BIOGRAPHICAL SKETCH

NAME: Paola Rizzo

POSITION TITLE: Associate Professor of Applied Biology, University of Ferrara

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	DATE	FIELD OF STUDY
University of Naples, Naples, Italy	Master of Sciences	1989	Molecular Biology
University of Ferrara, Ferrara, Italy	Ph.D.	2004	Endocrinology
University of Illinois at Chicago, Chicago, IL, USA	Post-doc	2005	Pharmaceutical Science

A. Personal Statement

From 1995 to 2009 I have been involved in cancer research, specifically focused on the role of viruses in human mesothelioma and then, cas an Assistant Professor at the Loyola University Cancer Center, Chicago, USA. on the role of the Notch pathway in estrogen-responsive breast cancer. Upon my return to Italy in 2009, I extended my studies on cross-talks between Notch and estrogens to the cells of cardiovascular and of the innate immune system. Particularly, I have been studying primarily the role of Notch in 1) the regulation of the endothelial function in the context of myocardial infarction, heart failure, atherosclerosis, and aortic stenosis and 2) cardiotoxicity of chemotherapeutic drugs. I have a demonstrated record of carrying out successful collaborative projects and mentoring undergraduates, <<<<<<<<<<<<<<graduate students, and post-doc.

B. Positions, Scientific Appointments, and Honors

- **University of Ferrara, Ferrara, Italy**
  Department of Translational Medicine
  Associate Professor Applied Biology **March 2018- Present**
  Assistant Professor Applied Biology *March 2015- February 2018*
  Department of Medical Sciences, UOL Cardiology
  Senior Scientific Consultant **Jan 2011-May 2014**
  Assistant Professor (not tenure) **May 2014- February 2015**

- **Loyola University Medical School, Chicago IL**
  Department of Pathology, Breast Cancer Program **2005 - 2009**
  Assistant Professor

- **University of Illinois, Chicago IL**
  Department of Biopharmaceutical Sciences, *Research Specialist* **2002 -2005**

- **Loyola University Medical School, Chicago IL**
  Department of Pathology, Thoracic Oncology Cancer Program **1996 - 2001**
  Research assistant III

- **University of Chicago, Chicago IL**
  Department of Pathology, *Research Project Professional* **1995 - 1996**

- **National Institutes of Health, Bethesda MD**
  Thoracic Oncology Section, Surgery Branch, *Adjunct Scientist* **1994 - 1995**

DNA Replication, Repair and Mutagenesis, NICHD, *Adjunct Scientist* **1993 - 1994**
Section on Protein Chemistry and Conformation, NIDDKD
Visiting Associate **1992 - 1993**
Visiting Fellow **1989 – 1992**

Honors: Recipient of Trotula De Ruggiero Award, Premio "Trotula De Ruggiero , prima donna medico della Scuola Medica Salernitana", dell'Ordine dei Medici Chirurghi e degli Odontoiatri della provincia di Salerno , La Nuova Scuola Medica Salernitana e Centro Studi Hippocratica Civitas 23-11-2012
Memberships: Italian Association of Biology and Genetics; Italian Association of Cell Biology& Differentiation

C. Contributions to Science

Studies on protein folding: During the years spent at the National Institutes of Digestive and Kidney Disease (NIDDK(NIH) I investigated the "core loop interaction hypothesis" in protein folding under the supervision of Dr. Hiroshi Taniuchi who contributed to demonstrate that the primary structure of ribonuclease determines its tridimensional structure. Our study was aimed to identify the driving force of protein folding by defining the details of the interactions between side chains of amino acids mainly involved in the stabilization of the protein structure. My contribution to the field has been the mapping of the amino acids critical for the antibody- antigen interaction (monoclonal antibodies to cytochrome c) through measurement of hydrogen-deuterium exchange at the interface between the antigen and the antigen-binding site of the antibody and site-directed mutagenesis in the variable region of the antibody.

a. **Rizzo P.**, Tinello C., Punturieri A., Taniuchi H. A Study of Hydrogen Exchange of Monoclonal Antibodies: Specificity of the Antigen-Binding Induced Conformational Stabilization. Biochimica et Biophysica Acta (1992) 1159, 169-178. PMID: 1327157

Role of SV40 in human cancer: The virus SV40 was a contaminant of poliovaccines produced in the sixties and immediately after vaccination it was discovered that SV40 was oncogenic in hamster. There were no evidence of SV40 playing the same role in human until the nineties when human mesothelioma was shown to contain SV40 sequences by our group. I worked on SV40 in human cancer from 1994 to 2000 and my contribution to the field were: 1) the detection of SV40 sequences in several human cancers, 2) the demonstration that viral proteins blocked pRB and p53 in mesothelioma biopsies and 3) the characterization by sequencing of the different strains of SV40 in tumor as and in poliovaccine samples.

a. Carbone M., **Rizzo P.**, Grimley P.M., Procopio A.Mew D.J.Y., Shridhar V., de Bartolomeis A., Esposito V., Giuliano M.T., Steimberg S.M., Levine A.S., Giordano A. and Pass H.I. Simian Virus-40 Large T antigen binds p53 in Human Mesotheliomas. Nature Medicine (1997) 3, 908-912. PMID: 9256284
b. **Rizzo P,** Di Resta I, Powers A, Ratner H, and Carbone M. Unique strains of SV40 in commercial poliovaccines from 1955 not readily identifiable with current testing for SV40 infection. Cancer Research (Advances in Brief) (1999) 59:6103-6105. PMID: 10626798

Estrogen-mediated regulation of Notch in breast cancer: We have demonstrated, for the first time, that tamoxifen inhibits the estrogen receptor but activates the oncogene Notch, thus, in order to shrink the tumor more effectively, anti-estrogens treatment should be combined to Notch inhibitors. Based on this work, a pilot Phase 1 clinical trial was conducted at Loyola University, Chicago, that showed no toxicity of a combination treatment of anti-estrogens and Notch 1 inhibitors in early-stage breast cancer patients. Moreover, molecular analysis of the breast biopsies showed that combinations of anti-estrogens and Notch inhibitors more efficiently inhibited proliferation and antiapoptotic genes compared to treatment with the single agent.

a. Weijzen S, **Rizzo P**, Braid M, Vaishnav R, Jonkheer SM, Zlobin A, Osborne BA, Gottipati S, Aster JC, Hahn WC, Rudolf M, Siziopikou K, Kast WM, Miele L Activation of Notch-1 signaling maintains the neoplastic phenotype in human Ras-transformed cells. Nat Med. 2002 Aug 19 . PMID: 12185362
b. **Rizzo P.,** Miao H., D'Souza G., Osipo C., Yun J., Whitehouse L., Zhao H., Mascarenhas J, Wyatt D, Antico G, Hao L, Yao K, Rajan P, Hicks C, Siziopikou K, Selvaggi S, Koerner F, Bashir A, Lendahl U, Chaturvedi U, Qin JZ, Tonetti D, Albain K, Nickoloff B and Miele L Cross-Talk Between Notch And The Estrogen Receptor In Breast Cancer Suggests New Therapeutic Approaches. Cancer Res. 2008 Jul 1;68(13):5226-35. PMID: 18593923

Molecular mechanisms underlying endothelial dysfunctions and atherosclerosis wth special emphasis on the role on the Notch pathway: Our studies *in vitro* showed that estrogens protect the endothelium from inflammation-induced apoptosis by activating the Notch signaling. Furthermore, in a mouse model of atherosclerosis, we found that laminar shear stress protects the endothelium by activating Notch. We also showed, for the first time, that the expression levels of Notch ligand DLL4 in atherosclerotic plaques is involved in the progression of peripheral artery disease.

a. Aquila G, Fortini C, Pannuti A, Delbue S, Pannella M, Morelli MB, Caliceti C, Castriota F, De Mattei M, Ongaro A, Pellati A, Ferrante P, Miele L, Tavazzi L, Ferrari R**, Rizzo P,** Cremonesi A. Distinct gene expression profiles associated with Notch ligands Delta-like 4 and Jagged1 in plaque material from peripheral artery disease patients. J Translational Medicine. 2017 May 4;15(1):98. doi: 10.1186/s12967-017-1199-3. PMID: 28472949
b. Fortini F, Vieceli Dalla Sega F, Caliceti C, Aquila G, Pannella M, Pannuti A, Miele L, Ferrari R**, Rizzo P**. Estrogen receptor β-dependent Notch1 activation protects vascular endothelium against tumor necrosis factor α (TNFα)-induced apoptosis. J Biol Chem. 2017 Nov 3; 292(44):18178-18191. doi: 10.1074/jbc.M117.790121. PMID: 28893903
c. Aquila G, Morelli MB, Vieceli Dalla Sega F, Fortini F, Nigro P, Caliceti C, Ferracin M, Negrini M, Pannuti A, Bonora M, Pinton P, Ferrari R, **Rizzo P.** Heart rate reduction with ivabradine in the early phase of atherosclerosis is protective in the endothelium of ApoE-deficient mice. J Physiol Pharmacol. 2018 Feb; 69(1):35-52. doi: 10.26402/jpp.2018.1.04. Epub 2018 May 8. PMID: 29769419

Molecular mechanisms underlying the ischemia-reperfusion damage in the heart: Ischemia-reperfusion damage amplifies apoptotic death of cardiomyocytes caused by the occlusion of a coronary artery. We identified two effective approaches to reduce the ischemia-reperfusion damage; 1) treatment with estrogens and a G protein- coupled estrogen receptors agonist and 2) treatment with small molecules that prevent the formation of mitochondrial pore.

a. Rocca C, Femminò S, Aquila G, Granieri MC, De Francesco EM, Pasqua T, Rigiracciolo DC Fortini F, Cerra MC, Maggiolini M, Pagliaro P, **Rizzo P**, Angelone T, Penna C. Notch1 Mediates Preconditioning Protection Induced by GPER in Normotensive and Hypertensive Female Rat Hearts Front. Physiol., 2018, 15. PMID: 29867564

Nutraceutics and reduction of the cardiovascular risk: Efforts are being made in the attempt to understand the molecular mechanisms by which nutraceuticals exert vascular protection. We characterized *in vitro* the antiatherogenic activity of berberine, of papaia and berries fermented with probiotics. In normal subjects with mild dyslipidemia, we found a protective effect on the endothelium following 6 months dietary consumption of a novel nutraceutical compound containing Red Yeast Rice.

a. Marracino L, Punzo A, Severi P, Nganwouo Tchoutang R, Vargas-De-la-Cruz C, Fortini F, Vieceli Dalla Sega F, Silla A, Porru E, Simoni P, Rosta V, Trentini A, Ouambo Talla AW, Hrelia S, Cervellati C, **Rizzo P,** Caliceti. Fermentation of *Vaccinium floribundum* Berries with *Lactiplantibacillus plantarum* Reduces Oxidative Stress in Endothelial Cells and Modulates Macrophages Function. Nutrients. 2022 April 8, PMID: 35458122

Complete List of Published work: https://scholar.google.com/citations?hl=en&user=aFc_5FwAAAAJ