BIOGRAPHICAL SKETCH

NAME: Ng, Yin Shan Eric

eRA COMMONS USER NAME (agency login):

POSITION TITLE: Assistant Professor of Ophthalmology

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date YYYY	FIELD OF STUDY
Boston University, Boston, MA	BA	1991	Biology
Boston University, Boston, MA	MA	1992	Biotechnology
Harvard Medical School, Boston, MA	PHD	2000	Cell & Developmental Biology
D'Amore Lab, Schepens Eye Research Institute (SERI) of Mass. Eye and Ear, Boston, MA	Postdoctoral Fellow	2003	Vascular Biology & Molecular Genetics

A. PERSONAL STATEMENT

For more than fifteen years, my research has focused on the molecular regulation of neovascularization both in normal development and in pathological conditions. In particular, I have been studying the diverse functional roles of the angiogenic growth factor, VEGF, in normal vasculature as well as its translational research in pathological angiogenesis in the eye[1]. My research formed the foundation for my drug development efforts, and I have been directly involved in the development of novel vascular therapeutics in the biotech industry for nearly seven years. Through my experience in applying basic scientific research approaches in a translational research environment, I have applied new insights of VEGF biology into the creation of therapeutic approaches for treating pathological ocular neovascularization[2]. More recently, I was involved in therapeutic targets discovery and drug development research for various neuro-vascular pathologies affecting the eye[3] through a research collaboration with an industrial partner GSK, while building my research as an Lecturer/Assistant Professor at UCL in London, UK. My long-term goal is to develop a program of biomedical research that will help refine our current use of anti-VEGF therapeutics[4] and define new targets for developing the next generation of pharmacotherapies. My current research projects include investigating the neuroprotective function of VEGF-A in ischemia- and inflammation-driven retinopathies and in glaucoma; identifying novel targets for anti-angiogenesis and anti-inflammation in neovascular AMD, diabetic retinopathy and retinopathy of prematurity; and, characterizing a novel anti-inflammatory strategy for ocular disease. Because I have worked in both pharma/biotech and academic environment as a research scientist in the last 13 years, I have been benefited tremendously and thus recognize the importance and the values of building translational research on the foundation of basic research. And I strongly believe that the Schepens Eye Research Institute provides a uniquely effective environment for me to be successful in pursuing my research goal.

1. Carmeliet, P., **Ng, Y.-S.**, Nuyens, D., Theilmeter, G., Brusselmans, K., Cornelissen, I., Ehler, E., Kakkar, V., Stalmans, I., Mattot, V., Perriard, J.-C., Dewerchin, M., Flameng, W., Nagy, A., Lupu, F., Moons, L., Collen, D., D'Amore, P., and Shima, D. (1999). Impaired myocardial angiogenesis and ischemic cardiomyopathy in mice lacking the vascular endothelial growth factor isoforms VEGF164 and VEGF188. Nature Medicine 5, 495-502. PMID: 10229225

2. Jucker, F, Lee, J-H, Canny, M, DeErkenez, A, Krilleke, D, **Ng, Y-S**, Shima, DT, Pardi, A. A therapeutic aptamer inhibits angiogenesis by specifically targeting the heparin binding domain of VEGF165. Proc Natl Acad Sci USA, 2005, 102(52):18902-7. PMID: 16357200

3. Norihiro Nagai, Peter Lundh von Leithner, Kanako Izumi-Nagai, Brett Hosking, Bo Chang, Ron Hurd, Peter Adamson, Anthony P. Adamis, Richard H. Foxton, **Yin Shan Ng**, and David T. Shima. Spontaneous CNV in a novel mutant mouse is associated with early VEGF-A driven angiogenesis and late stage focal edema, neural cell loss and dysfunction. Invest Ophthalmol Vis Sci, 2014, 55:3709-19. PMCID: PMC4059080.

4. R.H. Foxton, A. Finkelstein, S. Vijay, A. Dahlmann-Noor, P.T. Khaw, J.E. Morgan, D.T. Shima and **YS Ng#** (corresponding author). VEGF-A is necessary and sufficient for retinal neuroprotection in models of experimental glaucoma. Am J Pathol, 2013, 182(4):1379-90. PMID: 23416159

B. POSITIONS AND HONORS

Positions and Employment

1994 - 2000	Graduate Student, D'Amore Lab, Harvard Medical School (HMS), Boston, MA
2000 - 2003	Research Fellow in Ophthalmology, HMS, Boston, MA
2003 - 2004	Senior Research Scientist, (OSI) Eyetech, Lexington, MA
2004 - 2006	Senior Research Scientist, Group Leader, (OSI) Eyetech, Lexington, MA
2006 - 2006	Associate Director, Drug Discovery, (OSI) Eyetech , Lexington, MA
2006 - 2009	Associate Director and Director, Research & Development, Pervasis Therapeutics, Cambridge, MA
2009 - 2013	Lecturer/Assistant Professor, ORBIT, UCL Institute of Ophthalmology, London
2013 -	Assistant Scientist, SERI/Mass Eye and Ear (MEE), Boston, MA
2013 -	Assistant Professor, HMS, Boston, MA

Other Experience and Professional Memberships

1999 -	Reviewer, American Journal of Pathology and Microvascular Research
2003 -	Member, Association for Research in Vision and Ophthalmology
2004	Participant, , The Laboratory Mouse in Vision Research Workshop, the Jackson Laboratory, ME
2005	Participant, Management and Leadership Skills for Supervisors and Managers, National Seminars Group, Rockhurst University Continuing Education Center, Inc.
2005	Participant, Bioinformatics for Biologists Mini-courses, Whitehead Institute for Biomedical Research
2008	Participant, Basic Training Course in Drug Development, Pharmaceutical Education & Research Institute, Inc.
2009 -	Reviewer, PLoS One Journal, Investigative Ophthalmology & Vision Science, and Journal of Cell Transplantation
2013 -	Member, North American Vascular Biology Organization
2014 -	Reviewer, Cell Death & Disease, Biomaterials, Journal of Neuroinflammation

Honors

1991	Selected Member , Golden Key National Honor Society
1991	Elected Member, Phi Betta Kappa Society
1991	Graduation with Distinction, summa cum laude, Boston University
1993 - 1994	Cancer Research Award Fellowship, Cutaneous Biology Research Center, MGH
1995 - 1996	John Stauffer Fellow, HMS
1998	Student Prize, Xth International Vascular Biology Meeting
2003	Business and Science Award, Eyetech Pharmaceuticals
2004	Inventor Achievement Award, Eyetech Pharmaceuticals

C. Contribution to Science

1. The biology of different VEGF isoforms in development and in disease.

   By alternative mRNA splicing, the VEGF gene gives rise to multiple protein isoforms with distinct biochemistry properties in terms of binding to heparan sulfate proteoglycans. In collaboration with Dr. Patricia D'Amore, Dr. David Shima and Dr. Peter Carmeliet, we examined the potential functional differences between the various VEGF forms. Using a gene-targeting approach, three different VEGF isoform-specific lines of mice were created, and we demonstrated that the dissimilar VEGF isoforms have differential functions during vascular development. More interestingly, I showed that the heparin-binding

VEGF165 isoform is associated more with pathologies, and contributed to the concept that targeting the pathological heparin-binding isoform of VEGF could result in better therapy.

a. Carmeliet P**, Ng YS**, Nuyens D, Theilmeier G, Brusselmans K, Cornelissen I, Ehler E, Kakkar VV, Stalmans I, Mattot V, Perriard JC, Dewerchin M, Flameng W, Nagy A, Lupu F, Moons L, Collen D, D'Amore PA, Shima DT. Impaired myocardial angiogenesis and ischemic cardiomyopathy in mice lacking the vascular endothelial growth factor isoforms VEGF164 and VEGF188. Nat Med. 1999 May;5(5):495-502. PubMed PMID: 10229225.

b. **Ng YS**, Rohan R, Sunday ME, Demello DE, D'Amore PA. Differential expression of VEGF isoforms in mouse during development and in the adult. Dev Dyn. 2001 Feb;220(2):112-21. PubMed PMID: 11169844.

c. Stalmans, I, **Ng, YS**, Rohan, R, Fruttiger, M, Bouché, A, Fujisawa, H, Hermans, B, Shani, M, Jansen, S, Hicklin, D, Anderson, D, Moons, L, Dewerchin, M, Collen, D, Carmeliet, P, and D'Amore, PA. Deficiency of the VEGF164- but not of the VEGF188- or VEGF120-isoforms impairs retinal arterial development in mice. 2002, *J Clin Invest*., 2002, 109:327-336.

d. Ishida S, Usui T, Yamashiro K, Kaji Y, Amano S, Ogura Y, Hida T, Oguchi Y, Ambati J, Miller JW, Gragoudas ES, **Ng YS**, D'Amore PA, Shima DT, Adamis AP. VEGF164-mediated inflammation is required for pathological, but not physiological, ischemia-induced retinal neovascularization. J Exp Med. 2003 Aug 4;198(3):483-9. PubMed PMID: 12900522; PubMed Central PMCID: PMC2194095.

2. The first anti-VEGF therapy for neovascular AMD and developmental study for the first PDGFBB-specific aptamer for ocular neovascular pathologies.

When the critical role of VEGF in the pathogenesis of neovascular AMD was established around 1996, VEGF-targeting therapeutics had not been developed. In 2003, while working at Eyetech Pharmaceuticals, Inc., I was involved in pre-clinical and IND-enabling research of Macugen®, which identified the drug's mechanism of action as VEGF165-specific antagonism. My findings directly contributed to the NDA filing of Macugen®. While at Eyetech, I was also involved in the pre-clinical development and IND-enabling characterization study of the first anti-PDGFBB aptamer, which is currently under clinical investigation with the trade name Fovista®.

a. Lee JH, Canny MD, De Erkenez A, Krilleke D, **Ng YS**, Shima DT, Pardi A, Jucker F. A therapeutic aptamer inhibits angiogenesis by specifically targeting the heparin binding domain of VEGF165. Proc Natl Acad Sci U S A. 2005 Dec 27;102(52):18902-7. PubMed PMID: 16357200; PubMed Central PMCID: PMC1323181.

b. Patent US20050260651 A1 - Sterically Enhanced Antagonist Aptamer Conjugates (Shrubbery) Anthony P. Adamis, Pericles Calias, David Shima, Gregory S. Robinson, **Yin-Shan Ng**.

c. Patent EP1776479 A2 - Sequencing of Modified Nucleic Acid Molecules (Enzymatic Sequencing of a Pegylated Modified RNA Aptamer) **Yin-Shan Ng**, David Shima, Pericles Calias, Francine Wincott, Gregory S. Robinson, Corinna Krinos.

d. Mitchell TS, Bradley J, Robinson GS, Shima DT, **Ng YS**. RGS5 expression is a quantitative measure of pericyte coverage of blood vessels. Angiogenesis. 2008;11(2):141-51. PubMed PMID: 18038251.

3. A critical neuroprotective function of endogenous and exogenous VEGF for the retina.

When VEGF was first discovered, it was thought to be a vascular endothelial cell-specific growth factor. Since then, strong evidence has shown that additional cell types, especially neuronal cells, express the receptors for and response to VEGF. We were interested in the functional role of VEGF in the adult retina, and in particular, during hypoxia pre-conditioning (HP) since VEGF expression is highly upregulated. We determined that VEGF is neuroprotective for the retina and is part of the adaptive response during HP. Furthermore, endogenous VEGF in the normal retina plays an important role in maintaining neuronal health, and chronic VEGF antagonism resulted in retinal ganglion cell death and retinal degeneration. Recently, we further illustrated the critical neuroprotective function of endogenous and exogenous VEGF in experimental models of diabetic retinopathy and ocular hypertensive glaucoma. Our findings have important implications for the clinical usage of anti-VEGF therapies for neovascular pathologies in the eye, as well as the validation of using VEGF as a potential therapeutic agent for retinal neuroprotection.

a. Nishijima K, **Ng YS**, Zhong L, Bradley J, Schubert W, Jo N, Akita J, Samuelsson SJ, Robinson GS, Adamis AP, Shima DT. Vascular endothelial growth factor-A is a survival factor for retinal neurons and

a critical neuroprotectant during the adaptive response to ischemic injury. Am J Pathol. 2007 Jul;171(1):53-67. PubMed PMID: 17591953; PubMed Central PMCID: PMC1941589.

b. Foxton RH, Finkelstein A, Vijay S, Dahlmann-Noor A, Khaw PT, Morgan JE, Shima DT, **Ng YS**. VEGF-A is necessary and sufficient for retinal neuroprotection in models of experimental glaucoma. Am J Pathol. 2013 Apr;182(4):1379-90. PubMed PMID: 23416159; PubMed Central PMCID: PMC3608027.

c. XX Biennial Meeting of the International Society for Eye Research 2012, Invited Speaker: "*Probing the neuroprotective function of VEGF-A for retinal neurons.*"

d. 2010-2012, Medical Research Council (UK) Project Grant: VEGF Mediated Retinal Neuroprotection: mechanistic studies and implications for the clinical use of VEGF antagonists.

4. Novel animal model and discovery of new therapeutic targets for wet AMD.

One of the major obstacles for discovering new therapies for AMD is the lack of animal models that can recapitulate the pathogenesis of the human disease. In collaboration with Dr. Bo Chang and colleagues at the Jackson Laboratory, we have identified a novel model of spontaneous choroidal neovascularization (CNV), with similar pathobiology of the CNV in human. Using the novel spontaneous CNV mice, we confirmed the C-C chemokine receptor 3 (CCR3) as a novel therapeutic target for CNV, and the CCR3 pathway is at least partly distinct from that of VEGF in CNV pathogenesis. Furthermore, we also identified and validated that toll-like receptor 2 and angiopoietin 2 play a functional role in CNV pathogenesis, and that they could be novel therapeutic targets for CNV.

a. Nagai N, Lundh von Leithner P, Izumi-Nagai K, Hosking B, Chang B, Hurd R, Adamson P, Adamis AP, Foxton RH, **Ng YS**, Shima DT. Spontaneous CNV in a novel mutant mouse is associated with early VEGF-A-driven angiogenesis and late-stage focal edema, neural cell loss, and dysfunction. Invest Ophthalmol Vis Sci. 2014 May 20;55(6):3709-19. PubMed PMID: 24845632; PubMed Central PMCID: PMC4059080.

b. Nagai N, Ju M, Izumi-Nagai K, Robbie SJ, Bainbridge JW, Gale DC, Pierre E, Krauss AH, Adamson P, Shima DT, **Ng YS**. Novel CCR3 antagonists are effective mono- and combination inhibitors of choroidal neovascular growth and vascular permeability. *Am J Pathol,* 2015, 185(9):2534-49. PMID: 26188133.

c. Ju M, Iwata D, Foxton RH, Bunker S, Belich M, Gough G, Adamson P, Shima DT and **Ng YS**. Functional role of TLR in choroidal neovascularization. ARVO Conference 2014, poster presentation.

d. Lundh von Leithner P, Iwata D, **Ng YS**, Regula J, Hartmann G, Shima DT. Bispecific anti-VEGF/ANG2 antibody exhibits superior efficacy to VEGF monotherapy in a model of spontaneous CNV, ARVO Conference 2014, poster presentation.

Complete List of Published Work in My Bibliography:
http://www.ncbi.nlm.nih.gov/myncbi/eric.ng.1/bibliography/48009433/public/?sort=date&direction=ascending

D. Research Support

Ongoing Research Support

Bright Focus Foundation AMD Research Grant Ng (PI) 07/01/2015-06/30/2017
Title: "TLR2 as a novel therapeutic target for CNV pathogenesis"
The objective of this proposal is to validate the functional role of toll-like receptor 2 (TLR2), a component of the innate immune system, in CNV pathogenesis, and to evaluate TLR2 as a novel, effective and safe therapeutic target for the treatment of CNV. Ng (10% effort) is overseeing the overall project, managing the day-to-day execution of experiments, designing and conducting proof of concept experiments, and is responsible for supervising and working with the fellow in charge of the project and liaising with any collaborators to ensure a timely progression of the study.

Grimshaw Foundation AMD Research Grant Ng (PI) 06/01/2016-05/31/2017
Title: "Microbial activation of TLR2 and oxidized lipids: a potential mechanism for CNV pathogenesis"
The major aim for this study is to validate a functional role of chronic TLR2 activation by oxidized lipids and bacterial infection in CNV pathogenesis. Ng (5% effort) is overseeing the overall project, designing and conducting proof of concept experiments, working with the fellow in charge of the project.

Department of Defense PRMRP Discovery Award Ng (PI) 07/01/2016-12/31/2017
Title: “Developing a novel therapeutic for diabetic retinopathy by targeting the heparin-binding domain of VEGF: anti-inflammation and protection of the diabetic retina”
The studies in the application aim to determine the therapeutic potential of targeting the heparin-binding domain of VEGF for treating vascular inflammation associated with diabetic retinopathy. Ng (20% effort) will oversee the direction of the project and manage the day-to-day execution of experiments, design and conduct proof of concept experiments, and supervise and work with the post-doctoral fellow driving the project.

Completed Research Support

Grimshaw Foundation AMD Research Grant Ng (PI) 06/01/2015-05/31/2016
Title: “PPAR agonist protects RPE from degeneration- a potential therapy for dry AMD

Curing Kids Research Grant Ng (PI) 08/01/2014-07/31/2015
Title: “Developing a Novel Therapeutic for ROP by Targeting the Heparin-binding Domain of VEGF: Anti-inflammation and Normalization of the Hypoxic Retina”

Juvenile Diabetes Research Foundation Ng (PI) 08/01/2014-07/31/2015
Title: “Developing a rodent model of PDR” (1-PNF-2014-118-a-N)

Diabetes UK Project Grant (UK) Ng (co-Investigator) 08/01/2013-12/31/2013*
Title: “The role of VEGF-A in retinal neuron survival in diabetic retinopathy: functional assessment and potential neuroprotection solutions”
*Funding stopped upon completion of moving the Ng lab to the USA.