BIOGRAPHICAL SKETCH

NAME: D'Amore, Patricia

eRA COMMONS USER NAME (agency login):

POSITION TITLE: Professor of Ophthalmology & Pathology

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date YYYY	FIELD OF STUDY
Regis College, Weston, MA	BA	1973	Biology
Boston University, Boston, MA	PHD	1977	Cell Biology
John Hopkins Univ. Sch. Med., Baltimore, MD	Postdoctoral Fellow	1987	Ophthal & Physiol Chem
Northeastern University, Boston, MA	MBA	1987	Finance

A. PERSONAL STATEMENT

For over 30 years, I have been investigating angiogenesis. The work conducted in my laboratory and in collaboration with investigators at Massachusetts Eye and Ear Infirmary, formed the basis for the current use of anti-angiogenic therapies for diabetic retinopathy. Throughout my career, I have also been committed to the training of students and fellows and have mentored over 60 trainees in my laboratory. Seven of these trainees are now full Professors at universities, which include: University of North Carolina, Baylor, University College London, Washington University, and the University of Massachusetts. Eight of the trainees are Senior Scientists at companies or institutions such as Genzyme and Invitrogen. I have been the Chair of the Training Committee at the Schepens Eye Research Institute (SERI) for ten years and I am a recipient of the A. Clifford Barger Excellence in Mentoring Award, the Everett Mendelsohn Excellence in Mentoring Award from Harvard Medical School, the American Medical Association Women Physicians Sector Mentorship Award, and the Williiam Silen Lifetime Achievement Award in Mentoring.

B. POSITIONS AND HONORS

Positions and Employment

1981 - present Research Associate, Surgery, The Children's Hospital, Boston, MA
1982 - 1988 Assistant Professor, Pathology, Harvard Medical School (HMS), Boston, MA
1983 - present Faculty of the Cell & Developmental Biology, Biological & Biomedical Sciences Program, HMS, Boston, MA
1989 - 1998 Associate Professor of Ophthalmology (Pathology), HMS, MA
1991 - 1994 Member, Cell Biology and Physiology Study Section II
1998 - 2013 Professor of Ophthalmology (Pathology), HMS, Boston, MA
1998 - present Senior Scientist, Schepens Eye Research Institute (SERI), Boston, MA
1998 - 2003 Professorship, Jules and Doris Stein Research to Prevent Blindness
2002 - present Ankeny Scholar of Retinal Molecular Biology, SERI, Boston, MA
2002 - 2009 Associate Director of Research, SERI, Boston, MA
2009 - 2012 Co-Director of Research, SERI, Boston, MA
2009 - present Vice Chair of Basic and Translational Research, Depart. of Ophthalmology, HMS, Boston, MA
2012 - present Charles L. Schepens Professor of Ophthalmology, SERI, Boston, MA
2012 - present Director of Research, SERI, Mass Eye and Ear (MEE), Boston, MA
2013 - present Professor of Pathology, HMS, Boston, MA
2014 - present Director, Howe Laboratory, MEE, Boston, MA
2014 - present Associate Chief of Basic and Translational Research, MEE, Boston, MA

Other Experience and Professional Memberships

2003 - 2005 Reviewer, Cellular Aspects of Diabetes and Obesity Study Section (CAD0), NIH

2005	Reviewer, Drug Development Group Review Panel, NCI, NIH
2006	Ad hoc member, Program Project Review Committee, NHLB Institute
2006 - present	Co-Editor-in-Chief, Microvascular Research
2006 - 2008	Member, Study Section, Susan G. Komen Breast Cancer Foundation Grant Review
2007	Member, American Association for Cancer Research
2008	Member, Special Emphasis Panel, NIH Cardiovascular Sciences Review Group
2009	Review, Massachusetts Life Sciences Center, New Investigator Matching Grant Program
2009	Member, Shared Equipment (S10) Instrumentation Study Section, ZRG1CBQ31, NIH
2009 - 2013	Member, Biology and Diseases of the Posterior Eye Study Section, NIH, CSR
2013 - present	Grant Review & Awards Committee, Global Ophthalmology Awards Program
2015 - present	Member, Vision Academy, Bayer Healthcare
2016 - present	Member, Scientific Review Committee, Fight for Sight

Honors

1979	Myers Honor Award for Research in Ophthalmology, Baltimore, MD
1986	American Heart Association Established Investigatorship
1993	Cogan Award, Association for Research in Vision and Ophthalmology
1994	Alcon Research Institute Award
2004 - present	Member, The Academy at Harvard Medical School
2005	Excellence Award, Schepens Eye Research Institute
2006	Senior Scientific Investigator Award, Research to Prevent Blindness
2006	First Annual David Shepro Lecture, Boston, University
2007	A. Clifford Barger Excellence in Mentoring Award, Harvard Medical School
2009	Gold Fellow, Association for Research in Vision and Ophthalmology
2010	5th Annual Jeffrey M. Isner, M.D. Endowed Memorial Lectureship
2010	Distinguished Lecturer in Vision Science, State University of New York, Buffalo, NY
2012	Rous-Whipple Award, American Society of Investigative Pathology
2013	Everett Mendelsohn Mentoring Award, Harvard Medical School
2013	American Medical Association Women Physicians Sector Mentorship Award
2014	Endre A. Balazs Prize, International Society for Eye Research
2014	Laureate, Antonio Champalimaud Award
2015	Proctor Medal, Association for Research & Vision Ophthalmology
2016	William Silen Lifeteime Achievement in Mentoring Award, Harvard Medical School

C. Contribution to Science

1. Pericyte-endothelial cell interactions

   Capillaries are composed of endothelial cells (EC) and pericytes. Little was known about the nature of the interactions, if any, between these two cells; however, loss of pericytes during background retinopathy pointed to a role in the regulation of vessel integrity and stabilization. We demonstrated that EC recruit pericytes (or their precursors) via the release of PDGFB, which also stimulates the proliferation of pericytes/smooth muscle. We showed that the association between EC and pericytes leads to the inhibition of endothelial proliferation, to the induction of pericyte differentiation, and to the production of VEGF by pericytes, all processes that are mediated by the contact-dependent activation of TGFß1. Our work paved the way for the understanding that pericyte association with capillary endothelium mediates vessel stabilization and maturation. In addition, it forms the basis for the current use of anti-PDGFB (Fovista®) in combination with anti-VEGF (Avastin® or Lucentis®) for the treatment of wet age-related macular degeneration. This work was conducted in my laboratory under my direction.

   a. Orlidge A, D'Amore PA. Inhibition of capillary endothelial cell growth by pericytes and smooth muscle cells. J Cell Biol. 1987 Sep;105(3):1455-62. PubMed PMID: 3654761; PubMed Central PMCID: PMC2114828.

b. Antonelli-Orlidge A, Saunders KB, Smith SR, D'Amore PA. An activated form of transforming growth factor beta is produced by cocultures of endothelial cells and pericytes. Proc Natl Acad Sci U S A. 1989 Jun;86(12):4544-8. PubMed PMID: 2734305; PubMed Central PMCID: PMC287307.

c. Hirschi KK, Rohovsky SA, D'Amore PA. PDGF, TGF-beta, and heterotypic cell-cell interactions mediate endothelial cell-induced recruitment of 10T1/2 cells and their differentiation to a smooth muscle fate. J Cell Biol. 1998 May 4;141(3):805-14. PubMed PMID: 9566978; PubMed Central PMCID: PMC2132737.

d. Darland DC, Massingham LJ, Smith SR, Piek E, Saint-Geniez M, et al. Pericyte production of cell-associated VEGF is differentiation-dependent and is associated with endothelial survival. Dev Biol. 2003 Dec 1;264(1):275-88. PubMed PMID: 14623248.

2. Role of VEGF in ischemic retinal neovascularization

Clinical observations have suggested that ischemic retinal tissue was a source of an angiogenic activity, that more 65 years ago was referred to as “factor x.” Working with my clinical colleagues, Drs. Anthony Adamis and Joan Miller, my laboratory demonstrated that this factor was VEGF. Using non-human primates we showed that rendering the retina ischemic led to neovascularization that was associated with increases in VEGF mRNA and protein, and that neutralization of VEGF blocked the new vessel growth. This work formed a major portion of the basic work that led to the use of anti-VEGF therapies for the treatment of age-related macular degeneration and diabetic macular edema, treatments that have revolutionized their management.

a. Miller JW, Adamis AP, Shima DT, D'Amore PA, Moulton RS, et al. Vascular endothelial growth factor/vascular permeability factor is temporally and spatially correlated with ocular angiogenesis in a primate model. Am J Pathol. 1994 Sep;145(3):574-84. PubMed PMID: 7521577; PubMed Central PMCID: PMC1890317.

b. Shima DT, Adamis AP, Ferrara N, Yeo KT, Yeo TK, et al. Hypoxic induction of endothelial cell growth factors in retinal cells: identification and characterization of vascular endothelial growth factor (VEGF) as the mitogen. Mol Med. 1995 Jan;1(2):182-93. PubMed PMID: 8529097; PubMed Central PMCID: PMC2229943.

c. Shima DT, Deutsch U, D'Amore PA. Hypoxic induction of vascular endothelial growth factor (VEGF) in human epithelial cells is mediated by increases in mRNA stability. FEBS Lett. 1995 Aug 21;370(3):203-8. PubMed PMID: 7656977.

d. Adamis AP, Shima DT, Tolentino MJ, Gragoudas ES, Ferrara N, et al. Inhibition of vascular endothelial growth factor prevents retinal ischemia-associated iris neovascularization in a nonhuman primate. Arch Ophthalmol. 1996 Jan;114(1):66-71. PubMed PMID: 8540853.

3. Role of VEGF and VEGF isoforms in the adult

VEGF proteins are encoded by a single gene that is alternatively spliced to generate multiple isoforms (three in mice). Whether the isoforms served different functions was unknown. In addition, early studies demonstrated a critical role for VEGF in vascular development and pathology, but there was little consideration of a possible role for VEGF in the adult. Our observation that virtually all adult tissues expressed VEGF mRNA, in the absence of active angiogenesis, led us to hypothesize a physiologic role for VEGF. Using in vivo and in vitro models we showed that VEGF was produced by a subset of cells in all tissues examined. In addition, we noted that the profile of VEGF isoforms varied widely among adult tissues. We demonstrated that neutralization of VEGF or that lack of specific VEGF isoforms in the normal adult led to tissue dysfunction and degeneration. Finally, we reported that VEGF acts as a survival factor not only for vascular endothelial but also for a wide variety of non-vascular cells.

a. Stalmans I, Ng YS, Rohan R, Fruttiger M, Bouché A, et al. Arteriolar and venular patterning in retinas of mice selectively expressing VEGF isoforms. J Clin Invest. 2002 Feb;109(3):327-36. PubMed PMID: 11827992; PubMed Central PMCID: PMC150858.

b. Saint-Geniez M, Maharaj AS, Walshe TE, Tucker BA, Sekiyama E, et al. Endogenous VEGF is required for visual function: evidence for a survival role on Müller cells and photoreceptors. PLoS One. 2008;3(11):e3554. PubMed PMID: 18978936; PubMed Central PMCID: PMC2571983.

c. Maharaj AS, Walshe TE, Saint-Geniez M, Venkatesha S, Maldonado AE, et al. VEGF and TGF-beta are required for the maintenance of the choroid plexus and ependyma. J Exp Med. 2008 Feb 18;205(2):491-501. PubMed PMID: 18268040; PubMed Central PMCID: PMC2271023.

d. dela Paz NG, Walshe TE, Leach LL, Saint-Geniez M, D'Amore PA. Role of shear-stress-induced VEGF expression in endothelial cell survival. J Cell Sci. 2012 Feb 15;125(Pt 4):831-43. PubMed PMID: 22399811; PubMed Central PMCID: PMC3311927.

4. Role and regulation of inflammation in ocular pathogenesis

It is widely believed that chronic low-level inflammation (often termed para-inflammation) is a major contributor to most degenerative pathologies such as AMD and diabetic retinopathy. In spite of this, little is known about the mechanisms that underlie the pathogenesis. We have been studying the role of inflammation at the level of both the vasculature and the retinal pigment epithelium. The vascular is the site of leukocyte extravasation into tissue, and as such, represents a rate-limiting step in the process. We have shown that two factor, VEGF and TGFß, which are both involved in microvascular stabilization participate in maintaining a non-inflammatory endothelium. We have also demonstrated a role for endomucin, a mucin apically expressed by venous and capillary but not by arterial endothelium in preventing leukocyte adhesion under quiescent conditions. We are also examining the role of innate immunity in the pathogenesis of geographic atrophy and have reported NLRP3 activation in RPE of donor eye with AMD, but not in age-matched controls, and have demonstrated NLPR3 activation in human RPE in vitro.

a. Walshe TE, Dole VS, Maharaj AS, Patten IS, Wagner DD, D'Amore PA. Inhibition of VEGF or TGF-ß signaling activates endothelium and increases leukocyte rolling. Arterioscler Thromb Vasc Biol, 2009 Aug; 29:1185-1192. Epub 2009 May 21. PMC2775449.

b. Tseng WA, Thein T, Kinnunen K, Lashkari K, Gregory MS, *D'Amore PA, *Ksander BR (co-corresponding authors). NLRP3 inflammasome activation in retinal pigment epithelial cells by lysosomal destabilization: implications for age-related macular degeneration. Invest Ophthalmol Vis Sci, 2013 Jan 7; 54:110-120. PMC3544415.

c. Zahr A, Alcaide P, Yang J, Jones A, Gregory M, dela Paz NG, Patel-Hett S, Nevers T. Luscinskas FW, Saint-Geniez M, Ksander B, * D'Amore PA, * Argueso P (co-corresponding authors). Endomucin prevents leukocyte–endothelial cell adhesion and has a critical role under resting and inflammatory conditions. Nat Commun 2016. PMC4740757.

Complete List of Published Work in My Bibliography:
http://www.ncbi.nlm.nih.gov/myncbi/patricia.d'amore.1/bibliography/41153600/public/?sort=date&direction=ascending

D. RESEARCH SUPPORT

Ongoing Research Support

5R01EY012509-15 (Lei, PI) 02/01/2014-01/31/2018
NIH/NEI
PDGF and PVR
The major goals of this project are to investigate the mechanism by which growth factors drive biochemical and cellular responses intrinsic to proliferative vitreoretinopathy (PVR), and apply this information to the development of new therapeutic options to prevent PVR.
Role: Co-investigator

P30 EY03790-33 (Argueso, PI) 08/01/97-07/31/17
NIH/NEI
Core Grant for Vision Research
Role: Director, Animal Core
The major goal of this project is to provide support for four (4) core modules available for all investigators at SERI. The four modules are Morphology, Animal Resources, Lab Computer Applications and Flow Cytometry.
Role: Co-investigator

RO1 EY005318-26 (D'Amore, PI) 04/01/11-03/31/17
NIH/NEI no cost extension
Cell-cell Interactions in the Retinal Vasculature
The major goal of this project is to understand the mechanisms that regulate vessel assembly and stability.

1R13 EY027181-01 (D'Amore, PI) 08/01/2016-07/31/2017
NIH/NEI
Fourth Biennial Symposium on Age Related Macular Degeneration
The objective of this multidisciplinary conference is to stimulate discussions and collaborations aimed at elucidating the mechanisms that underlie the development of AMD and, thus, to identify means to treat, cure, and ultimately prevent AMD.

Completed Research Support

5T32EY007145-17 (D'Amore, PI) 02/01/1997-06/30/16
NIH/NEI
Molecular Bases of the Eye Disease
The major goal of this project is to train the next generation of scientists who will address the problems of eye disease by identifying new means of diagnosis, prevention and treatment.

1R13EY024813 (D'Amore, PI) 08/01/2014-07/31/2015
NIH/NEI
Third Biennial Symposium on Age Related Macular Degeneration
The objective of this multidisciplinary conference is to stimulate discussions and collaborations aimed at elucidating the mechanisms that underlie the development of AMD and, thus, to identify means to treat, cure, and ultimately prevent AMD.

7-12-IN-11 (D'Amore, PI) 07/01/2012-06/30/2014
American Diabetes Association
Notch-mediated cell-cell interactions in the pathophysiology of diabetic retinopathy
The major goal of this study is to test the hypothesis that Notch signaling between retinal endothelial cells (EC) and retinal pericytes (RP) is essential to the development of diabetic retinopathy.

R01EY015435 (D'Amore, PI) 05/01/2008-11/30/2014
NEI/NIH
Role of RPE-derived VEGF in Choroid Development & Stability
The goal of this study is to investigate the role of VEGF in choroidal vascular development and stability.