BIOGRAPHICAL SKETCH

NAME: Federico Bussolino

POSITION TITLE: Professor of Biochemistry -University of Torino

DATE AND PLACE OF BIRTH: June 7, 1954, Torino (Italy)

WORK ADDRESS: Department of Oncology- sp. 142, Km 3.95 10060 Candiolo

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EDUCATION AND TRAINING (DEGREES)

Duration (from/to)	Degree and Field of study	Institution	Supervisor/ Mentor	City	Country
Nov 1980/ Oct 1985	Specialization in Nephrology - Immunopathology of kidney diseases	Università di Torino	Vercellone Antonio	Torino	I
Nov 1973/ Feb 1980	MD - Immunopathology and Nephrology	Università di Torino	Camussi Giovanni	Torino	I
Sep 1976/ Jun 1978	Visiting_EMBO fellow Inflammation	INSERM U200	Bach Francois	Paris	F

RESEARCH AND PROFESSIONAL EXPERIENCE (INCLUDES POST--DOCTORAL TRAINING)

Duration	Position	Institution	Supervisor/ Mentor	City	Country
Jan 2013- Present	Deputy Rector for translational research	Università di Torino	-	Torino	I
Nov 2017- present	Director of Department of Oncology	Università di Torino		Torino	I
January 2014- November 2015	Visiting Professor	Humanitas University		Milano	I

Nov 2002-Present	Chair of the PhD Programme "Complex systems in life sciences" (Former: Complexity in post--genomic biology)	Università di Torino	-	Torino	I
Dec 1994-Present	Professor of Biochemistry--Medical School.	Università di Torino	-	Torino	I
Jan 2009-Apr 2012	Scientific Director	IRCC Candiolo -- Fondazione Piemontese per la Ricerca sul Cancro Onlus (FPRC)	-	Torino	I
Jan 2007/-Dec 2009	President of the Evaluation Board	Università di Torino	-	Torino	I
April 2002-Oct 2006	Member of the Evaluation Board	Università di Torino	·	Torino	I
Nov 2002-Oct 2007	Director of the Department of Oncological Sciences.	Università di Torino	-	Torino	I
Mar 1991-Nov 1994	Assistant Professor	Università di Torino	-	Torino	I
Nov 1985-Feb 1991	Post-doc	Università di Torino	P. Arese	Torino	I
Oct 1984-Sep 1985	Visiting	ETH	H. Lutz	Zurigo	CH
Feb 1983-Oct 1983	Visiting	Erfurt University	U.Till	Erfurt	D

A. Research Performance

Publications: 266 international peer reviewed papers;
H index –ISI: 66; >15700 citations (without auto-citations).
H index Scopus: 69; >17500 (without auto-citations)
orcid.org/0000-0002-5348-1341

Patents:

- F. Bussolino, S. Marchio (2003). A novel mechanism of HIV-1 entry into host cells and peptides inhibiting this mechanism. 02020649.6, Università di Torino
- F. Bussolino, S. Marchio (2006). Peptidi metastasi-specifici e loro applicazioni diagnostiche e terapeutiche. PCT/EP2007/010428, Università di Torino
- Marchiò S, Bussolino F (2012). Inhibitors of alpha 6/ E cadherin complex. EP12182994, Università di TorinoFondazione Piemontese per la Ricerca sul Cancro-ONLUS

Awards:

- 2004- Lega Italiana Contro i Tumori

- 2014- Academia dei Lincei- Award Luigi Feltrinelli

B. Leadership

Co-founder of 2 SMEs. Chair of the Department of Oncological Sciences (2003-2007) and Scientific Director of Institute for Cancer Research at Candiolo (2009- 2012). Co-founder of PhD Programme: Complex Systems in Life Scinences aimed at implementing cross-activities between Biologists, MDs, Physics, Computer scientists. President of the "Evaluation Board" of the University of Torino (2007-2009); President of the Evaluation Committee nominated by the University Ministry for the national professorship selection in Biochemistry (Nov 2016-Oct 2018).

C. Personal Statement

My expertise in tumor angiogenesis and in understanding the cellular and molecular circuits occurring between cancer and stroma cells have been developed over three decades. I have led national and international projects on vascular development, on tumor angiogenesis, fibrosis and the microenvironment. In my own research I have concentrated on the molecular and cellular mechanisms involved in the role of vasculature in tumor progression and metastatic spreading, by focusing on how oncogenic hits impact on the angiogenic mechanisms characterizing singular tumor subtypes and contributing to the onset of acquired resistance to anti-angiogenic regimens.
My major interest is in driving the field of the microenvironment in tumor biology forward technically and conceptually. In particular, I'm absolutely convinced that significant progresses in cancer fight, including the route of therapeutic personalized approaches, have to consider cancer as a tissue characterized by cells generally carrying somatic mutations and stroma cells, which differently interact with cancer cells and dynamically influence their behaviour in the host. My research program has been characterized by innovation and thoroughness. I have considerable experience in administering projects with collaborations and co-authored publications. I have also put considerable effort into mentoring young scientists and have trained more than 60 students and postdoctoral fellows. We have developed and used a variety of new technologies and models ranging from molecular biology to genetically engineered mouse models, to high-tech microscope approaches, to network analysis and 3D culture models. Now, my Lab is moving to single cell transcriptomics.

D. Positions and Honors (partial list)

Professional activities

1998 Chair of the Task Force of the Ottolenghi Foundation (Torino) to organize an Institute for Neurosceince Research;
1999-2008: Chair of Molecular Angiogenesis Division at Institute for Cancer Research and Treatment (University of Torino);
2001-2005 Member of the Board of International School of Advanced Study of University of Turin;
2003-2007: Member of the Scientific Board of "Associazione per lo sviluppo scientifico e tecnologico del Piemonte (ASP)"
2004-2008: Member of Scientific Board of Italian Society of Cancerology
2010.-2012 Member of the Scientific Board of Armenise Foundation (Boston)
2010-2015: Member of the Scientific Board of Italian Society of Biochemistry and Molecular Biology

Editorial Boards

2007-present: Associated Editor of Angiogenesis
2007-2010: member of the Editorial Board of Circulation Research
2012-present: member of the Editorial Board of Arteriosclerosis, Thrombosis and Vascular Biology
2014-present: member of the Editorial Board of Journal of Immunological Research

International Meetings- Invited Speakers (partial list of the most recent)

- XIIIth International Vascular Biology Meeting June 1 - 5, 2004. Toronto
- The 3rd Kloster Seeon Meeting "Angiogenesis" of the SPP 1069. Sep. 18-21, 2004, Munich (D)
- Gordon Conference- Fibronectin, Integrins & Related Molecules, January 30 - February 4, 2005-Ventura, CA (USA)
- Gordon Conference-Angiogenesis and Microcirculation, August 14-19, 2005, Salve Regina University, Newport, RI (USA)
- Elso Meeting , September 3-6, 2005, Dresden, (D)
- Gordon Conference-Vascular Cell Biology, February 11-16, 2007, Ventura, CA
- American Heart Association- Cardiovascula Development August 1-4, Keystone, CO (USA)
- 9th International Conference "Angiogenesis:Basic Science and Clinical Applications", June 22-26,2008, Patras (G)
- EVGN Summer School, September 15-19, 2008. Krakow (PL)
- 3rd European Conference on Tumor Angiogenesis and Antiangiogenic Therapy November 6-8, 2008. Abano Terme (I)
- Faseb Summer Research Conference: Thrombospondins and other extracellular matrix proteins. June 16-21, 2009, Tucson (USA)
- European Society of Endocrinology. Endocrinology mets Science, September 23-26, 2009, Torino (I)
- Lorentz Center- Modeling angiogenesis: joinging cells, maths and computers, Oct 6-9, 2010, Leiden (B)
- Nottingham University. Angionet meeting, April 20-22, 2009 , Dundee (UK).
- EMBO Molecular Medicine Workshop: Cell Guidance in Cancer, May 6-10, 2010. Portofino (I)
- Beatson International Cancer Conference. July 6-9,2011. Glasgow (UK)
- University of Heidelberg. Keplero Conference, May 16-18, 2011, Heidelberg (D)
- The A. Falaschi Molecular Medicine Conference, May 30-June 2, 2012, Trieste (I)
- I NEMB Venice Workshop on Cancer Nanotechnology, October 11-12, 2012 , Venice (I)
- III International Thoracic Oncology Congress, September 13-15, 2012 Dresden (D)
- XXXIII Annual Meeting of the European Section of IHSR, July 1-3, 2015 Bordeaux (F)
- Angiogenesis and Vascular Disease- Keystone Symposia, May 8-12, 2017 Santa Fe (USA)

E. Industrial appointments
2002: Co-Founder of Creabilis Therapeutics
2007: Co- Founder of Apavadis Biotechnology

F. Research Funding
Current
2012 (60 months): Advanced nanosystems for a new era in molecular oncology. (granted by Ministero dell' Università) (1500000 €)
2014 (36 months) Transcription Factor EB (TFEB) regulation of lysosome--autophagy pathway in tumor angiogenesis (granted by Italian Association for Cancer Research) (510000 €)
2015 (36 months): Innovative Tools for Cancer Risk Assessment and Early Diagnosis for Pancreatic Cancer (granted by AIRC) (540000 €)

2016 (24 months) The Global Network Analysis of Regulatory RNAs in Sprouting Angiogenesis (granted by Copmagnia di San Paolo Foundation (100000 €)
2016 (24 months) Innovative strategies to improve the clinical use of anti--angiogenic compunds in patients with colorectal cancer (granted by CRT Foundation) (100000 €)
2017 (36 months) Regulation of cancer fibrosis by a Tfeb--mediated transcriptional program (granted by Italian Association for Cancer Research) (800000 €)

Pending

2017 (36 months) Role of TFEB in fabry's disease (granted by Telethon) (580000 €)
2017 Molecular and cellular circuits sustaining myofibroblast activation in chronic pulmonary disease and lung fibrosis (granted by Cariplo Foundation (350000 €)
2017 (36 months) Anti-angiogenic response in colorectal cancer predicted by investigational studies with patient-derived xenografts granted by World wide cancer association (185000 £)
2017: (36 months) Comprehensive profiling of circulating biomarkers to detect residual disease and relapse in early-stage (stage i-iii) non-small-cell lung cancer (granted by ERA-NET Transcan-2) (300000 Euro)

Previous (2003-2009)

2012 (36 months) Bloch electromagnetic surface wave Bio-sensors for early diagnosis (granted by EU-FP7) (400000 €)
2010 (36 months): Molecular and cellular mechanisms of the normalization of tumor vasculature by anti-cancer therapies (granted by AIRC) (750000 €)
2010 (36 months): Lab-on-chip for angiogenic markers detection (granted by Regione Piemonte) (240000 €)
2008(36 months): Photonic biosensors for early cancer diagnotics (granted by Regione Piemonte) (300000 €)
2007 (36 months): Deciphering cell signaling networks to target cell motility in tumor angiogenesis (granted by AIRC) (600000 €)
2007 (48 months:) Establishment of a functional genomic screening platform for cancer research (granted by Heath Ministry, Special Project Oncology) (320000 €)
2006 (24 months): Bacteriophages as biological sensors and cell-targeting agents in vascular biology (Granted by Ministero Università) (107000 €)
2004 (36 months): Molecular pathways regulating endothelial cell motility during vascular vessel assembly (granted by AIRC) (500000 €)
2004 (60 months): European Vascular Genomic Network (FP6) (820000 €)
2004 (24 months): Role of HMGB1 in vascular development (Granted by Ministero Università) (52000 €)

G. Contributions to Science (selected) (Paper with > 200 citations are indicated)

1. I contributed to create the groundwork for the role of endothelial cells in inflammation and innate immunity. This includes the elucidation of paracrine and autocrine circuits between inflammatory cytokines (IL-1, IL-6, TNFα) in activating a pro-thrombotic and a pro-inflammatory program changing the surface properties of endothelial cells with the final result to recruit different subsets of leukocytes at site of tissue injuries including tumors.

a) Bussolino F, Breviario F, Tetta C, Aglietta M, Mantovani A, Dejana E. Interleukin 1 stimulates platelet-activating factor production in cultured human endothelial cells. J Clin Invest. 1986 Jun;77(6):2027-33. (258 citations)
b) Bussolino F, Camussi G, Aglietta M, Braquet P, Bosia A, Pescarmona G, Sanavio F, D'Urso N, Marchisio PC. Human endothelial cells are target for
c) platelet-activating factor. I. Platelet-activating factor induces changes in cytoskeleton structures. J Immunol. 1987 Oct 1;139(7):2439-46. (209 citations)
d) Bussolino F, Camussi G, Baglioni C. Synthesis and release of platelet-activating factor by human vascular endothelial cells treated with tumor necrosis factor or interleukin 1 alpha. J Biol Chem. 1988 Aug 25;263(24):11856-61. (201 citations)
e) Camussi G, Bussolino F, Salvidio G, Baglioni C. Tumor necrosis factor/cachectin stimulates peritoneal macrophages, polymorphonuclear neutrophils, and vascular endothelial cells to synthesize and release platelet-activating factor. J Exp Med. 1987 Nov 1;166(5):1390-404. (383 citations)
f) Mantovani A, Bussolino F, Introna M. Cytokine regulation of endothelial cell function: from molecular level to the bedside. Immunol Today. 1997 May;18(5):231-40 (602 citations).

2. In the 80' the current think was that hematopoiesis was governed by molecules that specifically and exclusively acted on precursors. I contributed to dismantle this dogma showing the vascular properties of colony stimulating factors (G-CSF, CM-CSF). After 25 years the proangiogenic roles of these molecules clarify their fundamental role in the fitness of bone marrow vascular niche.

a) Bussolino F, Wang JM, Defilippi P, Turrini F, Sanavio F, Edgell CJ, Aglietta M, Arese P, Mantovani A. Granulocyte- and granulocyte-macrophage-colonystimulating factors induce human endothelial cells to migrate and proliferate. Nature. 1989 Feb 2;337(6206):471-3 (550 citations)
b) Bussolino F, Ziche M, Wang JM, Alessi D, Morbidelli L, Cremona O, Bosia A, Marchisio PC, Mantovani A. In vitro and in vivo activation of endothelial cells by colony-stimulating factors. J Clin Invest. 1991 Mar;87(3):986-95 (253 citations).
c) Valdembri D, Serini G, Vacca A, Ribatti D, Bussolino F. In vivo activation of JAK2/STAT-3 pathway during angiogenesis induced by GM-CSF. FASEB J. 2002 Feb;16(2):225-7.
d) Soldi R, Primo L, Brizzi MF, Sanavio F, Aglietta M, Polentarutti N, Pegoraro L, Mantovani A, Bussolino F. Activation of JAK2 in human vascular endothelial cells by granulocyte-macrophage colony-stimulating factor. Blood. 1997 Feb 1;89(3):863-72.

3. I was the first to propose that HGF/MET axis regulates the angiogenic properties of tumor vascular capillaries thus contributing to characterize the cancer invasive program triggered by this couple of ligand-receptor.

a) Camussi G, Montrucchio G, Lupia E, Soldi R, Comoglio PM, Bussolino F. Angiogenesis induced in vivo by hepatocyte growth factor is mediated by platelet-activating factor synthesis from macrophages. J Immunol. 1997 Feb 1;158(3):1302-9.
b) Silvagno F, Follenzi A, Arese M, Prat M, Giraudo E, Gaudino G, Camussi G, Comoglio PM, Bussolino F. In vivo activation of met tyrosine kinase by heterodimeric hepatocyte growth factor molecule promotes angiogenesis. Arterioscler Thromb Vasc Biol. 1995 Nov;15(11):1857-65.

c) Bussolino F, Di Renzo MF, Ziche M, Bocchietto E, Olivero M, Naldini L, Gaudino G, Tamagnone L, Coffer A, Comoglio PM. Hepatocyte growth factor is a potent angiogenic factor which stimulates endothelial cell motility and growth. J Cell Biol. 1992 Nov;119(3):629-41. (1068 citations)

4.In 1996 I successfully coordinated a grant on angiogenesis funded by EU and I started to work on VEGFs. I showed that HIV-1 Tat activates VEGFR-2 and promotes angiogenesis, an important observation for HIV-associated tumors. It was one of the first demonstration of the partial specificity of VEGF receptors for the ligands belonging to VEGF family. This concept was further extended on VEGFR-1 showing that HIV-1 Tat regulates the recruitment of monocytes in inflamed tissues and the motility of Burkit lymphoma cells by triggering VEGFR-1. Furthermore the demonstration that HIV-1-Tat activated angiogenesis gave a relevant boost in understanding the mechanisms of epidemic Kaposi's sarcoma. A second and seminal contribution was the demonstration for the first time that the functions of VEGFR-2 in vascular cells are regulated by co-receptors. I reported that alphav-beta3 integrin forms a hetero-complex with VEGFR-2, and positively enhances the catalytic and biological function of VEGFA/VEGFR-2 axis.

a) Sgadari C, Barillari G, Toschi E, Carlei D, Bacigalupo I, Baccarini S, Palladino C, Leone P, Bugarini R, Malavasi L, Cafaro A, Falchi M, Valdembri D, Rezza G, Bussolino F, Monini P, Ensoli B. HIV protease inhibitors are potent anti-angiogenic molecules and promote regression of Kaposi sarcoma. Nat Med. 2002 Mar;8(3):225-32 (201citations).
b) Soldi R, Mitola S, Strasly M, Defilippi P, Tarone G, Bussolino F. Role of alphavbeta3 integrin in the activation of vascular endothelial growth factor receptor-2. EMBO J. 1999 Feb 15;18(4):882-92 (436 citations).
c) Mitola S, Sozzani S, Luini W, Primo L, Borsatti A, Weich H, Bussolino F. Tat-human immunodeficiency virus-1 induces human monocyte chemotaxis by activation of vascular endothelial growth factor receptor-1. Blood. 1997 Aug 15;90(4):1365-72.
d) Bussolino F, Mantovani A, Persico G. Molecular mechanisms of blood vessel formation. Trends Biochem Sci. 1997 Jul;22(7):251-6. (339 citations).
e) Albini A, Soldi R, Giunciuglio D, Giraudo E, Benelli R, Primo L, Noonan D, Salio M, Camussi G, Rockl W, Bussolino F. The angiogenesis induced by HIV-1 tat protein is mediated by the Flk-1/KDR receptor on vascular endothelial cells. Nat Med. 1996 Dec;2(12):1371-5. (302 citations).

5. Our studies exploiting phage display technology allowed identifying new molecules involved in the interactions between stroma and cancer cells in colorectal cancer. These studies laid the groundwork for thinking about new mechanisms to target tumor metastatization.

a) Bartolini A, Cardaci S, Lamba S, Oddo D, Marchiò C, Cassoni P, Amoreo CA, Corti G, Testori A, Bussolino F, Pasqualini R, Arap W, Corà D, Di Nicolantonio F, Marchiò S. BCAM and LAMA5 Mediate the Recognition between Tumor Cells and the Endothelium in the Metastatic Spreading of KRAS-Mutant Colorectal Cancer. Clin Cancer Res. 2016 Oct 1;22(19):4923-4933
b) Marchiò S, Soster M, Cardaci S, Muratore A, Bartolini A, Barone V, Ribero D, Monti M, Bovino P, Sun J, Giavazzi R, Asioli S, Cassoni P, Capussotti L, Pucci P, Bugatti A, Rusnati M, Pasqualini R, Arap W, Bussolino F. A complex of α6 integrin and E-cadherin drives liver metastasis of colorectal cancer cells through hepatic angiopoietin-like 6. EMBO Mol Med. 2012 Nov;4(11):1156-75.
c) Soster M, Juris R, Bonacchi S, Genovese D, Montalti M, Rampazzo E, Zaccheroni N, Garagnani P, Bussolino F, Prodi L, Marchiò S. Targeted dual-color silica nanoparticles

provide univocal identification of micrometastases in preclinical models of colorectal cancer. Int J Nanomedicine. 2012;7:4797-807.

6. We contributed to shape the concept that vascular architecture is regulated by the same molecules that define the trajectories of axons in central and peripheral nervous systems. In particular we described the first endogenous mechanism of inhibition of integrin function analyzing the role of the axon guidance cue semaphorin 3A in vascular system. Both in vascular development and in tumor angiogenesis semaphorins and more in general axon guidance cues play a significant role in vascular maturation and stabilization and represent druggable targets in cancer preclinical models. Furthermore these findings have contributed to open a new vision on how exploit anti-angiogenic regimens in clinical oncology based on the concept of vascular normalization. During the treatment with anti-angiogenic compounds there is a temporal window during the which the chaotic architecture of tumor capillaries normalizes with subsequent improvement of drug delivery and oxygenation. This phenomenon can be used to improve the efficacy of other therapies, reduce the dosages and the subsequent adverse effects.

a) Maione F, Capano S, Regano D, Zentilin L, Giacca M, Casanovas O, Bussolino F, Serini G, Giraudo E. Semaphorin 3A overcomes cancer hypoxia and metastaticdissemination induced by antiangiogenic treatment in mice. J Clin Invest. 2012 May;122(5):1832-48.
b) Maione F, Molla F, Meda C, Latini R, Zentilin L, Giacca M, Seano G, Serini G, *Bussolino F, Giraudo E. Semaphorin 3A is an endogenous angiogenesis inhibitor that blocks tumor growth and normalizes tumor vasculature in transgenic mouse models. J Clin Invest. 2009 Nov;119(11):3356-72.
c) Serini G, Valdembri D, Zanivan S, Morterra G, Burkhardt C, Caccavari F, Zammataro L, Primo L, Tamagnone L, Logan M, Tessier-Lavigne M, Taniguchi M,Püschel AW, Bussolino F. Class 3 semaphorins control vascular morphogenesis by inhibiting integrin function. Nature. 2003 Jul 24;424(6947):391-7 (393 citations)
d) Bottos A, Destro E, Rissone A, Graziano S, Cordara G, Assenzio B, Cera MR, Mascia L, *Bussolino F, Arese M. The synaptic proteins neurexins and neuroligins are widely expressed in the vascular system and contribute to its functions. Proc Natl Acad Sci U S A. 2009 Dec 8;106(49):20782-7
e) Comunanza V, Corà D, Orso F, Consonni FM, Middonti E, Di Nicolantonio F, Buzdin A, Sica A, Medico E, Sangiolo D, Taverna D, Bussolino F. VEGF blockadeenhances the antitumor effect of BRAFV600E inhibition. EMBO Mol Med. 2017 Feb;9(2):219-237.
f) Bottos A, Martini M, Di Nicolantonio F, Comunanza V, Maione F, Minassi A, Appendino G, *Bussolino F, Bardelli A. Targeting oncogenic serine/threonine-protein kinase BRAF in cancer cells inhibits angiogenesis and abrogates hypoxia. Proc Natl Acad Sci U S A. 2012 Feb 7;109(6):E353-9.

Complete list of my published work in PubMed: https://www-ncbi-nlm-nih-gov.offcampus.dam.unito.it/pubmed/?term=Bussolino+F+%5Bauthor%5D

H. Major contributions to early careers of excellent researchers

•Sara Zanivan: PhD in my lab, then Post-doc in Mann' Lab (Max-Plank Institute of Biochemistry), now PI at Beatson Institute (Glasgow)
Ilaria Cascone: PhD in my lab, then Post-doc in Camonis Lab (Institut Curie, Paris), now Associated Professor. Université Paris Est (F)
Enrico Giraudo: PhD in my lab, then Post-doc in Hanahan Lab (UCSF at San Francisco), now Assistant Professor at Department of Pharmacy, University of Torino
Marco Arese: PhD in my lab, then Post-doc in Griffin Lab (NYU in New York), now Associated Professor Department of Oncology, University of Torino

Mattia Pelizzola: PhD in my lab, then Post-doc in Yale University, now Team Leader at Istituto Italiano di Tecnologia (Genova, I)
Andrea Picco:PhD in my Lab, now assistant professor at the Department of Biochemistry-University of Geneva (CH)
Giorgio Seano: PhD Student in my Lab, now post Doc in Jain's Lab (Harvard University).
Luca Primo: Post-doc in my Lab, now Associated Professor at Department of Oncology, University of Torino
Stefania Mitola: Post-doc in my Lab, now Associated Professor at Department of Biomedical Sciences, University of Brescia
Alberto Rissone: PhD Student in my Lab, now post doc at NIH, Genetics Molecular Biology Branch (Bethesda)
Simona Pavan: PhD Student in my Lab, now post doc at Department of Biomedicine , University of Basel (CH).
Davide Corà: Post-doc in my Lab, now Assistant Professor in Molecular Biology, University A.Avogadro (Novara)