BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.

NAME **Pozzi, Ambra**	POSITION TITLE **Professor** **Depts. of Medicine, Cancer Biology, and Molecular Physiology and Biophysics**
eRA COMMONS USER NAME: pozzia	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
University of Milan, Italy	Master	1990	Biochemistry
The Scripps Research Institute, La Jolla, CA, USA	PhD student	1993-1996	Cell Biology
University of Florence, Italy	PhD	1996	Experimental Pathology
The Scripps Research Institute, La Jolla, CA, USA	Post Doc.	1996-2000	Cell Biology

A. Personal Statement

Our laboratory has established two major lines of research.

To study the molecular mechanisms of kidney fibrosis, focusing on cell-matrix interactions and arachidonic acid-derived eicosanoids in kidney injury.

Cell-matrix interaction in kidney homeostasis: As progressive accumulation of extracellular matrix (ECM), mainly collagens, leads to fibrosis, our goal is to determine how interactions between ECM and cells via specific ECM receptors control ECM synthesis/remodeling in health and disease. Among the collagen receptors, we study integrins and discodin domain receptors (DDRs). We have identified integrin α1β1 as an anti-fibrotic integrin whose activation leads to downregulation of endogenous collagen synthesis and negatively modulates fibrosis. Recently, we have identified integrin α2β1 and DDR1 as a positive regulator of kidney fibrosis and provide evidence that mice lacking these receptors are protected from fibrosis following injury. Finally, we study how these matrix receptors crosstalk with pro-fibrotic growth factor receptors, including EGF and TGF-b receptors.

Arachidonic acid-derived eicosanoids in kidney homeostasis: The P450 arachidonic acid monooxygenases oxidize arachidonic acid to a) 19- or 20-HETE (w-hydroxylase or CYP4 isoforms), or b) 5,6-, 8,9-, 11,12-, or 14,15-EET (epoxygenase or CYP2 isoforms). Both EETs and HETEs have markedly divergent biological effects depending on the tissue of origin. For example, 20-HETE causes vasoconstriction and promotes hypertension, while EETs are vasodilators and lower blood pressure. As hypertension and kidney injury are frequently associated, a goal of our research is to determine the relative contribution of EETs vs. HETE to kidney homeostasis by using mice lacking and/or overexpressing key enzymes involved in the synthesis of EETs and/or HETEs. Using these in vivo tools we intend to test the hypothesis that EETs protects from, while 20-HETEs contributes to kidney injury.

To study the molecular mechanisms controlling endothelial cell functions in order to devise valid and better tolerated anti-angiogenic therapy.

In the past 10 years our laboratory has investigated the role of cell-matrix interaction in the control of endothelial cell functions in vivo and in vitro and provide the first evidence that the collagen binding integrin alpha1beta1 is pro-angiogenic and pro-tumorigenic and its inhibition and/or down-regulation is beneficial in the setting of tumor associated angiogenesis. More recently, we have started to investigate the role of arachidonic acid P450 epoxygenases in the control of endothelial cell function in vitro and tumorigenesis in vivo. We provide evidence that the products of P450 epoxygenases are pro-angiogenic in vivo and in vitro and maneuvers to prevent their synthesis plays a beneficial effect in slowing cancer progression in vivo.

B. Positions and Honors

Professional Positions

1996-2000: Res. Fellow. Department of Cell Biology, The Scripps Research Institute, LA Jolla, CA, USA.
2000-2007: Assistant Professor, Departments of Medicine and Cancer Biology, Division of Nephrology and Hypertension, Vanderbilt University.

2007-2012: Associate Professor, Departments of Medicine and Cancer Biology, Division of Nephrology and Hypertension, Vanderbilt University.
2008-2013: Research Scientist, VA Tennessee Valley Healthcare System, Nashville, TN.
2011-2012: Associate Professor, Department of Molecular Physiology and Biophysics, Vanderbilt University.
2012-present: Professor, Depts. of Medicine, Cancer Biology and Molecular Physiology and Biophysics, Vanderbilt University
2013-2019: Senior Research Career Scientist, VA Tennessee Valley Healthcare System, Nashville, TN.

Other Professional activities
2000-present: member, American Society of Nephrology
2004-present: member, American Society of Matrix Biology
2004-present: IACUC, voting member
2005: AACR: Grants sub-Committee for Clinical and Translational Cancer Research Grant Awards DOD: Pathobiology Panel #2 (PBY-2) for Breast Cancer Grant Merit Awards.
2006: NIH-NIDDK. Ad hoc, Pathobiology of Kidney Disease (PBKD): RO1 study sections NIH-NIDDK. Special Emphasis Panel for P01 grants
2007: DOD: Pathobiology Panel #2 (PBY-2) for Breast Cancer Grant Merit Awards
2007-2011: NIH-NIDDK. Permanent member, Pathobiology of Kidney Disease (PBKD): RO1 study section
2008: VA Career Development Awards: Ad hoc reviewer
2008-present: Associate Director of the p30-NIH Vanderbilt O'Brien Mouse Kidney Physiology and Disease Center
2008-present: member of the editorial board of *The Journal of Biological Chemistry*
2008-2011: VA: permanent member of the VA Merit Award study section (nephrology branch)
2009-present: Director of the Renal Research Conference, Nephrology Division, Vanderbilt University
2009-present: member of the editorial board of *The American Journal of Nephrology*
2010: DOD: Pathobiology Panel #2 (PBY-2) for Breast Cancer postdoctoral ideas
2010-2013: Member of the Council for the American Society of Matrix Biology
2011: DOD: Pathobiology Panel #2 (PBY-2) for Breast Cancer postdoctoral ideas
2011-present: member of the editorial board of *Current Angiogenesis*
2011-present: Executive Member of the Vanderbilt Vascular Biology Center (VVBC)
2012: DOD: Lung Cancer Research Program (LCRP) cellular and molecular biology Concepts
2011-2012: Member of the organizing committee for the 12th American Society of Matrix Biology meeting
2012-2013: Member of the organizing committee for the 2013 American Society of Nephrology meeting
2012-present: Member of the Vanderbilt Institutional Biomedical/Biological Sciences internal review committee for limited submission opportunity
2012-present: Member of the Vanderbilt Internal Shared Resources Oversight Committee (ISROC)
2013-2016: Treasurer of the American Society of Matrix Biology
2013-2015: member of the American Diabetes Association's Research Grant Review Committee (RGRC).
2013-present: Associate Editor of *Matrix Biology*
2013-present: Associate Director of the Vanderbilt Center of Matrix Biology
2014-present: Associate Director of the Vanderbilt Center for Kidney Disease

C. Selected peer-reviewed publications (in chronological order from more than 100 publications).

1. **Pozzi, A**. 2011. Diseased renal glomeruli are getting soft. Focus on "Biophysical properties of normal and diseased renal glomeruli". Am J Physiol Cell Physiol 300:C394-396.
2. **Pozzi, A.**, and Zent, R. 2011. TGF-beta sequestration by mesangial cell integrin alphavbeta8: A novel mechanism of glomerular endothelial cell regulation. Am J Pathol 178:485-489.
3. Borza, C.M., and **Pozzi, A.** 2012. The role of cell-extracellular matrix interactions in glomerular injury. Exp Cell Res 318:1001-1010.
4. Borza, C.M., Su, Y., Chen, X., Yu, L., Mont, S., Chetyrkin, S., Voziyan, P., Hudson, B.G., Billings, P.C., Jo, H., et al. 2012. Inhibition of Integrin alpha2beta1 Ameliorates Glomerular Injury. J Am Soc Nephrol Mar 22. [Epub ahead of print]
5. Gewin, L., Vadivelu, S., Neelisetty, S., Srichai, M.B., Paueksakon, P., **Pozzi, A.**, Harris, R.C., and Zent, R. 2012. Deleting the TGF-beta receptor attenuates acute proximal tubule injury. J Am Soc Nephrol 23:2001-2011.
6. Mathew, S., Chen, X., **Pozzi, A.**, and Zent, R. 2012. Integrins in renal development. Pediatr Nephrol 27:891-900.
7. **Pozzi, A.**, and Zent, R. 2012. Hold tight or you'll fall off: CD151 helps podocytes stick in high-pressure situations. J Clin Invest 122:13-16.

8. Shi, M., Pedchenko, V., Greer, B.H., Van Horn, W.D., Santoro, S.A., Sanders, C.R., Hudson, B.G., Eichman, B.F., Zent, R., and **Pozzi, A.** 2012. Enhancing integrin alpha1 inserted (I) domain affinity to ligand potentiates integrin alpha1beta1-mediated down-regulation of collagen synthesis. J Biol Chem 287:35139-35152.
9. Yu, L., Su, Y., Paueksakon, P., Cheng, H., Chen, X., Wang, H., Harris, R.C., Zent, R., and **Pozzi, A.** 2012. Integrin alpha1/Akita double-knockout mice on a Balb/c background develop advanced features of human diabetic nephropathy. Kidney Int.
10. Borza, C.M., and **Pozzi, A.** 2013. Discoidin domain receptors in disease. Matrix Biol.
11. **Pozzi, A**., and Zent, R. 2013. Integrins in Kidney Disease. J Am Soc Nephrol.
12. Elias, B.C., Mathew, S., Srichai, M.B., Palamuttam, R., Bulus, N., Mernaugh, G., Singh, A., Sanders, C.R., Harris, R.C., **Pozzi, A**., et al. 2014. The integrin beta 1 subunit regulates paracellular permeability of kidney proximal tubule cells. J Biol Chem.
13. Jablonski, C.L., Ferguson, S., **Pozzi, A.**, and Clark, A.L. 2014. Integrin alpha1beta1 participates in chondrocyte transduction of osmotic stress. Biochem Biophys Res Commun.
14. Parekh, R., Lorenzo, M.K., Shin, S.Y., **Pozzi, A.**, and Clark, A.L. 2014. Integrin alpha1beta1 differentially regulates cytokine-mediated responses in chondrocytes. Osteoarthritis Cartilage.
15. Skrypnyk, N., Chen, X., Hu, W., Su, Y., Mont, S., Yang, S., Gangadhariah, M., Wei, S., Falck, J.R., Jat, J.L., et al. 2014. PPARalpha Activation Can Help Prevent and Treat Non-Small Cell Lung Cancer. Cancer Res 74:621-631.

D. Research Support

Ongoing research projects

Veteran Administration Merit Award (**Pozzi, A)** 12/01/08 - 11/30/17
Role of Collagen Binding Receptors in Glomerulosclerosis
The goal of this grant is to determine how integrins, receptors for extracellular matrix components, and growth factors receptors cooperate in controlling collagen homeostasis in the course of diabetic nephropathy.
Role: PI

1R01CA162433-01A1 (**Pozzi, A**) 08/01/12-07/31/17
NIH-NCI
"The P450 Epoxygenases as Pro-Oncogenic Enzymes"
*T*he goal of this proposal is to determine how epoxygenases control lung cancer progression
Role: PI

1R01DK095761-01A1 (**Pozzi, A**) 04/01/13-03/31/17
NIH-NIDDK
"Integrin/TGF-beta Axis in Tubulointerstitial Fibrosis"
The goal of this proposal is to determine the role of TGF-beta activation in renal injury.
Role: PI

NIH/NIDDK 5P01 DK038226-24 (Brown, N) 09/05/09-06/30/14
Role of Eicosanoids in Renal Function
Project 2 (Pozzi, A): P450 monooxygenases and the regulation of renal function
The long term goal of this project is to provide a molecular understanding of role(s) of P450 eicosanoids in renal physiological, their mechanism and site of action, and relevance to human disease.
Role: PI of Project 2

R01 NIDDK DK069221 (Zent) 12/01/04-11/30/15
The role Laminins in renal development
This project looks at the role of MT-MMPs in renal development.
Role: Co-Investigator

R01 NIDDK DK075594 (Zent) 02/01/08-01/31/17
Beta1 integrin and renal tubulogenesis
This project studies the mechanisms whereby □1 integrins regulate branching morphogenesis of the kidney.
Role: Co-Investigator

5R01 NCI CA122620-03 (Zhang) 05/01/09-04/30/14

Type II 11B-Hydroxysteroid Dehydrogenase and Colorectal Tumorigenesis

In the current proposal, we will test whether inhibition of type 2 11ss-hydroxysteroid dehydrogenase activity may provide a new strategy for CRC chemoprevention and chemotherapy with minimal side effects.

Role: Co-investigator

5R01 NIH/NIDDK DK054902-12 (Wasserman) 07/01/10-05/31/15

Integrated Control of Muscle Glucose Uptake in Vivo

The goal of this study is to determine: (i) How selective phosphodiesterae-5A inhibition prevents and reverses high fat (HF) diet-induced muscle insulin resistance; (ii) how mitochondrial-targeted catalase prevents insulin resistance in HF-fed mice; (iii) how regular physical exercise, protects against HF-fed insulin resistance; and (iv) the relative importance of endothelial dysfunction and extracellular matrix modifications to the extramyocellular defects associated with insulin resistance and interventions that enhance insulin action.

Role: Co-investigator