

CURRICULUM VITAE



INFORMAZIONI PERSONALI/PERSONAL INFORMATION

Nome, Cognome/ Name, Surname Cristina Bottino
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Nazionalità/Nationality Italiana/Italian

Luogo-Data di nascita/Birthplace-Date of birth Genova 23 ottobre1958/Genoa October 23,1958

ISTRUZIONE E FORMAZIONE/ EDUCATION AND TRAINING

Data/Date 1985
Qualifica conseguita/Title and professional qualification obtained Laurea in Medicina e Chirurgia (summa cum laude)/M.D. degree (summa cum laude)

• Nome e tipo di istituto di istruzione o formazione/ Name and type of organization providing education and training Facoltà di Medicina e Chirurgia, Università degli studi di Genova, Italia/School of Medicine, University of Genova, Italy

ESPERIENZA LAVORATIVA/ Work EXPERIENCE

- Date (da – a)/ Dates (from - to) 1986-88
- Nome Istituzione/ Name of the company Ludwig Institute for Cancer Research, Lausanne, Switzerland
- Incarico ricoperto/ occupational skills covered Postdoctoral fellow
- Date (da – a)/ Dates (from - to) 1989-2001
- Nome Istituzione/ Name of the company Istituto Scientifico Tumori (IST), Genova
- Incarico ricoperto/ occupational skills covered Dirigente medico, Laboratorio di Immunologia/ Staff Member, Laboratory of Immunology
- Date (da – a)/ Dates (from - to) 2002-2006
- Nome Istituzione/ Name of the company IRCCS Istituto G. Gaslini, Genova.
- Incarico ricoperto/ occupational Responsabile Modulo Funzionale “Immunologia Molecolare”, Laboratorio di Immunologia Clinica

skills covered	e Sperimentale/Head Molecular Immunology Unit, Laboratory of Clinical and Experimental Immunology
• Date (da – a)/ Dates (from - to)	2006-oggi/today
• Nome Istituzione/ Name of the company	IRCCS Istituto G. Gaslini, Genova
• Incarico ricoperto/ occupational skills covered	Direttore Laboratorio di Immunologia Clinica e Sperimentale/ Head Laboratory of Clinical and Experimental Immunology
• Date (da – a)/ Dates (from - to)	2006-oggi/today
• Nome Istituzione/ Name of the company	Università di Genova, Scuola di Medicina, Dipartimento di Medicina Sperimentale/University of Genova, School of Medicine, Dep. of Experimental Medicine
• Incarico ricoperto/ occupational skills covered	Professore Ordinario di Patologia generale/ Full Professor of General Pathology

**ATTIVITÀ DI RICERCA/RESEARCH
ACTIVITY**

Le ricerche di Cristina Bottino sono volte all'identificazione dei meccanismi molecolari che regolano la risposta immunitaria nell'uomo. In particolare ha focalizzato i suoi studi sull'immunità innata e sui linfociti Natural Killer (NK). Ha contribuito alla scoperta e alla caratterizzazione molecolare della maggior parte dei recettori (inibitori o attivatori) delle cellule NK e dei loro ligandi. Ha studiato la funzione delle cellule NK nella risposta immunitaria contro cellule infettate da virus, nei tumori pediatrici e dell'adulto (neuroblastoma, leucemie) e in alcune immunodeficienze primitive (PID) (XLP1, FHL).

L'attività di ricerca di C. Bottino è documentata da oltre 170 pubblicazioni scientifiche, la maggior parte su riviste internazionali di grande prestigio (<http://www.ncbi.nlm.nih.gov/pubmed/>).

Nel 2006 è stata inclusa nell'elenco dei ricercatori più citati al mondo (elenchi compilati per le diverse discipline dall'Institute for Scientific Information, ISI, di Philadelphia), nella categoria Immunologia (<http://isihighlycited.com>). H-index 69, Citations 16.632 (Web of Science, WoS)

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The research activity of Cristina Bottino is focused on the analysis of the molecular mechanisms involved in immune responses in humans. In particular, a major object of her research has been the study of Innate Immunity and Natural Killer (NK) cells. She contributed to the discovery and the molecular characterization of the inhibitory and activating NK receptors and of their ligands. She analyzed the NK cell function in immune responses against virus-infected cells, tumors in children and adults (neuroblastoma, leukemia) as well as in primary immunodeficiencies (PID) (XLP1, FHL).

The research activity of C. Bottino is documented by over 170 publications in high rank International Journals (<http://www.ncbi.nlm.nih.gov/pubmed/>).

In 2006 she has been included among the highly cited researchers (Institute for Scientific Information, ISI, Philadelphia), subject category; Immunology (<http://isihighlycited.com>). H-index 69, Citations 16.632 (Web of Science, WoS)

ORCID iD: 0000-0001-6695-1739; Scopus Author ID: 7005786002; Researcher ID: J-9977-2016

**PUBBLICAZIONI
SELEZIONATE/SELECTED PUBLICATIONS**

1. Bottino, C., G. Tambussi, S. Ferrini, E. Ciccone, P. Varese, M.C. Mingari, L. Moretta, and A. Moretta, *Two subsets of human T lymphocytes expressing gamma/delta antigen receptor are identifiable by monoclonal antibodies directed to two distinct molecular forms of the receptor*. J Exp Med, 1988. **168**(2): p. 491-505.
2. Moretta, A., C. Bottino, D. Pende, G. Tripodi, G. Tambussi, O. Viale, A. Orengo, M.

Barbaresi, A. Merli, E. Ciccone, and et al., *Identification of four subsets of human CD3-CD16+ natural killer (NK) cells by the expression of clonally distributed functional surface molecules: correlation between subset assignment of NK clones and ability to mediate specific alloantigen recognition*. J Exp Med, 1990. **172**(6): p. 1589-98.

3. Moretta, A., M. Vitale, C. Bottino, A.M. Orengo, L. Morelli, R. Augugliaro, M. Barbaresi, E. Ciccone, and L. Moretta, *P58 molecules as putative receptors for major histocompatibility complex (MHC) class I molecules in human natural killer (NK) cells. Anti-p58 antibodies reconstitute lysis of MHC class I-protected cells in NK clones displaying different specificities*. J Exp Med, 1993. **178**(2): p. 597-604.

4. Moretta, A., M. Vitale, S. Sivori, C. Bottino, L. Morelli, R. Augugliaro, M. Barbaresi, D. Pende, E. Ciccone, M. Lopez-Botet, and L. Moretta, *Human natural killer cell receptors for HLA-class I molecules. Evidence that the Kp43 (CD94) molecule functions as receptor for HLA-B alleles*. J Exp Med, 1994. **180**(2): p. 545-55.

5. Bottino, C., M. Vitale, D. Pende, R. Biassoni, and A. Moretta, *Receptors for HLA class I molecules in human NK cells*. Semin Immunol, 1995. **7**(2): p. 67-73.

6. Moretta, A., S. Sivori, M. Vitale, D. Pende, L. Morelli, R. Augugliaro, C. Bottino, and L. Moretta, *Existence of both inhibitory (p58) and activatory (p50) receptors for HLA-C molecules in human natural killer cells*. J Exp Med, 1995. **182**(3): p. 875-84.

7. Bottino, C., S. Sivori, M. Vitale, C. Cantoni, M. Falco, D. Pende, L. Morelli, R. Augugliaro, G. Semenzato, R. Biassoni, L. Moretta, and A. Moretta, *A novel surface molecule homologous to the p58/p50 family of receptors is selectively expressed on a subset of human natural killer cells and induces both triggering of cell functions and proliferation*. Eur J Immunol, 1996. **26**(8): p. 1816-24.

8. Moretta, A., C. Bottino, M. Vitale, D. Pende, R. Biassoni, M.C. Mingari, and L. Moretta, *Receptors for HLA class-I molecules in human natural killer cells*. Annu Rev Immunol, 1996. **14**: p. 619-48.

9. Sivori, S., M. Vitale, L. Morelli, L. Sanseverino, R. Augugliaro, C. Bottino, L. Moretta, and A. Moretta, *p46, a novel natural killer cell-specific surface molecule that mediates cell activation*. J Exp Med, 1997. **186**(7): p. 1129-36.

10. Cantoni, C., R. Biassoni, D. Pende, S. Sivori, L. Accame, L. Pareti, G. Semenzato, L. Moretta, A. Moretta, and C. Bottino, *The activating form of CD94 receptor complex: CD94 covalently associates with the Kp39 protein that represents the product of the NKG2-C gene*. Eur J Immunol, 1998. **28**(1): p. 327-38.

11. Cantoni, C., C. Bottino, M. Vitale, A. Pessino, R. Augugliaro, A. Malaspina, S. Parolini, L. Moretta, A. Moretta, and R. Biassoni, *NKp44, a triggering receptor involved in tumor cell lysis by activated human natural killer cells, is a novel member of the immunoglobulin superfamily*. J Exp Med, 1999. **189**(5): p. 787-96.

12. Pende, D., S. Parolini, A. Pessino, S. Sivori, R. Augugliaro, L. Morelli, E. Marcenaro, L. Accame, A. Malaspina, R. Biassoni, C. Bottino, L. Moretta, and A. Moretta, *Identification and molecular characterization of NKp30, a novel triggering receptor involved in natural cytotoxicity mediated by human natural killer cells*. J Exp Med, 1999. **190**(10): p. 1505-16.

13. Bottino, C., R. Augugliaro, R. Castriconi, M. Nanni, R. Biassoni, L. Moretta, and A. Moretta, *Analysis of the molecular mechanism involved in 2B4-mediated NK cell activation: evidence that human 2B4 is physically and functionally associated with the linker for activation of T cells*. Eur J Immunol, 2000. **30**(12): p. 3718-22.

14. Moretta, A., R. Biassoni, C. Bottino, M.C. Mingari, and L. Moretta, *Natural cytotoxicity receptors that trigger human NK-cell-mediated cytotoxicity*. Immunol Today, 2000. **21**(5): p. 228-34.

15. Parolini, S., C. Bottino, M. Falco, R. Augugliaro, S. Giliani, R. Franceschini, H.D. Ochs, H. Wolf, J.Y. Bonnefoy, R. Biassoni, L. Moretta, L.D. Notarangelo, and A. Moretta, *X-linked lymphoproliferative disease. 2B4 molecules displaying inhibitory rather than activating function are responsible for the inability of natural killer cells to kill Epstein-Barr virus-infected cells*. J Exp Med, 2000. **192**(3): p. 337-46.

16. Bottino, C., M. Falco, S. Parolini, E. Marcenaro, R. Augugliaro, S. Sivori, E. Landi, R. Biassoni, L.D. Notarangelo, L. Moretta, and A. Moretta, *NTB-A, a novel SH2D1A-associated surface molecule contributing to the inability of natural killer cells to kill Epstein-Barr virus-infected B cells in X-linked lymphoproliferative disease*. J Exp Med, 2001. **194**(3): p. 235-46.

17. Moretta, A., C. Bottino, M. Vitale, D. Pende, C. Cantoni, M.C. Mingari, R. Biassoni, and L. Moretta, *Activating receptors and coreceptors involved in human natural killer cell-mediated cytotoxicity*. Annu Rev Immunol, 2001. **19**: p. 197-223.

18. Pende, D., C. Cantoni, P. Rivera, M. Vitale, R. Castriconi, S. Marcenaro, M. Nanni, R. Biassoni, C. Bottino, A. Moretta, and L. Moretta, *Role of NKG2D in tumor cell lysis mediated by human NK cells: cooperation with natural cytotoxicity receptors and capability of recognizing tumors of nonepithelial origin*. Eur J Immunol, 2001. **31**(4): p. 1076-86.

19. Moretta, A., C. Bottino, M.C. Mingari, R. Biassoni, and L. Moretta, *What is a natural killer cell?* Nat Immunol, 2002. **3**(1): p. 6-8.

20. Vitale, M., J. Zimmer, R. Castriconi, D. Hanau, L. Donato, C. Bottino, L. Moretta, H. de la Salle, and A. Moretta, *Analysis of natural killer cells in TAP2-deficient patients: expression of functional triggering receptors and evidence for the existence of inhibitory receptor(s) that prevent lysis of normal autologous cells*. Blood, 2002. **99**(5): p. 1723-9.
21. Bottino, C., R. Castriconi, D. Pende, P. Rivera, M. Nanni, B. Carnemolla, C. Cantoni, J. Grassi, S. Marcenaro, N. Reymond, M. Vitale, L. Moretta, M. Lopez, and A. Moretta, *Identification of PVR (CD155) and Nectin-2 (CD112) as cell surface ligands for the human DNAM-1 (CD226) activating molecule*. J Exp Med, 2003. **198**(4): p. 557-67.
22. Bottino, C., L. Moretta, D. Pende, M. Vitale, and A. Moretta, *Learning how to discriminate between friends and enemies, a lesson from Natural Killer cells*. Mol Immunol, 2004. **41**(6-7): p. 569-75.
23. Castriconi, R., A. Dondero, R. Augugliaro, C. Cantoni, B. Carnemolla, A.R. Sementa, F. Negri, R. Conte, M.V. Corrias, L. Moretta, A. Moretta, and C. Bottino, *Identification of 4Ig-B7-H3 as a neuroblastoma-associated molecule that exerts a protective role from an NK cell-mediated lysis*. Proc Natl Acad Sci U S A, 2004. **101**(34): p. 12640-5.
24. Castriconi, R., A. Dondero, M.V. Corrias, E. Lanino, D. Pende, L. Moretta, C. Bottino, and A. Moretta, *Natural killer cell-mediated killing of freshly isolated neuroblastoma cells: critical role of DNAX accessory molecule-1-poliovirus receptor interaction*. Cancer Res, 2004. **64**(24): p. 9180-4.
25. Falco, M., E. Marcenaro, E. Romeo, F. Bellora, D. Marras, F. Vely, G. Ferracci, L. Moretta, A. Moretta, and C. Bottino, *Homophilic interaction of NTBA, a member of the CD2 molecular family: induction of cytotoxicity and cytokine release in human NK cells*. Eur J Immunol, 2004. **34**(6): p. 1663-72.
26. Moretta, A. and C. Bottino, *Commentary: Regulated equilibrium between opposite signals: a general paradigm for T cell function?* Eur J Immunol, 2004. **34**(8): p. 2084-8.
27. Reymond, N., A.M. Imbert, E. Devilard, S. Fabre, C. Chabannon, L. Xerri, C. Farnarier, C. Cantoni, C. Bottino, A. Moretta, P. Dubreuil, and M. Lopez, *DNAM-1 and PVR regulate monocyte migration through endothelial junctions*. J Exp Med, 2004. **199**(10): p. 1331-41.
28. Bottino, C., R. Castriconi, L. Moretta, and A. Moretta, *Cellular ligands of activating NK receptors*. Trends Immunol, 2005. **26**(4): p. 221-6.
29. Bottino, C., L. Moretta, and A. Moretta, *NK cell activating receptors and tumor recognition in humans*. Curr Top Microbiol Immunol, 2006. **298**: p. 175-82.
30. Pende, D., R. Castriconi, P. Romagnani, G.M. Spaggiari, S. Marcenaro, A. Dondero, E. Lazzeri, L. Lasagni, S. Martini, P. Rivera, A. Capobianco, L. Moretta, A. Moretta, and C. Bottino, *Expression of the DNAM-1 ligands, Nectin-2 (CD112) and poliovirus receptor (CD155), on dendritic cells: relevance for natural killer-dendritic cell interaction*. Blood, 2006. **107**(5): p. 2030-6.
31. Castriconi, R., A. Dondero, C. Cantoni, M. Della Chiesa, C. Prato, M. Nanni, M. Fiorini, L. Notarangelo, S. Parolini, L. Moretta, L. Notarangelo, A. Moretta, and C. Bottino, *Functional characterization of natural killer cells in type I leukocyte adhesion deficiency*. Blood, 2007. **109**(11): p. 4873-81.
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34. Gregorio, A., M.V. Corrias, R. Castriconi, A. Dondero, M. Mosconi, C. Gambini, A. Moretta, L. Moretta, and C. Bottino, *Small round blue cell tumours: diagnostic and prognostic usefulness of the expression of B7-H3 surface molecule*. Histopathology, 2008. **53**(1): p. 73-80.
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36. Bellora, F., R. Castriconi, A. Dondero, G. Reggiardo, L. Moretta, A. Mantovani, A. Moretta, and C. Bottino, *The interaction of human natural killer cells with either unpolarized or polarized macrophages results in different functional outcomes*. Proc Natl Acad Sci U S A, 2010. **107**(50): p. 21659-64.
37. Falco, M., E. Romeo, S. Marcenaro, S. Martini, M. Vitale, C. Bottino, M.C. Mingari, L. Moretta, A. Moretta, and D. Pende, *Combined genotypic and phenotypic killer cell Ig-like receptor analyses reveal KIR2DL3 alleles displaying unexpected monoclonal antibody reactivity: identification of the amino acid residues critical for staining*. J Immunol, 2010. **185**(1): p. 433-41.
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- Baud, H. Authier, S. Kerdine-Romer, M. Pallardy, I. Cremer, L. Peaudecerf, B. Rocha, D. Valteau-Couanet, J.C. Gutierrez, J.A. Nunes, F. Commo, S. Bonvalot, N. Ibrahim, P. Terrier, P. Opolon, C. Bottino, A. Moretta, J. Tavernier, P. Rihet, J.M. Coindre, J.Y. Blay, N. Isambert, J.F. Emile, E. Vivier, A. Lecesne, G. Kroemer, and L. Zitvogel, *Alternatively spliced NKp30 isoforms affect the prognosis of gastrointestinal stromal tumors*. Nat Med, 2011. **17**(6): p. 700-7.
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41. Castriconi, R., A. Dondero, F. Bellora, L. Moretta, A. Castellano, F. Locatelli, M.V. Corrias, A. Moretta, and C. Bottino, *Neuroblastoma-Derived TGF-beta1 Modulates the Chemokine Receptor Repertoire of Human Resting NK Cells*. J Immunol, 2013. **190**(10): p. 5321-8.
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51. Bellora F, Dondero A, Corrias MV, Casu B, Regis S, Caliendo F, Moretta A, Cazzola M, Elena C, Vinti L, Locatelli F, Bottino C and Castriconi R. Imatinib and Nilotinib Off-Target Effects on Human NK Cells, Monocytes, and M2 Macrophages. J Immunol. 2017; 199(4):1516-1525.
52. Dondero A, Casu B, Bellora F, Vacca A, De Luisi A, Frassanito MA, Cantoni C, Gaggero S, Olive D, Moretta A, Bottino C and Castriconi R. NK cells and multiple myeloma-associated endothelial cells: molecular interactions and influence of IL-27. Oncotarget. 2017; 8(21):35088-35102.
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BREVETTI/PATENTS

1. THERAPEUTIC AND DIAGNOSTIC METHODS AND COMPOSITIONS TARGETING 4IG-B7-H3 AND ITS COUNTERPART NK CELL RECEPTOR. Publication info:ES2534288 (T3)

2015-04-21

2. NTB-A, A SURFACE MOLECULE INVOLVED IN NATURAL KILLER CELLS ACTIVITY.
Publication info:AT464320 (T) 2010-04-15
3. Novel Triggering Receptor Involved in Natural Cytotoxicity Mediated by Human Natural Killer Cells and Antibodies That Identify the Same
4. Publication info:US2010015153 (A1) 2010-01-21
5. NOVEL TRIGGERING RECEPTOR INVOLVED IN NATURAL CYTOTOXICITY MEDIATED BY HUMAN NATURAL KILLER CELLS, AND ANTIBODIES THAT IDENTIFY THE SAME.
Publication info:ES2321687 (T3) 2009-06-10
6. Polypeptides having a triggering NK activity and biological applications. Publication info: US2006246068 (A1) 2006-11-02
7. NOVEL TRIGGERING RECEPTOR INVOLVED IN NATURAL CYTOTOXICITY MEDIATED BY HUMAN NATURAL KILLER CELLS AND ANTIBODIES THAT IDENTIFY THE SAME.
Publication info:CA2288307 (A1) 2001-05-15

<http://worldwide.espacenet.com>

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