Deborah Fratantonio, Ph.D.

Department of Biosciences, Biotechnologies and Biopharmaceutics University of Bari "Aldo Moro", Italy Date of birth: January 28th, 1987 Email: deborah.fratantonio@uniba.it

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Education

- **Doctor of Philosophy** in Social and environmental toxicology. University of Messina, Italy. March, 2015
- Qualification to practice the pharmacist profession. University of Pavia, Italy.
 June, 2011
- **Bachelor degree** in Pharmacy and industrial pharmacy. University of Pavia, Italy. May 2011.

Research Experience

- Researcher (RTD a) SSD BIO/10 PON AIM1893457 (attività 2) Linea 2.1. "D.D.G. n. 407 del 27/02/2018 Programma Operativo Nazionale (PON) Ricerca e Innovazione 2014-2020. Avviso "AIM: Attrazione e Mobilità Internazionale" nell'ambito dell'Asse I "Capitale umano" e nel rispetto della Strategia Nazionale di Specializzazione Intelligente 2014-2020 azioni volte a favorire la mobilità e l'attrazione di ricercatori in ambito universitario". Department of Biosciences, Biotechnologies and Biopharmaceutics University of Bari, Italy. August 2019- present
 - Project: Characterize the pathogenic mechanism of neuromuscular diseases, related to mitochondrial homeostasis (respirometry, membrane potential, ROS content, metabolomics and flux) and post-translational modifications of mitochondrial proteins and/or mediators of mitochondrial biogenesis in 2D and 3D cellular models.
- **AIRC Researcher fellowship** in "Investigating MKK3 as novel molecular target for therapeutic strategy in microsatellite in stable colorectal cancer. *Regina Elena National Cancer Institute, IRCCS, Rome. July 2019-august*
- **Researcher collaborator** in Delivery and imaging of circulating miRNAs as innovative therapeutic and diagnostic tools for pediatric pulmonary hypertension" and "The protective effect of plant-derived extracellular vesicles and their miRNA cargo against TNF-α-induced inflammatory genes expression in cell culture models".

 **Bambino Gesù Children's Hospital, IRCCS, Vatican City. September 2018-June 2019
- **Postdoctoral research assistant** in Molecular Nutrition, funded by National Institutes of Health (NIH) and National Institute of Food and Agriculture (NIFA).

 Nebraska Center for the Prevention of Obesity Diseases, Department of Nutrition and Health Sciences. University of Nebraska-Lincoln, USA. June 2016- August 2018

Scientific research: Bioavailability, distribution and activity of exosomes and microvesicles cargo (non-coding RNA, mRNA, proteins and lipids) of dietary items (milk, eggs) in humans and mice. The relevance of this research is to understand how exogenous and endogenous extracellular vesicles and their cargo exert a role in gene expression regulating metabolism, pregnancy, fecundity, cognitive performance and brain development. This new field of research has high relevance and impact for the understanding of molecular mechanisms underlying the role of microvesicles cargo in health and disease.

- Project title: "Role of miRNAs in the early stage of chicken embryo development"
- Project Title: "Identification of mechanisms though which exosomes and their RNA cargos in chicken eggs improve spatial learning and memory in mice".
 Role: *Principal investigator (PI)*. 2017-2018
- Project title: "Egg-Born miRNAs regulate gene network and contribute toward reproductive success in Humans and Mice",
 Role: *Principal investigator (PI)*. 2016-2017
- Project title: "Methamphetamine exposure alters the number and destinations of exosomes originating in the *nucleus accumbens* (NAc) in ECT mice. Role: **Co-investigator**. 2017-2018
- **Postdoctoral research** at *University of Messina, Italy.* 2015-2016
 - Project title: Curcumin potentiates antitumor activity of Paclitaxel in rat glioma C6 cells Role: *Scholar fellowship. June 2015- May 2016*

Scientific research: Aim to evaluate the synergistic effect of curcumin, a yellow pigment of spicy curcuma (Curiosa longa), known for its effectiveness chemopreventive and chemotherapeutic activity through the influence on cell cycle intervention, differentiation and apoptosis in different types of cancer, a major role will be played in the control of oncogenesis, tumor progression and resistance to chemotherapy of different types of malignancy. Paclitaxel (PTX), a microtubule stabilizing agent with very potent antitumor potential, is recommended as a first line strategy chemotherapeutic agent against many types of tumors. However, the clinical experience of PTX in brain tumor is limited by drug resistance. In conclusion, the data of our research indicated that the combinational strategy exerted much higher efficacy in glioma growth delay than single administration of Cur or PTX, thus it may help in reducing dosage and in minimizing side effects of cytotoxic therapy.

- Project title: Alpha-lipoic acid, but not dihydrolipoic acid, activates Nrf2 pathway in TNF- α -challenged HUVECs.

Role: Scholar fellowship. 2015-2016

Scientific research: Alpha-Lipoic acid (ALA) is a sulfur-containing coenzyme required for the mitochondrial dehydrogenase reactions leading to ATP formation. LA is readily taken up by a variety of cells and tissues and is reduced in mitochondria to the potent antioxidant dihydrolipoic acid (DHLA). Due to their antioxidant properties ALA and DHLA have been recently proposed as pleiotropic compounds with potential therapeutic use in many inflammatory diseases. In this study, we investigated the in vitro effect of physiological concentrations of ALA and DHLA (250-500 nM) against endothelial dysfunction induced by TNF-alpha in human umbilical vessel endothelial cells (HUVECs). Our data show that ALA, but not DHLA, inhibits TNF-α-induced activation of NF-kB pathway, as observed by reduced p65 nuclear levels and cytoplasmic IkB-α phosphorylation. At the same extent, only ALA is able to reduce, in a dose-dependent way, the TNF-α-induced downstream expression of the endothelial adhesion molecules ICAM-1 and E-selectin. Part of these effects can be explained by the observed specific stimulatory activity on Nrf2 pathway. Nrf2 is the master of redox homeostasis, acting as regulator or inducer for the expression of several antioxidants and cytoprotective genes.

- Project title: "Development of micro/nano technologies and advanced systems for human health".

Role: Scholar fellowship. 2015

Scientific Research: Transport of nanoparticles through systems of biomimetic cell barriers such as the blood-brain barrier (BEE). The study envisaged the use of cell line bEND.3 of murine cerebral microvascular endothelial cells for transport studies using a BEE model in vitro. The confluent monolayers of endothelial cells obtained were examined under a microscope to verify their integrity and subsequently the permeability to albumin was measured. The biocompatibility of the P-PLGA and P-PLGA-PEG nanoparticles was evaluated on the HUVEC and NIH / 3T3 cell lines by means of the viability tests and subsequently the transport through the BEE was evaluated.

• Ph.D. student 2012-2015

Scientific research: mechanisms by which molecules of nutritional interest modulate endothelial cellular response to different stimuli, affecting gene expression pathways at transcriptomic and proteomic level, by using techniques such as mammalian cell culture and transfection, *in vitro* protein analysis like western, immunoprecipitation, immunofluorescence etc.

• **Visiting Researcher** in Potential health benefits of polyphenol and antocyanindins in Human disease: in vitro study".

Department of Nutrition and Christian-Albrechts-University, Kiel, Germany. 2013-2014

• **Visiting Researcher** in Physiological concentration of Caffeic Acid in endothelial dysfunction caused by high-glucose exposure.

Council for Agricultural Research and Economics Food and Nutrition Center (CREA-NUT), Roma, Italy. 2013

Scientific Research: preventing the alterations induced by highglucose in endothelial cells using molecules of nutritional interest and widely present in nature. Specifically, the effect of caffeic acid, an abundant hydroxycinnamic acid in coffee and other foods, in human endothelial cells (HUVEC) exposed to high concentrations of glucose (HG). At this purpose the levels of the main markers of the intracellular redox state were examined, such as glutathione (GSH), the activity of superoxide dismutase (SOD) and intracellular antioxidant activity (TAA), focusing on the central role that the increase of oxidative stress plays in metabolic disorders such as diabetes mellitus and its prevention thought dietary molecules.

• Graduate student

Scientific research: Antifungal activity of natural extracts and pure compounds, in culture fungal colonies, responsible for major human parasitosis, the most studied has been the Mycrosporum. Preparation and evaluation of microbial assays: dilution in agar and determination of Minimum Inhibitory Concentration (MIC) and (MFC); antibiogram. Studies have been developed within the research progect on Etnopharmacology, characterization and study of compounds used in the traditional medicine.

 Project title: Saponins activity from Medicago Sativa L. against dermatophytes of microsporum species.

University of Pavia, Italy. 2010-2011

Awards and Honors

- **Invited speaker** at School, Chemistry, Food & Pharmacy, University of Reading, Reading UK. August, 2018
- Invited speaker at Translational Genomics Research Institute (TGen) and affiliate of City of Hope, Phoenix, Arizona, USA. June, 2018
- Front cover award in "BioFactor" Vol 44 No 3, May/June 2018 related to the article Deborah Fratantonio, Francesco Cimino, Antonio Speciale and Fabio Virgili: *Need (more than) two to Tango: multiple tools to adapt to changes in oxygen availability.* Biofactors (2018) DOI: 10.1002/biof.1419.

- **Travel grant** to attend the 2018 "Nutrigenetics, Nutrigenomics, & Precision Nutrition Workshop", Speaker: Jose M. Ordovas, PhD, Senior Scientist. *University of North Carolina at Chapel Hill, Nutrition Research Institute, Kannapolis, NC.* June 4-7, 2018
- **Invited Speaker** at 22nd International FFC Conference, Beth Israel Deaconess Medical Center, *Harvard Medical School, Boston, MA, USA*. September 22-24, 2017. Link: http://functionalfoodscenter.net/22nd-int--conference-of-ffc.html

Teaching experience

- Provide Lecture and interactive class in "NUTR820 Molecular Nutrition"
- Teaching laboratory techniques within the class "NUTR821 Molecular Nutrition Techniques".

Role: **Graduate Teaching Assistant and Laboratory Tutor of Molecular Biology** Department of Nutrition and Health Sciences, University of Nebraska at Lincoln. 2017-2018.

Responsibility: Follow and guide students in the learning molecular biology techniques in the course "NUTR821 Molecular Nutrition Techniques"

• "Expert technologist in the development of nano enabling Technologies for drug delivery". PON 02 00355 2964193- HIPPOCRATES.

Role: **Graduate Teaching Assistant and Laboratory Tutor of Molecular Biology** University of Messina, Italy. 2014-2015

Responsibility: Follow and guide students in the activity of "Transport study, material and release of active compound of drug delivery": Introduction of good laboratory practices, *in vitro* models, cultures of animal cells, vitality and genotoxicity tests, biomimetic cell cultures of biological barriers; Dissertation review.

Other academic activity

• Poster judge for ungraduated and graduated students at "Spring 2018 Research Fair". April 10-11, 2018. Nebraska Union, University of Nebraska, Lincoln.

Research Funding

 Project title: Identification of mechanisms though which exosomes and their RNA cargos in chicken eggs improve spatial learning and memory in mice US\$ 57,500/1 year from Egg Nutrition Center (ENC)

Role: Co-Investigator / Scientific principal Investigator of the project

2017, Department of Nutrition and Health Sciences, University of Nebraska Lincoln

 Project title: Egg-borne microRNAs regulate gene networks and contribute toward reproductive success in humans and mice US\$ 75,000/1 year from Egg Nutrition Center (ENC)

Role: Postdoctoral research assistant (Scientific principal Investigator of the project) 2016, Department of Nutrition and Health Sciences, University of Nebraska Lincoln

Publications List

- 1. Salman Ahmed, Haroon Khan*, **Deborah Fratantonio***, Muhammad Mohtasheemul Hasan, Samin Sharifi, Nazanin Fathi, Hammad Ullah, Luca Rastrelli (*corresponding author). Apoptosis induced by luteolin in breast cancer: Mechanistic and therapeutic perspectives. Phytomedicine (available on line 10 March 2019) (**IF 3.61**)
- 2. <u>Deborah Fratantonio</u>, Maria Sofia Molonia, Romina Bashllari, Claudia Muscarà, Guido Ferlazzo, Gregorio Costa, Antonina Saija, Francesco Cimino, Antonio Speciale. Curcumin potentiates antitumor activity of Paclitaxel in rat glioma cell targeting P53 and Nf-kB pathways. **Phytomedicine** (2018) https://doi.org/10.1016/j.phymed.2018.08.009 (**IF 3.61**)
- 3. <u>Deborah Fratantonio</u>, Antonio Speciale, Maria S. Molonia, Romina Bashllari, Marco Palumbo, Antonina saija, Giovanni Monastra, Francesco Cimino, Fabio Virgili. Alphalipoic acid, but not dihydrolipoic acid, activates Nrf2 pathway in TNF-α-challenged HUVECs.
 - Archives of Biochemistry and Biophysics (2018) doi: 10.1016/j.abb.2018.08.003. (IF 3.11)
- 4. <u>Frantantonio D</u>., Shu J., Cui J., Zempleni J.; "*MicroRNAs in chicken egg exosomes: content and bioavailability in healthy humans*". FFC's 22nd International Conference; Boston, MA, USA; Organized by FFC and BIDMC/ Harvard Medical School Teaching Hospital; Volume 1; Supplement 1: 111-112 (**IF N.D**)
- 5. <u>Deborah Fratantonio</u>, Francesco Cimino, Antonio Speciale and Fabio Virgili: *Need (more than) two to Tango: multiple tools to adapt to changes in oxygen availability.* Biofactors (2018) DOI: 10.1002/biof.1419. (**IF 3.03**)
- Daniela Ferrari, Francesco Cimino, <u>Deborah Fratantonio</u>, Maria Sofia Molonia, Romina Bashllari, Rossana Busà, Antonina Saija, Antonio Speciale: *Cyanidin-3-O-Glucoside Modulates the In Vitro Inflammatory Crosstalk between Intestinal Epithelial and Endothelial Cells*. Mediators of Inflammation (2017). DOI:10.1155/2017/3454023 (IF 3.54)

- 7. <u>Deborah Fratantonio</u>, Francesco Cimino, Maria Sofia Molonia, Daniela Ferrari, Antonina Saija, Fabio Virgili, Antonio Speciale: *Cyanidin-3-O-glucoside ameliorates palmitate-induced insulin resistance by modulating IRS-1 phosphorylation and release of endothelial derived vasoactive factors*. Biochimica et Biophysica Acta (BBA) Molecular and Cell Biology of Lipids (2016) DOI:10.1016/j.bbalip.2016.12.008 (**IF 3.67**)
- Daniela Ferrari, Antonio Speciale, Mariateresa Cristani, <u>Deborah Fratantonio</u>, Maria Sofia Molonia, Giulia Ranaldi, Antonella Saija, Francesco Cimino: *Cyanidin-3-O-glucoside inhibits NF-kB signalling in intestinal epithelial cells exposed to TNF-α and exerts protective effects via Nrf2 pathway activation*. Toxicology Letters (2016). DOI:10.1016/j.toxlet.2016.10.014 (IF 3.16)
- 9. <u>Deborah Fratantonio</u>, Antonio Speciale, Raffaella Canali, Lucia Natarelli, Daniela Ferrari, Antonina Saija, Fabio Virgili, Francesco Cimino: *Low nanomolar caffeic acid attenuates high glucose-induced endothelial dysfunction in primary human umbilical-vein endothelial cells by affecting NF-κB and Nrf2 pathways*. BioFactors (2016). DOI:10.1002/biof.1312 (IF 3.03)
- 10. Sirajudheen Anwar, <u>Deborah Fratantonio</u>, Daniela Ferrari, Antonella Saija, Francesco Cimino, Antonio Speciale: *Berry anthocyanins reduce proliferation of human colorectal carcinoma cells by inducing caspase-3 activation and p21 upregulation*. Molecular Medicine Reports (2016). DOI:10.3892/mmr.2016.5397 (**IF 1.92**)
- 11. Mariateresa Cristani, Antonio Speciale, Ferdinando Mancari, Teresita Arcoraci, Daniela Ferrari, **Deborah Fratantonio**, Antonina Saija, Francesco Cimino, Domenico Trombetta: *Protective activity of an anthocyanin-rich extract from bilberries and blackcurrants on acute acetaminophen-induced hepatotoxicity in rats*. Natural product research (2016). DOI:10.1080/14786419.2016.1160235 (**IF 1.92**)
- 12. <u>Deborah Fratantonio</u>, Antonio Speciale, Daniela Ferrari, Mariateresa Cristani, Antonina Saija, Francesco Cimino: *Palmitate-induced endothelial dysfunction is attenuated by cyanidin-3-O-glucoside through modulation of Nrf2/Bach1 and NF-κB pathways*.

 Toxicology Letters (2015) DOI:10.1016/j.toxlet.2015.09.020 (**IF 3.16**)

- 13. Antonino Germanò, Lucia Merlo, Francesco Cimino, Speciale Antonio, Mariateresa Cristani, **Deborah Fratantonio**, Giovanni Raffa, RV Abritti, Antonina Saija, A David: *A preliminary study serum & Actin as potential biomarker of diffuse axonal injury in severe traumatic brain injury*.. Journal of neurotrauma, 2014. Vol. 31. No. 5. 140. DOI: 10.1089/neu.2014.9937 (**IF 5.00**)
- 14. Sirajudheen Anwar, Antonio Speciale, <u>Deborah Fratantonio</u>, Mariateresa Cristani, Antonina Saija, Fabio Virgili, Francesco Cimino: *Cyanidin-3-O-glucoside modulates intracellular redox status and prevents HIF-1 stabilization in endothelial cells in vitro exposed to chronic hypoxia*. Toxicology Letters 02/2014; 226(2). DOI:10.1016/j.toxlet.2014.01.048 (**IF 3.16**)

Google scholar citation: https://scholar.google.it/citations?user=2T QWo0AAAAJ&hl=it

Submitted peer reviewed paper

Raffaella Comitato, Guido Leoni, Roberto Ambra, Sonia Manca, Barbara Guantario, <u>Deborah</u> <u>Fratantonio</u>, Raffaella Canali and Fabio Virgili. *miRNA-190b modulates apoptotic response in HeLa cancer cells induced by γ-Tocotrienol*. **Scientific Report- Nature** (submitted)

<u>Deborah Fratantonio</u>, Jiang Shu, Katherine Howard, Scott R. Baier, David Giraud, Juan Cui, and Janos Zempleni. *MicroRNAs from chicken eggs are bioavailable and alter gene expression in peripheral blood mononuclear cells in humans*. **Scientific Report- Nature** (under revision)

<u>Deborah Fratantonio</u>, Jiang Shu, Juan Cui, and Janos Zempleni. *Dietary chicken egg exosomes and their cargo improve spatial and learning memory in C57BL mice during life cycle through microRNA-target gene in hippocampus*. **Journal of Nutrition** (submitted)

<u>Deborah Fratantonio</u>, Jiang Shu, Juan Cui, and Janos Zempleni. *MiRNAs and gene expression profile during the early stage of chicken embryo development*. **Journal of Experimental Biology** (submitted)

Oral Comunications

1. **D. Fratantonio**, J. Chu, J. Cui and J. Zempleni. *Dietary depletion of chicken egg exosome* and their cargo affects the gene expression profile in right and left hippocampus and impairs cognitive performace in C57BL/6 mice. Convegno monotematico "Le basi

- farmacologiche dei Nutraceutici" della Società Italian di Farmacologia. 29-30 Marzo 2019, Napoli.
- 2. <u>D.Fratantonio</u>. Chicken egg exosomes and their cargos are bioavailable in humans and contribute toward spatial learning and memory in mice. Translational Genomics Research Institute (TGen) and affiliate of City of Hope, Phoenix, Arizona, USA.
- 3. <u>D. Fratantonio</u>, J. Shu, J. Cui and J. Zempleni. *MicroRNAs in chicken egg exosomes:* content and bioavailability in healthy humans. 22nd International Conference of FFC 10th International Symposium of ASFFBC Functional Foods and Chronic Diseases: Science and Practice. September 22-23, 2017, at Harvard Medical School, Boston, MA, USA
- 4. <u>D.Fratantonio</u>, A. Speciale, D. Ferrari, A. Saija, F. Cimino. *Cyanidin-3-Oglucoside* protects endothelial cells against palmitic acid-induced injury in vitro through Nrf-2 modulation. In: 17° Seminario SIF dottorandi, assegnisti di ricerca, postdottorandi e specializzandi in Farmacologia e Scienze affini. 16-18 settembre 2014, Rimini.

Proceedings of the conference

- 1. CIMINO F, ANWAR S, CANALI R, **FRATANTONIO D**, RICCIARDI E, SAIJA A, VIRGILI F, SPECIALE A. (2012). Cellular adaptive response to glutathione depletion modulates endothelial dysfunction triggered by TNF-α: involvement of Nrf2/ARE pathway. In: Oxygen Club of California World "Oxidants and Antioxidants in Biology: Cell Signaling and Nutrient-Gene Interactions", Alba, Italia, 20-23 Giugno 2012.
- 2. SPECIALE A, ANWAR S, **FRATANTONIO D**, AZZERBONI A, SAIJA A, VIRGILI F, CIMINO F. (2012). Nrf2 transcription factor activation modulates endothelial inflammatory response triggered by TNF-alpha. In: X Convegno Nazionale I.N.B.B. "Scienze della Vita", Roma, Italia, 22-23 Ottobre 2012.
- 3. **FRATANTONIO D**, ANWAR S, AZZERBONI A, CANALI R, SAIJA A, SPECIALE A, VIRGILI F, CIMINO F. (2013) Caffeic Acid modulates oxidative stress induced by high-glucose exposure in endothelial cells: involvement of Nrf2 pathway. In: 5th International Symposium Nutrition, Oxygen Biology and Medicine. Development and Ageing Nutrition, Epigenetics and Lifestyle and the Healthspan. Parigi, Francia, 5-7 giugno 2013.
- 4. LO CASCIO P, PALOMBIERI D, CALABRO' C, ZENA R, **FRATANTONIO D**, SPECIALE A, SAIJA A. (2013) Effetti citotossici in vitro di estratti di Mytilus galloprovincialis e Sparus aurata esposti a Benzo(a)pirene. In: 74° Congresso Nazionale dell'Unione Zoologica Italiana, Modena, 30 Settembre 3 Ottobre 2013.
- 5. **FRATANTONIO D**, SPECIALE A, FERRARI D, AZZERBONI A, ANWAR S, SAIJA A, CIMINO F. (2013) Cyanidin-3-O-glucoside protects endothelial cells from Palmitic acid-induced oxidative stress by activating Nrf2 pathway. In: Proceedings 36° Congresso Nazionale della Società Italiana di Farmacologia. Il ruolo della ricerca farmacologica per la crescita e la salute in Italia. Torino, Italia, 23-26 ottobre 2013.
- 6. **FRATANTONIO D**, SPECIALE A, AZZERBONI A, CRISTANI M, CANALI R, NATARELLI L, SAIJA A, VIRGILI F, CIMINO F. (2013) Caffeic Acid modulates oxidative stress induced by hyperglycemia in endothelial cells: involvement of Nrf2 pathway. In: Proceedings 36° Congresso Nazionale della Società Italiana di Farmacologia. Il

- ruolo della ricerca farmacologica per la crescita e la salute in Italia. Torino, Italia, 23-26 ottobre 2013.
- 7. S. OURGHEMMI, H.SEBEI, **D. FRATANTONIO**, R. ZENA, F. CIMINO, M. CRISTANI (2013) Comparative studies on antioxidant activity of extract from three wild Rosa Species grown in different Tunisia regions. Volume II ruolo della ricerca RICERCA farmacologica per la CRESCITA e la Salute in Italia, pp 131-131, In: 36° CONGRESSO NAZIONALE DELLA SOCIETÀ ITALIANA DI FARMACOLOGIA. 23-26 ottobre 2013, Torino.
- 8. MERLO L, CIMINO F, SPECIALE A, CRISTANI M, **FRATANTONIO D**, RAFFA G, PRIOLA S, ABRITTI R.V., SAIJA A, DAVID A, GERMANO'A. (2014) A Preliminary Study Serum β-Actin as Potential Biomarker of Diffuse Axonal Injury in Severe Traumatic Brain Injury. INTS Budapestl Marzo 2014.
- 9. **FRATANTONIO D**, SPECIALE A, FERRARI D, ANWAR S, SAIJA A, CIMINO F. (2014) Caffeic Acid attenuates high glucose-induced oxidative stress and endothelial dysfunction in human endothelial cells via modulating NF-κB pathway. In: Abstract book "FARMACOGNOSIA: nuove opportunità terapeutiche dal mondo vegetale". Convegno Monotematico della Società Italiana di Farmacognosia. Napoli, Italia, 20-21 Giugno 2014.
- 10. SPECIALE A, **FRATANTONIO D**, FERRARI D, ANWAR S, SAIJA A, CIMINO F (2014). Cyanidin-3-O-glucoside prevents endothelial cells dysfunction via Nrf2 pathway. In: "FARMACOGNOSIA: nuove opportunità terapeutiche dal mondo vegetale". Convegno Monotematico della Società Italiana di Farmacognosia. Napoli, Italia, 20-21 Giugno 2014.
- 11. FERRARI D, SPECIALE A, **FRATANTONIO D**, CRISTANI M, , SAIJA A, CIMINO F (2014) Protective effects of Cyanidin-3-O-glucoside against LPS-induced damage in Caco-2 intestinal cells. In: Abstract book "FARMACOGNOSIA: nuove opportunità terapeutiche dal mondo vegetale". Convegno Monotematico della Società Italiana di Farmacognosia. Napoli, Italia, 20-21 Giugno 2014
- 12. **FRATANTONIO D**, CIMINO F, FERRARI D, CIANCIMINO L, ANANIA F, SAIJA A, SPECIALE A. (2014) Caffeic acid protects the endothelium from high glucose-induced dysfunction through Nrf2 and HO-1 activation. In: Cellular Environmental Stressors in Biology and Medicine: Focus on Redox Reactions. Ferrara, Italia, 25-27 Giugno, 2014.
- 13. FERRARI D, **FRATANTONIO D**, CRISTANI M, SAIJA A, CIMINO F, SPECIALE A (2014) Cyanidin-3-O-glucoside modulates intracellular redox status and inflammation induced by LPS in Caco-2 intestinal cells through activation of Nrf-2 Pathway. In: 17° Seminario SIF dottorandi, assegnisti di ricerca, postdottorandi e specializzandi in Farmacologia e Scienze affini. 16-18 settembre 2014, Rimini,
- 14. SPECIALE A, FERRARI D, **FRATANTONIO D**, BASHLLARI R, BUSA' R, SAIJA A, CIMINO F, (2015). Modulation of nuclear factor-kB signalling pathway by anthocyanins in human intestinal Caco-2 cells exposed to Tnf-α. In: Oxidant and antioxidant in biology, Oxygen Club of California World Congress 24-26 Giugno, Valencia, Spain
- 15. **FRATANTONIO D**, FERRARI D, SPECIALE A, MOLONIA S, SAIJA A, CIMINO F. (2015) Cyanidin-3-O-glucoside inhibits palmitate-induced endothelial insulin resistance via blocking IKKβ and serine phosphorylation of IRS-1. In: Oxidant and antioxidant in biology, Oxygen Club of California World Congress 24-26 Giugno, Valencia, Spain.
- 16. FRATANTONIO D, SPECIALE A, MOLONIA S, FERRARI D, TRIOLO O, IMBESI G, SAIJA A, CIMINO F. (2015). Cyanidin-3-O-glucoside ameliorates palmitate-induced insulin resistance: modulation of IKK and JNK induced serine IRS-1 phosphorylation. In: 37° Congresso Nazionale SIF, I NUOVI ORIZZONTI DELLA RICERCA FARMACOLOGICA: TRA ETICA E SCIENZA. Napoli 27-30 Ottobre 2015.

- 17. FERRARI D, **FRATANTONIO D**, BASHLLARI R, SAIJA A, CIMINO F, SPECIALE A. Cyanidin-3-O-glucoside exhibits anti-inflammatory properties and improves intestinal epithelial barrier integrity in Caco-2 cells exposed to TNF-α. In: 37° Congresso Nazionale SIF, I NUOVI ORIZZONTI DELLA RICERCA FARMACOLOGICA: TRA ETICA E SCIENZA. Napoli 27-30 Ottobre 2015.
- 18. SPECIALE A, FERRARI D, **FRATANTONIO D**, BUSA' R, SAIJA A, CIMINO F, Cyanidin-3-O-glucoside modulates intestinal inflammatory response induced by TNF-α: an approach based on in vitro epithelial and epithelial-endothelial co-culture models. In: 37° Congresso Nazionale SIF, I NUOVI ORIZZONTI DELLA RICERCA FARMACOLOGICA: TRA ETICA E SCIENZA. Napoli 27-30 Ottobre 2015.
- 19. **FRATANTONIO D,** FERRARI D, SPECIALE A, MOLONIA S, SAIJA A, VIRGILI F, CIMINO F. Cyanidin-3-O-glucoside ameliorates palmitate-induced insulin resistance by modulating IKK and JNK induced serine IRS-1 phosphorylation. In: Redox Medicine and Nutrition, Oxygen Club of California World Congress 4-6 Maggio 2016, University of California, Davis, USA.
- 20. **Fratantonio D**. and Zempleni J. MicroRNAs in chicken egg exosomes are bioavailable in humans and contribute toward spatial learning and memory in mice. University of Nebraska, NPOD 3rd Annual Fall Symposium, September 20, 2017, Lincoln, NE.
- 21. **FRATANTONIO D**. and ZEMPLENI J. MicroRNAs in chicken egg exosomes are bioavailable in humans and contribute toward spatial learning and memory in mice. In: ASEMV2017 meeting Oct.8-12, 2017, Asilomar, Pacific Grove-CA, USA.
- 22. BASHLLARI R, **FRATANTONIO D**, MOLONIA MS, MUSCARA' C SAIJA A, CIMINO F, SPECIALE A. Curcumin potentiates antitumor activity of Paclitaxel in rat glioma C6 cells. In 38° Congresso Nazionale della Società Italiana di Farmacologia: Farmaci, salute e qualità della vita. Rimini 25-28 Ottobre 2017.
- 23. SPECIALE A, **FRATANTONIO D**, BASHLLARI R, MUSCARA' C, MOLONIA MS, VIRGILI F, SAIJA A, CIMINO F. Alpha-lipoic acid, but not dihydrolipoic acid, activates Nrf2 pathway in TNF-α-challenged HUVECs. In 38° Congresso Nazionale della Società Italiana di Farmacologia: Farmaci, salute e qualità della vita. Rimini 25-28 Ottobre 2017.
- 24. **Fratantonio D**, Shu J, Cui J and Zempleni J. Chicken egg exosomes and their cargo are bioavailable and dietary depletion affects the hippocampus gene expression in mice. UNL Spring Retreat, April 11, 2018, Lincoln, NE
- 25. **D. Fratantonio**, A. Speciale, M.S. Molonia, R. Bashllari, A. Saija, F. Cimino, G. Monastra, F. Virgili. Alpha-lipoic acid, but not di-hydrolipoic acid, activates Nrf2 response in primary human umbilical-vein endothelial cells and protects against TNF-α induced endothelium dysfunction. REDOX HOMEOSTASIS: FROM SIGNALLING TO DAMAGE, 19-21 June, Ferrara Italy.

Technical Skills

1) Molecular and Cell Biology

Cell cultures:

Primary lines: primary human endothelial cells (HUVEC); primary human leukocytes (PBMC).

Stabilized and tumor lines: myeloma (U266B1, MM-1R, MM-1S); endothelial stabilized (Ea.hy 926); Mouse Brain Endothelioma (bEnd.3); human neuroblastoma cells (SH-SY5Y); rat glioma (C6); murine fibroblasts (NIH-3T3); human keratinocytes (HaCaT); epithelial cells of colorectal adenocarcinoma (Caco- 2); human embryonic kidney 293 (HEK-293); pancreatic β cells (Beta-TC-6); adipocyte-like cells (3T3-L1); Astrocytes (C8-D1A)

Cell barrier System: Integrity and permeability measurements through analysis of transcellular electrical resistance (TEER); assessment of transport by fluorescent probes or macromolecules through the cell monolayer:

- **endothelial barrier**: human endothelial cells (HUVECs) cultured on PET and Transwell filters for cells permeability and endothelial absorption.
- **epithelial cells** of human adenocarcinoma (Caco-2) differentiated in a polarized cells monolayer for transport studies (cellular and paracellular) and alteration of cell permeability.
- **blood-brain barrier** in vitro (BBB) by co-culture of endothelial cells (b.End.3) with astrocytes (C6 glioma), for drug delivery study.
- **3D** Cell culture system: primary human leukocytes (PBMC) and endothelial cells HUVEC to study leukocyte adhesion in endothelial dysfunction.

Tests used:

- Viability and cell proliferation (Trypan Blue exclusion assay, Wound Healing assay)
- Cytotoxicity (sulforhodamine B, MTT, Neutral Red assay, clonogenic assay)
- Cell genotoxicity (DNA laddering assay, apoptotic markers related to the cascade of caspase).

Genomic techniques:

- Real-Time PCR for evaluation of gene expression and statistical analysis
- Gene and miRNAs array, open array- thermo scientific
- Droplet PCR
- Gene silencing: mechanical cell transfection (electroporation) and chemical (lipofectamine and jetPEI DNA transfection reagent); oligonucleotide sequences (siRNA) or expression vectors (plasmid).
- miRNA and gene primer design
- Cross link immunoprecipitation (CLIP) RNA-protein assay.

Proteomic techniques:

- Immunoblot and SDS page for the evaluation of normal proteins or modified by phosphorylation, ubiquitinizazione, nitration
- Immunoprecipitation using Sepharos, streptavidin beads for the purification of cell extracts
- Immunofluorescence staining for the identification of specific proteins present *in vitro* tissues or cells
- Zymography to determine enzymatic activity of specific proteins such as metalloproteinases in the angiogenic process
- Extraction and purification of nucleic acids, extraction of whole cell proteins or arising from fractionation (nucleus, cytoplasm, mitochondria, membranes animal tissue).

Markers evaluation of cellular oxidative stress:

- Glutathione (GSH), superoxide dismutase (SOD), total antioxidant potential (TAA) both in vitro and in vivo.
- Biomarkers of neuronal toxicity by evaluating plasma levels of specific proteins (β-actin) determined by ELISA and quantitative western blot
- Integrity assessment cell monolayer permeability through permeability to serum albumin by (Bromo cresol green test).

<u>In vitro experimental models</u> to study the ability of molecules of nutritional interest and its ability to modulate cellular responses induced different kind of stimuli, related to the onset of prepathological conditions, inflammation and oxidative stress:

- Damage induced by hyperglycaemia in primary endothelial cells (HUVEC): modulation of pathways involved in the cellular adaptive response (Nrf2 / EpRE pathway) by caffeic acid: evaluation of the cellular redox state (intracellular ROS); involvement of the transcription factor NF-kB in the damage induced by hyperglycaemia.
- Damage induced by elevating concentrations of free fatty acids (FFA) in primary endothelial cells (HUVEC): Modulation of Adaptive Response; Endothelial dysfunction (Gene expression of molecule accession, leukocyte MEMBERSHIP); Evaluation of cellular redox state (intracellular ROS; GSH and TAA levels); involvement of the transcription factor NF- kB.
- **Hyperoxia-induced damage** in primary human endothelial cells (HUVEC): activation of NF kB and HIF 1 and NRF 2 pathway, oxidative stress (SOD) and apoptosis (Caspase 3).
- **Angiogenesis activation** in primary human endothelial cells (HUVEC) induced by hyperoxia (metalloproteinases MMP 2, MMP 9).
- Alteration of the epithelial barrier permeability induced by TNF- α and LPS in epithelial cells of human differentiated adenocarcinoma (Caco 2), cultured on PET and Trans-well

- filters: involvement of the transcription factor NF-kB, modulation of Nrf2 expression of protein junction.
- **Genotoxic effect** of benzopyrene, present in fish extract, on human leukocytes PBMC (DNA laddering, Caspase-3).
- Transport study of molecules of nutritional interest, though a **blood-brain barrier** *in vitro* model. (co-culture bEnd.3 and C6 glioma).
- Assessment of damage caused by high concentrations of free fatty acids (FFA) in primary endothelial cells: **modulation of pathways involved insulin-mediated NO release** (PI3-K/AKT/ eNOS); Modulation of insulin receptor substrate (IRS-1), and of kinases among the most responsible for failure to respond to insulin (JNK, IKK and PKC-θ).
- **Biocompatibility study of nanoparticles** of polymeric and not polymeric nature on primary cell lines (HUVECs) and immortalized (3T3).
- **Permeability study** of nanoparticles through blood brain barrier (BBB) in vitro model.
- Evaluation of cell **monolayer integrity**, following exposure to nanoparticles after 24 and 48h, with albumin permeability assay.
- **Pharmacological synergism** *in vitro* between Taxol and curcumin on HT-29 and C6 cell line.
- Role of extracellular vesicle in cell to cell communication: trafficking and turnover in different physiological conditions.
- Isolation and characterization of apoptotic bodies from pancreatic β cells during Tnf-alpha-induced inflammation and apoptosis.
- **Dietary exosomes transport across the blood brain barrier:** b.end.3 cellular uptake, kinetic and time course, co-culture system b.end.3 and Astrocyte. Lucifer yellow permeability assay. Astrocytes migration assay.

<u>In vivo</u> experimental models (Certified by University of Nebraska-Lincoln Institutional Animal Care Program)

- **Fertility study in mice**: Breeding and maintenance of mice colony, preparation of AIN-93 modified diet, weaning litters, sacrifice, tissue collection and dissection, DEXA analysis, Metabolic cages and data analysis.
- **Spatial and learning memory in mice**: Animal training, Morris water maze, Barnes maze, startle response, Rotarod test. Brain collection and Hippocampus dissection, staining and processing tissue for sequencing Analysis.
- **Bioavailability and Biodistribution of Fluorophore-labeled Exosomes.** Intravenous and oral administration, iBox® Small Animal Imaging system analysis.
- Exosome and Cargo Tracking (ETC) mouse: Develop and test a tamoxifen-inducible ECT mouse model that allows investigators to exercise spatial and temporal control over the expression of endogenous exosomes in which the exosome marker CD63 is fused to near-infrared protein (iRFP). The transgene vector was designed to allow for sorting of tissue-specific, iRFP-labeled exosomes by streptavidin-coated magnetic beads for subsequent cargo analysis. Mice genotyping.
- Methamphetamine effect on ETC mouse: IP injection, mice training, place preference

chamber test.

<u>Human study</u>: Isolation of plasma and PBMCs from human blood. RT-qPCR, analysis after miRNAs and RNA isolation, small and seqRNA.

Ex vivo experimental models: Human BIOREACTOR as described by Canali et al., British Journal of Nutrition, 2007 doi: 10.1017/S0007114507657870.

Other Techniques

- Fluorimetric techniques: FACS,
- Thin layer chromatography (TLC)
- Size exclusion chromatography (SEC)
- Fluorescent Microscopy (EVOS)
- Nanoparticle Tracking Analysis (NTA)
- Seahorse XFe24 Analyzer: measure the oxygen consumption rate (OCR)
- Odyssey CLx imaging system
- Next Generation Sequencing (NGS) sample preparation.
- Exosome isolation and characterization
- Apoptotic body isolation and characterization

Memberships

- Italian Society of Pharmacology (SIF), senior member. 2019-present
- American Society for Nutrition (ASN), Early Career Nutrition interest group (ECN), postdoctoral/young professional member. 2017-present
- NuGO early career network (NuGO-ENC), member. 2017-present
- National Postdoctoral association (NTA), member. 2016-present
- Oxygen Club of California (OCC), member. 2015- present
- Young Pharmacist Association Messina (AGIFar), Boarding member. 2014-2017
- Italian Society of Pharmacology (SIF), young member. 2012-2016

Peer Reviewing

- Gene & Nutrition
- Functional Foods in Health and Disease (FFHD)

Workshop

- "An Introduction to MetaboAnalyst: a web-based tool for high throughput data analysis and interpretation", presented by Dr. Rosa Vázquez-Fresno, 2017
- "Using MetaCore: How to analyze omics data and better understand underlying biological mechanisms", presented by Dr. Olivia Alder, 2017
- Introduction to Statistical Analysis Software (SAS), 2017
- "How to Write a Winning CAREER Proposal", presented by Lucy Deckard. February 2, 2018 Est Union, University of Nebraska, Lincoln, NE.
- "Write Winning Grant Proposals" presented by John D. Robertson. Nebraska Innovation Campus Conference Center auditorium. March 16, 2018. University of Nebraska, Lincoln, NE.
- "2018 Nutrigenetics, Nutrigenomics, & Precision Nutrition Workshop", Speaker: Jose M. Ordovas, PhD, Senior Scientist. University of North Carolina at Chapel Hill, Nutrition Research Institute June 4-7, 2018 in Kannapolis, NC.

Languages

Italian (mother tongue), English (fluent) and Portuguese (basic)

October, 2019

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