Nome gruppo: LABORATORIO DI BIOLOGIA MOLECOLARE TRASLAZIONALE

Laboratori di Biologia Molecolare e Fisiopatologia vascolare
Laboratori di Biologia Cellulare Traslazionale

Area di afferenza:

MED09

Elenco componenti e qualifica:

Maria Felice Brizzi Prof. Associato responsabile dei laboratori
Arturo Rosso Dip. Tempo indeterminato D3
Ada Castelli Dip. Tempo indeterminato C3
Margherita Alba Carlotta Pomatto Post. Doc.
Saveria Femminò Borsista
Sharad Kholia PhD
Marta Tapparo PhD
Giovanni Barbieri tesista Biotecnologie
Debora Charrance tesista Biotecnologie
Francesco Ravera tesista MD/PhD
Andrea Caccioppo specializzando Med. Interna
Flavia Chiacchierini specializzando Med. Interna
Maddalena Gili specializzando Med. Interna

Indirizzo e contatti:
Corso Dogliotti 14 piano terra
Stanze: T143, T148, T149, T151, T153
Mail: mariafelice.brizzi@unito.it
Tel: 0116706653

Attività del gruppo:

1. Studio dei meccanismi molecolari associati alla malattia diabetica e alla aterosclerosi
2. Studio delle vescicole extracellulari originate da differenti cellule staminali come mediatori di danno e di protezione in patologie vascolari e renali associate o meno al diabete
3. Studio delle vescicole extracellulari originate da cellule tumorali endoteliali nella regolazione della crescita di tumori solidi con particolare attenzione al microambiente tumorale
4. Valutazione dell'efficacia terapeutica di vescicole extracellulari circolanti nella rigenerazione tissutale ed in particolare nella rigenerazione di ulcere vascolari (Studio clinico approvato dal Comitato Etico)

5. Valutazione delle caratteristiche funzionali delle vescicole extracellulari ottenute da sangue arterioso di pazienti sottoposti a PCI sottoposti o meno a precondizionamento remoto (Studio clinico approvato dal Comitato Etico in collaborazione con la Cardiologia)
6. Studio degli effetti di vescicole extracellulari liberate dalle cellule endoteliali umane sottoposte a stimolo pro-infiammatorio (IL-3) sul danno da Ischemia/Riperfusione miocardica in un modello ex-vivo ed in vivo.

5 Pubblicazioni

PDGF-BB Carried by Endothelial Cell-Derived Extracellular Vesicles Reduces Vascular Smooth Muscle Cell Apoptosis in Diabetes. Togliatto G, Dentelli P, Rosso A, Lombardo G, Gili M, Gallo S, Gai C, Solini A, Camussi G, **Brizzi MF**. **Diabetes.** 2018 Apr;67(4):704-716. doi: 10.2337/db17-0371.

IL-3R-alpha blockade inhibits tumor endothelial cell-derived extracellular vesicle (EV)-mediated vessel formation by targeting the β-catenin pathway.Lombardo G, Gili M, Grange C, Cavallari C, Dentelli P, Togliatto G, Taverna D, Camussi G, **Brizzi MF**. **Oncogene.** 2018 Mar;37(9):1175-1191. doi: 10.1038/s41388-017-0034-x.

Obesity reduces the pro-angiogenic potential of adipose tissue stem cell-derived extracellular vesicles (EVs) by impairing miR-126 content: impact on clinical applications. Togliatto G, Dentelli P, Gili M, Gallo S, Deregibus C, Biglieri E, Iavello A, Santini E, Rossi C, Solini A, Camussi G, **Brizzi MF**. **Int J Obes** (Lond). 2016 Jan;40(1):102-11. doi: 10.1038/ijo.2015.123.

Unacylated ghrelin induces oxidative stress resistance in a glucose intolerance and peripheral artery disease mouse model by restoring endothelial cell miR-126 expression. Togliatto G, Trombetta A, Dentelli P, Gallo S, Rosso A, Cotogni P, Granata R, Falcioni R, Delale T, Ghigo E, **Brizzi MF**. **Diabetes.** 2015 Apr;64(4):1370-82. doi: 10.2337/db14-0991.

DNA vaccination against membrane-bound Kit ligand: a new approach to inhibiting tumour growth and angiogenesis. Olgasi C, Dentelli P, Rosso A, Iavello A, Togliatto G, Toto V, Liberatore M, Barutello G, Musiani P, Cavallo F, **Brizzi MF**. **Eur J Cancer.** 2014 Jan;50(1):234-46. doi: 10.1016/j.ejca.2013.09.016.

Finanziamenti

1. **IG 2015 Id.17630 AIRC (PI Maria Felice Brizzi)** 01/01/16-01/01/19

Agency: Associazione Italiana per la ricerca sul Cancro
Targeting IL-3R interferes with tumor endothelial cell-derived extracellular vesicle (EV)-mediated tumor progression
The focus of the project is to investigate the role of EVs derived from tumor endothelial cells in mediating change in the tumor microenvironment and thus contribute to tumor growth

2. **-UH2TR000880, UH3TR000880-03S1 (PI Peter Quesenberry)** 01/06/2013-01/06/2019

-subaward N° 707-5553 **(PI Giovanni Camussi, co-PI Maria Felice Brizzi**)
Agency: NIH/NIDDK
Regulation of renal and bone marrow injury by extracellular vesicle non-coding RNA

The focus of this project is to characterize and identify the “healing” microRNA involved in acute renal and bone marrow injury and engineer extracellular vesicles enriched in this microRNA.

3. **STEM EV (PI Maria Felice Brizzi)** 01/01/2018-31/12/2020

Agency: 3i3T Scarl, UNITO/Unicyte
Pre-clinical development of stem cell- derived SC-EVs for treatment of chronic kidney injury and hind limb ischemia
The aim of the projects is to study stem cell-drived extracellular vesicles for treatment of renal and cardio-vascular diseases.

4. **HLSC-ISLETS (PI Maria Felice Brizzi)** 01/01/2018-31/12/2020

Agency: 3i3T Scarl, UNITO/Unicyte
Preclinical study HLSC-ILS-based treatment for Type 1 Diabetes
The aim of the projects is to study stem cell-derived extracellular vesicles for treatment of Type 1 Diabetes.

5. **PROGRAMMA OPERATIVO REGIONALE “INVESTIMENTI A FAVORE DELLA CRESCITA E DELL’OCCUPAZIONE” F.E.S.R. 2014/2020 (PI Maria Felice Brizzi) 31/07/2018-31/12/2020**

Agency: Regione Piemonte
EV-ER
The aim of the projects is to study stem cell-derived extracellular vesicles for treatment of Type 2 Diabetes.

NAME: **Maria Felice Brizzi**

POSITION TITLE: Associate Professor of Internal Medicine, Department of Medical Sciences, University of Torino, Corso Dogliotti, 10126 Torino, Italy.

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date MM/YYYY	FIELD OF STUDY
University of Torino	MD	1988	Medicine
University of Torino	Specialty	1993	Internal Medicine
University of Bologna	PhD	1997	Morphogenetic and Cytological Science

Biographical Sketch

A. Personal Statement

She has experience in studies of stem and vascular cell-derived exosomes/microvesicles. In addition, I have specifically worked on and published works on 1.) inflammatory and tumor experimental model of angiogenesis 2.) marrow and tissue derived leukemic and normal stem cell separation and characterization, 3.) renal damage 4.) purification and characterization of stem cell derived extracellular vesicles and characterization of their protein, mRNA and miRNA content. In particular, I investigated the tumor activity and proangiogenic potential of endothelial cell-derived extracellular vesicles. Particular attention has been devoted in defining mechanisms of disease and potential targets. I work with a highly skilled and dedicated research group and I collaborate with Professor Camussi and Dr. Quesenberry in the NIH grants UH2-TR000880, UH3TR000880-03S1 on "Regulation of renal and bone marrow injury by extracellular vesicle non-coding RNA"..

B. Positions and Honors

1984-1988: internal pupil in the "Cytogenetics and Oncoematology" Laboratory directed by Prof. Luigi Pegoraro, at the University of Turin.
1989-1990: "A. Bossolasco " fellowship in the" Cytogenetics and Oncoematology Laboratory at the University of Turin
1991-1993: Fellowship issued by AIRC (Italian Association for Cancer Research) in the Laboratory of "Cytogenetics and Oncoematology" at the University of Turin
1993: "Visiting scientist" in the laboratories of Prof. Yosef Yarden Department of Biochemistry of the Weizman Institute of Science, Israel, for a joint project on the c-kit receptor (spending alternative periods in Italy and in Israel)
1994-1997: PhD student in "Morphogenetic and Cytological Science" at the University of Bologna.
1998: "Visiting scientist" in the laboratories of Prof. Yosef Yarden Department of Biochemistry of the Weizman Institute of Science, Israel, for a joint project on the c-kit receptor (spending alternative periods in Italy and in Israel)
1998-1999: Post-graduate fellowship at the "Cytogenetics and Oncoematology" Laboratory at the University of Turin.
1999: Assistant Professor in Internal Medicine at the University of Turin.

2006: Associate Professor in Internal Medicine at the University of Turin.
2009: Stable Position of Associate Professor in Internal Medicine at the University of Turin.
2016: Invited Speaker at the "Gordon Research Conferences on Extracellular vesicles"

- ***Administrative Activites:*** Professor Brizzi has been MEMBER OF THE TECHNICAL PEDAGOGICAL COMMITTEE, School of Medicine of the University of Turin and VICE PRESIDENT of the School of Medicine, University of Turin. She is currently a member of the EDUCATIONAL AND SCIENTIFIC COMMITTEE of the "MD-PhD Programme " School of Medicine University of Turin; member OF THE BIOETHICS COMMITEE, University of Torino; and MEMBER OF THE SCIENTIFIC EDUCATIONAL COMMITEE of the ACCADEMIC PhD School "Medical Pathophysiology", School of Medicine.

- She serves as Peer Reviewer for - Arteriosclerosisis Thrombosis and Vascular Biology, Oncogene, Blood, Plos One, Diabetes, Frontiers in Oncology, J Molecular Endocrinology, Circulation, Am J Hypertension, Stem Cells, Am. J Pathology.
- She serves in the Editorial Board of "Nutrition, Metabolism and Cardiovascular Diseases"
- She served as referee for the following research agencies: "GRANTS": National Health and Medical Research Council (Australia, Holland), Castang Foundation (UK), and Cancer Research (Poland).

C. Contribution to Science

She lists **108 publications on PubMED** indexed journals**:**
https://www.ncbi.nlm.nih.gov/pubmed/?term=brizzi+mf

WEB of Sciences All Databases **h-index: 32;** n° of citations **3466** and **3155** without self-citations.
http://apps.webofknowledge.com/CitationReport.do?product=UA&search_mode=CitationReport&SID=E4ESKr4CdXLQKATFxqV&page=1&cr_pqid=6&viewType=summary

She began her research training by studying the effects of hematopoietic growth factors on leukemic blasts and their potential use, in combination with chemotherapeutic agents, in the treatment of acute leukemic. She was also involved in the study of the intracellular mechanisms associated with leukemic cell growth. She demonstrated that in leukemic cells mitogenic signals are activated by external stimuli, such as IL-3, GM-CSF, SCF, and Thrombopietin (Leuk Res. 1988, British Journal of Haematoogy. 1990, 1995; Journal of Cell Physiology 1991; Journal of Biological Chemistry 1994, 1996, 1999; Oncogene1994, 1995, 1996a 1996b; Experimental Hematoogy 1998). In parallel, she was involved in a number of studies aimed to evaluate the role of JAK/STAT signaling pathway in mediating IL-3, GM-CSF and Thrombopoietin effects on mature hematopoietic populations, such as neutrophils and platelets as well as on vascular cells (Journal of Clinical Investigation 1993, Journal of Biological Chemistry 1996, Blood 1997, Journal of Clinical Investigation 1997, Circulation Research 1999). She also focused her scientific activity on tumor and inflammatory angiogenesis with particular regards to IL-3 (Circulation 2001, Oncogene 2004, 2005, 2010, 2011, 2018 Blood 2007, 2008). She was also involved in the study of the mechanisms associated with metabolic diseases such as diabetes and obesity (Journal of Clinical Investigation 2002, Diabetes 2011, 2013, 2015, 2018 Diabetologia 2013)
.Specifically she carried out the following researches on **extracellular vesicles (EVs)**:

1) Studies on the mechanisms mediated by stem cell/progenitor-derived EVs. She demonstrated that EVs released by mesenchymal stem cells obtained from obese patients ' adipose tissue were impaired in their ability

to induce vascular remodeling. The in vitro analysis suggested that a crucial role, in changing EV content, is played by high fatty acid circulating concentrations, commonly found in these patients.
Selected references:

1. Togliatto G, Dentelli P, Gili M, Gallo S, Deregibus C, Biglieri E, Iavello A, Santini E, Rossi C, Solini A, Camussi G, Brizzi M.F. Obesity reduces the pro-angiogenic potential of adipose tissue stem cell-derived extracellular vesicles (EVs) by impairing miR-126 content: impact on clinical applications**. Int J Obe**s; 2016, 40:102-11.

2) Studies on the role of serum and stem-cell derived EVs on renal and vascular regeneration. She analysed the protective effects of EVs released from mesenchymal stem cells of different origin on diabetes-mediated kidney damage. This study demonstrated that EVs released from these cells protect mesangial cells from hyperglycemia-induced damage by reducing both the oxidative stress and the production of extracellular matrix proteins. She also demonstrated the proangiogenic activity of serum derived- EVs.
Selected references:

1. Gallo S, Gili M, Lombardo G, Rossetti A, Rosso A, Dentelli P, Togliatto G, Deregibus MC, Taverna D, Camussi G, Brizzi MF. Stem cell-derived, microrna-carrying extracellular vesicles: a novel approach to interfering with mesangial cell collagen production in a hyperglycaemic setting. **PLoS One**. 2016, 11:e0162417.
2. Cavallari C, Ranghino A, Tapparo M, Cedrino M, Figliolini F, Grange C, Giannachi V, Garneri P, Deregibus MC, Collino F, Rispoli P, Camussi G, **Brizzi M.F.** Serum-derived extracellular vesicles (EVs) impact on vascular remodeling and prevent muscle damage in acute hind limb ischemia. **Sci Rep.** 2017, 7:8180.
3. Kholia S, Herrera Sanchez MB, Cedrino M, Papadimitriou E, Tapparo M, Deregibus MC, **Brizzi MF**, Tetta C, Camussi G. Human Liver Stem Cell-Derived Extracellular Vesicles Prevent Aristolochic Acid-Induced Kidney Fibrosis. **Front Immunol.** 2018 Jul 19;9:1639. doi: 10.3389/fimmu.2018.01639.
4. Grange C, Tritta S, Tapparo M, Cedrino M, Tetta C, Camussi G, **Brizzi MF.** Stem cell-derived extracellular vesicles inhibit and revert fibrosis progression in a mouse model of diabetic nephropathy. **Sci Rep**. 2019 Mar 14;9(1):4468. doi: 10.1038/s41598-019-41100-9.

3) Studies on the role of EVs released by vascular cells in tumor growth and vascular restenosis. She demonstrated the pro-angiogenic effect of EVs released in inflammatory setting containing IL-3 both in physiological and pathological conditions. In particular she identify specific pathways involved in IL-3-mediated normal and tumor vessel growth. Moreover she identify the PDGF-enriched endothelial cell-derived-EVs as mediators of vascular injury in diabetic setting.
Selected references:

1. Lombardo G, Dentelli P, Togliatto G, Rosso A, Gili M, Gallo S, Deregibus MC, Camussi G, **Brizzi M.F.** Activated stat5 trafficking via endothelial cell-derived extracellular vesicles controls IL-3 pro-angiogenic paracrine action. **Sci Rep.** 2016,6:25689
2. Lombardo G, Gili M, Grange C, Cavallari C, Dentelli P, Togliatto G, Taverna D, Camussi G, **Brizzi M.F.** IL-3R-alpha blockade inhibits tumor endothelial cell-derived extracellular vesicle (EV)-mediated vessel formation by targeting the β-catenin pathway. **Oncogene**. 2018, 37:1175-1191.
3. Togliatto G, Dentelli P, Rosso A, Lombardo G, Gili M, Gallo S, Gai C, Solini A, Camussi G, **Brizzi M.F.** PDGF-BB carried by endothelial cell-derived extracellular vesicles reduces vascular smooth muscle cell apoptosis in diabetes. **Diabetes.** 2018, Jan 31. pii: db170371. doi: 10.2337/db17-0371.

.Additional Information: Research Support

Active projects:

1. **IG 2015 Id.17630 AIRC** (**PI** Maria Felice Brizzi) 01/01/16-01/01/19

Agency: Associazione Italiana per la ricerca sul Cancro (AIRC)

"Targeting IL-3R interferes with tumor endothelial cell-derived extracellular vesicle (EV)-mediated tumor progression"
The focus of the project is to investigate the role of EVs derived from tumor endothelial cells in mediating change in the tumor microenvironment and thus contribute to tumor growth.

2. **UH2TR000880, UH3TR000880-03S1** (PI Peter Quesenberry) 01/06/2013-01/06/2019
subaward N° 707-5553 (PI Giovanni Camussi, **co-PI** Maria Felice Brizzi)
Agency: NIH/NIDDK
Regulation of renal and bone marrow injury by extracellular vesicle non-coding RNA
The focus of this project is to characterize and identify the "healing" microRNA involved in acute renal and bone marrow injury and engineer extracellular vesicles enriched in this microRNA.

3. **STEM EV** (**PI** Maria Felice Brizzi) 01/01/2018-31/12/20120
Agency: **3i3T Scarl, UNITO/Unicyte**
Pre-clinical development of stem cell- derived SC-EVs for treatment of chronic kidney injury and hind limb ischemia
The aim of the projects is to study stem cell-drived extracellular vesicles for treatment of renal and cardio-vascular diseases.

4. **HLSC-ISLETS** (**PI** Maria Felice Brizzi) 01/01/2018-31/12/2020
Agency: **3i3T Scarl, UNITO/Unicyte**
Preclinical study HLSC-ILS-based treatment for Type 1 Diabetes
The aim of the projects is to study stem cell-drived extracellular vesicles for treatment of Type 1 Diabetes.

5. **PROGRAMMA OPERATIVO REGIONALE "INVESTIMENTI A FAVORE DELLA CRESCITA E DELL'OCCUPAZIONE" F.E.S.R. 2014/2020 (PI** Maria Felice Brizzi**)** 31/07/2018-31/12/2020
Agency: **Regione Piemonte**
EV-ER
The aim of the projects is to study stem cell-derived extracellular vesicles to treat Type 2 Diabetes.

PERSONAL INFORMATIONS

Name	**ADA CASTELLI**
Address	**70 VIA XXV APRILE 10099 SAN MAURO TORINESE TORINO ITALY**
Phone number	**011-6336037**
Fax	
E-mail	**adacastelli@unito.it**
Nationality	Italy
Date of Birth	30-05-1956

WORKING EXPERIENCE

• Date (from-to)	From January 1998 until today Lab. Translational Cell Biology
• Name and address of employer	University study of Turin Via Verdi 8 Torino
• Sector	Dep Medical Science
• Kind of employment	Research Tehnician cat. C4
• Main task and responsability	Cellular Biology

WORKING EXPERIENCE

• Date (from-to)	From December 1987 to December 1998 General Pathology
• Name and address of employer	University study of Turin Via Verdi 8 Torino
• Sector	Dep Experimental Medicine and Oncology
• Kind of employment	Research Tehnician
• Main task and responsability	Moleculr Biology

EDUCATION AND TRAINING

• Date (from-to)	1971 Middle School
• Name and type of scool	State School E. Fermi
	2011 Safe use of liquid nitrogen – DPI, DPC emergency procedures course
FIRST LANGUAGE	Italian **italian**
OTHER LANGUAGES	French
• Reading Ability	Elementary
• Writing Ability	Elementary

• Ability of Oral expression	Elementary excellent
	Ability to work in sterility and culture primary cells
ORGANIZATIONAL SKILLS	
THECNICAL SKILLS	Use of all laboratory equipments

PERSONAL INFORMATIONS

Name	**ARTURO ROSSO**
Address	**3 VIA SAN GIORGIO 12035 CASALGRASSO (CN) ITALY**
Phone number	**011-6336034/5539**
Fax	
E-mail	**arturo.rosso@unito.it**
Nationality	Italy
Date of Birth	22-10-1957

WORKING EXPERIENCE

• Date (from-to)	From January 1994 until today Lab. Molecular Biology of Atherosclerosis
• Name and address of employer	University study of Turin Via Verdi 8 Torino
• Sector	Dep Medical Science
• Kind of employment	Research Tehnician cat. D3
• Main task and responsability	Molecular and Cellular Biology

WORKING EXPERIENCE

• Date (from-to)	From August 1993 to December 1993 Lab. Pathological Anatomy
• Name and address of employer	University study of Turin Via Verdi 8 Torino
• Sector	Dep Human Oncology
• Kind of employment	Research Tehnician
• Main task and responsability	Moleculr Biology

WORKING EXPERIENCE

• Date (from-to)	From June 1990 to July 1993 Lab. Parasitology
• Name and address of employer	University study of Turin Via Verdi 8 Torino
• Sector	Dep. Animal Biology
• Kind of employment	Tehnician cat. C6
• Main task and responsability	Histological preparations

EDUCATION AND TRAINING

• Date (from-to)	1976 Secondary school diploma Industrial Expert
• Name and type of scool	ITIS Fossano
	1994 Moleculr Biology course
	University study of Turin
	1997 Internet course
	University study of Turin
	1999 Biological risk in the hospital labs course
	Hospital S. G. Battista Turin
	2001 Chemical risk in the hospital labs course
	Hospital S. G. Battista Turin
	2002 Cryopreservation course
	University study of Turin
	2003 Spanish basic course
	University study of Turin
	2003 Spanish intermediate course
	University study of Turin
	2003 Stamina cells course
	Training center BD Milano
	2003 Excel course
	University study of Turin
	2005 Powerpoint course
	University study of Turin
	2007 Creating and using of PDF documents course

University study of Turin

2008 Search of information in internet course
University study of Turin

2009 Cryopreservation of semen course
University study of Turin

2010 ACCESS course
University study of Turin

2010 Word course
University study of Turin

2016 ASPP-RSPP module A course
University study of Turin

2016 ASPP-RSPP module B course
University study of Turin.

FIRST LANGUAGE **italian**

OTHER LANGUAGES

	French	**English**	**Spanish**
• Reading Ability	excellent	elementary	good
• Writing Ability	good	elementary	good
• Ability of Oral expression	excellent	elementary	good

ORGANIZATIONAL SKILLS	Ability to manage thesis and support students in molecular biology thanks to ASPP-RSPP courses Ability to educate students
THECNICAL SKILLS	Use of all laboratory computers and equipments