D.**, Moruzzi M.S. (2005) "Spermidine/spermine N1-acetyltransferase transient over-expression restores sensitivity of resistant human ovarian cancer cells to N1,N12-bis(ethyl)spermine and to cisplatin". *Carcinogenesis*. 2005 Oct; 26(10):1677-86. Epub 2005 May 19.

Caccamo A.E., Scaltriti M., Caporali A., **D'Arca D.**, Scorcioni F., Candiano G., Mangiola M. and Bettuzzi S. (2004) "Cell detachment and apoptosis induction of immortalized human prostate epithelial cells are associated with early accumulation of 45 Kda nuclear isoform of clusterin". *Biochem J*. 2004 Aug 15; 382(Pt 1):157-68.

Scaltriti M., Brausi M., Amorosi A., **D'Arca D.**, Astancolle S., Corti A., Caporali A. and Bettuzzi S. (2004) "Pattern of clusterin (SGP-2, ApoJ) mRNA and protein-expression in low and high grade human prostate cancer". *Int. J. Cancer*. 2004 Jan 1; 108(1):23-30.

Caporali A., Davalli P., Astancolle S., **D'Arca D.**, Brausi M., Bettuzzi S. and Corti A. (2004) "The chemopreventive action of catechins in the TRAMP mouse model of prostate carcinogenesis involves clusterin overexpression". *Carcinogenesis*. 2004 Nov; 25(11):2217-24. Epub 2004 Sep 9.

Davalli P., Astancolle S., Caporali A., D'Arca D., Corti A., Brasi M.B (2003). Clusterin is down-regulated during the progression of prostate cancer in the tramp mouse model but up-regulated during chemioprevention by green tea catechins administration. EUROPEAN UROLOGY. SUPPLEMENTS, 2003, vol. 2, p. 25.

Caccamo A.E., Scaltriti M., Caporali A., **D'Arca D.**, Scorcioni F., Candiano G., Mangiola M. and Bettuzzi S. (2003) "Nuclear traslocation of a truncated clusterin isoform is associated to induction of anoikis in SV40-immortalized human prostate epithelial cells (PNT1A)". Ann NY Acad Sci. 2003 Dec; 1010:514-9.

Bettuzzi S., Scaltriti M., Caporali A., Brausi M., **D'Arca D.**, Astancolle S., Davalli P. and Corti A. (2003) "Successful prediction of prostate cancer recurrence by gene profiling in combination with clinical data: a 5 years follow-up study". Canc Res. 2003 Jul 1; 63(13):3469-72.

Selected abstracts

Lauriola Angela, Caporali Andrea, Mai Sabine, **D'Arca Domenico**. "The key role of Mitostatin in the maintenance of genome stability". American Association for Cancer Research (AACR), AACR Annual Meeting April 2017 Washington, D.C., USA (<http://www.aacr.org>).

Laura Taddia, Lorena Losi, Alessandra Gualandi, **Domenico D'Arca**, Gaia Gozzi, Leda Severi, Stefania Ferrari, Chiara Marraccini, Glauco Ponterini, Gaetano Marverti, Ioana Braicu, Jalid Sehouli, Maria Paola Costi.
"Identification of a protein panel characterizing the cellular activity of Pemetrexed in the treatment of ovarian cancer". European Network for Translational Research in Ovarian Cancer (EUTROC), 18 April 2015, Berlin, Germany.

D'Arca D., Caporali A., Martello A., Davalli P., Lauriola A., Rivasi F., Brausi M. "Mitostatin: a "Guardian of Mitochondrial integrity" in prostate gland". The 22nd Meeting of the EAU Section of Urological Research (ESUR), 9-11 October 2014 Glasgow, Scotland.

D'Arca Domenico, Caporali Andrea, Martello Andrea, Davalli Pierpaola, Lauriola Angela, Rivasi Francesco, Brausi Maurizio and Corti Arnaldo.
"MITOSTATIN: a "Guardian of Mitochondrial integrity" in prostate gland". The 5th International Forum of Regional and Targeting Therapies for Cancer (RTTC), 2013 November 15th-18th - Shanghai, China.

Marverti G., Pirondi S., Marraccini C., Frassinetti C., Helleman J., Berns E.M.J.J., Ferrari S., Luciani R., Martello A., M. Pelà, R.Guerrini and **D'Arca D.**, Costi, M.P. "Studies On The Effects Of A Novel Pteorate-Peptide Bioconjugate For Folate Receptor-Mediated Targeted Therapy In Human Ovarian Cancer Cell Lines". European Network for Translational Research in Ovarian Cancer (EUTROC), 2013.

M. Scaltriti, A. Caporali, **D. D'Arca**, A. Caccamo, E. Medico, A. Corti and S. Bettuzzi.
"Profiling of genes differentially regulated by clusterin in PC3 human prostate cancer cells by DNA microarray". 9th World congress on advances in oncology, and 7th International Symposium on molecular medicine, 14-16 October, 2004, Hersonissos, Crete, Greece.

G. Marverti, A. Ligabue, M.G. Monti, S. Bettuzzi, A. Caporali, **D. D'Arca** and M.S. Moruzzi. "Spermidine/Spermine N¹-Acetyltransferase transient over-expression increases sensitivity of resistant human ovarian cancer cells to N¹,N¹²-Bis(Ethyl)Spermine and cisplatin". Biogenic Amines, Health implications of dietary Amines, 22-26 May 2004, Trento.

S. Carnevali, S. Petruzzelli, **D. D'Arca**, A. Caporali, S. Astancolle, F. Luppi, A. Corti and L.M. Fabbri. "Cigarette smoke (CSE) induces clusterin expression in human lung fibroblasts". European Respiratory Society Annual Congress, 4-8 September 2004, Glasgow.

S. Bettuzzi, A. Caporali, P. Davalli, S. Astancolle, **D. D'Arca**, M. Brausi, A. Corti. "Catechins chemopreventive action on prostate cancer is mediated by Clusterin overexpression in the TRAMP model". XIXth Congress of EAU 24-27 March 2004, Wien.

A. E. Caccamo, M. Scaltriti, A. Caporali, **D. D'Arca**, F. Scorcioni, G. Candiano, M. Mangiola and S. Bettuzzi "Nuclear traslocation of a truncated clusterin isoform is associated to induction of anoikis in SV40-immortalized human prostate epithelial cells (PNT1A). Apoptosis 2003: From signaling pathways to therapeutic tools. Jan. 29 – Febr. 1st, 2003- European Parliament Conference Center (Luxembourg)

M. Scaltriti, A. Caporali, S. Astancolle, **D. D'Arca** and S. Bettuzzi
"Clusterin-expression is down-regulated in transformed epithelial cells but up-regulated in fibroblasts from prostate cancer". Biochemical Aspects of Health and Disease–Biochemical Society Christmas Meeting. Imperial College, London 16-18 December 2002

Speaker in meetings and conferences

- 2014 5th Shanghai International Forum of Regional and Targeting Therapies for Cancer (RTTC2013, 15-17 November 2014, Shanghai, China): Oral presentation
Session: Novel Markers for Diagnosis and Individualized Treatment
Speech title: MITOSTATIN: a "Guardian of Mitochondrial integrity" in prostate gland.
- 2014 22nd Meeting of the EAU Section of Urological Research (ESUR), 9-11 October 2014, Glasgow, Scotland: Oral presentation
Speech title: MITOSTATIN is a novel Mitochondria-Localized Tumor Suppressor, the "Guardian of Mitochondrial integrity"
- 2013 The Joint Round Table event: "Urology: How to provide the right prevention and treatment to the right patient at the right time?" at the European Parliament in Brussels, September 25th 2013. Organized by the European Alliance for Personalised Medicine (EAPM) and the European Association of Urology (EAU).
The key discussion addressed some of the most burning concerns in European health care. The representatives of the EAU and EAPM have met with Members of the European Parliament to discuss the role that urology research and practice play in the development of personalised medicine across Europe.

Memberships

Member, European Association of Urology (EAU) since 2013.

Member, Italian Society of Biochemistry and Molecular Biology (SIB) since 2013.

Member, Italian Association of Cell Cultures (AICC) since 2015.

Member, European Association for Cancer Research (EACR) since 2016.

Scientific Merit Scholarships and Fellowships

- 2007-2009 Ministero del Lavoro, delle Politiche Sociali e Agenzia Sanitaria della regione Campania, Research Fellowship.
- 2006 Department of Biomedical Sciences, Università di Modena e Reggio Emilia, Research Fellowship.
- 2004 Associazione "Angela Serra" per la ricerca sul cancro, Merit scholarship.

Languages

Italian: First language

English: Fluent reading, writing and speaking

References

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