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BIOGRAPHICAL SKETCH

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NAME: Lu, Qingxian

eRA COMMONS USER NAME (credential, e.g., agency login): Q0LU0001

POSITION TITLE: Associate Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Shandong University, Jinan, China	BS	1983	Biology
Peking Union Medical College, Beijing, China	MS	1988	Cell Biology
Univ. of Texas Health Science Ctr. Houston TX	MS	1992	Molecular Biology
Univ. of Texas, MD Anderson Cancer Center	PhD	1996	Gene & Development
Emory University, Atlanta GA	Post Doc	1997	Gene & Development
Salk Institute for Biological Studies, San Diego, CA	Research Associate/staff Scientist	1997-2006	Molecular Neurosciences and Immunology

A. Personal Statement

I obtained my Ph.D. from the MD Anderson cancer center and University of Texas at Houston and received my research associate training as well as my junior career development in the Dr. Greg Lemke's laboratory at the Salk Institute, where I started my research experience in molecular biology and immunology by characterizing the negative regulatory functions of TAM receptor on APCs and the clinical manifestation of autoimmune disorder developed in the *Tyro3*$^{-/-}$*Axl*$^{-/-}$*Mertk*$^{-/-}$ (TAM) triply knockout mice (Lu and Lemke, Nature 1999, Science 2001). My research skill in immunology was further developed when I started to collaborate with well-recognized immunologists, Drs. Clause Roth (Paris now) and David Raulet at UC Berkeley. In this collaboration, I contributed most part of characterization of the TKO mice for defective maturation and functions of NK cells by bone marrow transplantation and NK phenotype analysis (nature immunology, 2007). After I set up my own laboratory in the Department of Ophthalmology and Visual Sciences at University of Louisville, I have concentrated on the functional roles of TAM receptors in APCs activation and autoimmunity caused by hyperreactive TAM-deficient APCs to study pathogenesis of the sight-threatening eye inflammatory diseases, called uveitis in human; and found that mice lacking TAM receptors produced retinal autoantigen-reactive $CD4^+$ T cells that can survive for long period and preserve retinal autoantigen reactivity upon antigen restimulatio. My expertise in study receptor tyrosine kinase signal transduction has been accumulated from many years' studies of regulation and signaling pathway interaction of Tyro3/Axl/Mertk family of receptor tyrosine kinases in development of human diseases, such as systemic autoimmune diseases, uveitis, and *retinitis pigmentosa*.

B. Positions and Honors

Positions and Employments

1997 **Postdoctoral Fellow,** Emory Univ, Dept of Anatomy and Cell Biology, Atlanta GA
1997 - 2000 **Research Associate**, Salk Institute, Molec Neurobiol Lab, La Jolla CA
2000 - 2003 **Sr Research Associate**, Salk Institute, Molec Neurobiol Lab, La Jolla CA

2003 - 2006 **Staff Scientist**, Salk Institute for Biological Studies, Molec Neurobiol Lab, La Jolla CA
2006 - 2012 **Asst Professor**, Univ of Louisville, Dept of Ophthalmology, Louisville KY
2007 - 2012 **Joint Asst Professor**, Univ of Louisville, Dept of Biochem & Mole Biol
2009 - 2012 **Joint Asst Professor**, Univ of Louisville, Dept of Anat Sci & Neurobiol
2012 - Present **Associate Professor**, Univ of Louisville, Dept of Ophthalmology; and **Joint Associate Professor**, Univ of Louisville, Depts of Biochem & Mole Biol, and Anat Sci & Neurobiol

Other Experience and Professional Memberships

2000 Membership of **AAAS**
2008 Membership of the American Association of immunologists (**AAI**)
2010 Membership of Research to Prevent Blindness (**RPB**)
2008 Membership for the Association for Research in Vision and Ophthalmology (**ARVO**).
2008 Membership for Society for Neuroscience (**SFN**)

Honors

1989 Max-Planck-Institut Training Fellowship, Germany
1990 Outstanding Research Award. Chinese Family Planning Council, China
1992 Endocrine Society Research Fellowship
1996 Research Achievement Award, UT MD Anderson Cancer Center at Houston
1999 Clontech Travel Award
2002-2005 Jerry Zweig Fellowship, the Salk Institute, CA
2010-2011 Special Scholar Award, Research to Prevent Blindness

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C. Contribution to Science

1. **Knockout of a single nucleotide from mouse genome**. As a Ph. D. student in the laboratory of Dr. Barry Shur at MD Anderson Cancer Center and U. of Texas at Houston, I learned homologous recombination and gene knockout in ES cells, and single-handedly practiced the ES cell culture, manipulation and microinjection. I successfully knocked-out β1, 4-Galactotransferase (Galtase), an essential enzyme for carbohydrate modification of proteins. However, whether a lectin-like, cell surface isoform of β1,4-Galtase was required for sperm-egg recognition and fertilization had been debating for many years. β1,4-Galtase gene makes two isoforms of enzymes using two different in-frame translation start codons with a N-terminal 13-amino acid (aa) extension at the long isoform of protein. To selectively knocked-out the surface form of Galtase without affecting the short enzymatic form, I adapted a newly-developed insertional recombination vector to mutate a single aa coding codon from the mouse genome, at the first time in the field for a functional protein before the Loxp-Cre technique was developed.
    a. **Lu Q**, Hasty P, Shur BD. Targeted mutation in beta1,4-galactosyltransferase leads to pituitary insufficiency and neonatal lethality. **Dev Biol.** 1997 Jan 15;181(2):257-67. PMID:9013935
    b. **Lu Q**, Shur BD. Sperm from beta 1,4-galactosyltransferase-null mice are refractory to ZP3-induced acrosome reactions and penetrate the zona pellucida poorly. **Development**. 1997 Oct;124(20):4121-31. PMID:9374408
2. **"Knockout" of the masks for a novel family of receptor-tyrosine kinases, consisting of Tyro3, Axl and Mertk (TAM).** My interest in cell-cell interaction/recognition and signal transduction prompted me to join Dr. Greg Lemke's lab and the Salk Institute as a research associate and then staff (non-tenure track) scientist. Once again, my contribution to uncover the functional roles for a novel family of the receptor tyrosine kinases through generation and study of multiple gene knockout compound mice paved a solid foundation and open several avenues leading to rapid development of few hot research areas, such as tyrosine kinase receptors in regulation of reproductive stem cell development/differentiation, immune responses, autoimmune diseases, retinal degeneration, phagocytosis and differentiation of myeloid derived leukocytes. My pioneer works in discovery of the TAM's negative regulation of DCs/macrophage immune responses immediately led to establishment of a novel working model for receptor tyrosine kinases to control appropriate immunoreceptor signaling and cytokine expression, and to maintain a homeostatic immune response to infectious and pathogenic stimuli without causing abnormal autoimmunity.
    a. **Lu Q**, Gore M, Zhang Q, Camenisch T, Boast S, Casagranda F, Lai C, Skinner MK, Klein R, Matsushima GK, Earp HS, Goff SP, Lemke G. Tyro-3 family receptors are essential regulators of mammalian spermatogenesis. **Nature.** 1999 Apr 22;398(6729):723-8. PMID:10227296.

b. **Lu Q**, Lemke G. Homeostatic regulation of the immune system by receptor tyrosine kinases of the Tyro 3 family. **Science**. 2001 Jul 13;293(5528):306-11. PMID:11452127.
c. Caraux A, **Lu Q** (Co-1st author), Fernandez N, Riou S, Di Santo JP, Raulet DH, Lemke G, Roth C. Natural killer cell differentiation driven by Tyro3 receptor tyrosine kinases. **Nat Immunol.** 2006 Jul;7(7):747-54.PMID:16751775.
d. Tang Y, Lu Q-J, Wei Y., Han L., Ji R, Li Q, **Lu Q**. Mertk deficiency alters expression of microRNAs in the retinal pigment epithelium cells. **Metab Brain Dis**. 2015, Jan 22. PMID: 25604732.

3. **Discovering the existence of the long-term survived and ocular autoantigen reactive memory CD4 T cells in the TAM null mice, and negatively regulation of innate immunity by TAM in the CNS immune system** After I joint the Department of Ophthalmology at UofL, I mainly focus on tyrosine kinase regulation of retinal epithelium cell function and retinal degeneration, and the molecular mechanism of vision-threaten autoimmune diseases. Through detailed studies of Uveitis in the gene knockout mice, we found that access exposure of retinal autoantigens and lacking negative regulation of antigen-presenting cells (APC) led to spontaneously production of retinal autoantigen-specific $CD4^+$ T cells, and some of these T cells could be converted to resting, long-lived retinal autoantigen-specific memory T cells that rendered the mutant mice more susceptible to retinal autoantigen stimulation. The significance of this discovery is to mimic relapse in the recurrent types of uveitis in patients, such as Behcet's, Ocular sarcoidosis and Vogt-Koyanagi-Harada diseases, and to elicit a dominant memory T helper-mediated inflammatory response in eye, which we link to hyperactivation of APCs and generation of antigen-specific memory T cells in our mutant mice. In addition, I discovered that APCs without TAM family of receptors produced increased helper T cell polarization cytokines and promoted a disease causing Th1 effector immune response. These findings are not only in agreement with clinical observations that alterations in HLA molecules in APCs are closely linked to higher risks of uveitis and systemic autoimmune diseases in human, but also deep our understanding of etiology of visual-threaten autoimmune diseases In addition, I have further discovered that the TAM receptors also negatively regulate inflammatory response by the CNS resident macrophage, i.e., microglia, to assure a healthy environment for adult neuronal stem cell proliferation and differentiation, and neuron function. This contribution may directly benefit to understanding the underlying mechanism on how to control chronic inflammation in the CNS for a long lived healthy ageing brain and preventing ageing-related CNS diseases.
    a. Ye F, Li Q, Ke Y, Lu Q, Han L, Kaplan HJ, Shao H**, Lu Q**. TAM receptor knockout mice are susceptible to retinal autoimmune induction. **Invest Ophthalmol Vis Sci**. 2011 Jun 16;52(7):4239-46. PMID:21467176. PMCID: PMC3175940.
    b. Ye F, Han L, Lu Q, Dong W, Chen Z, Shao H, Kaplan HJ, Li Q, **Lu Q**. Retinal self-antigen induces a predominantly Th1 effector response in Axl and Mertk double-knockout mice. **J Immunol**. 2011 Oct 15;187(8):4178-86. PMID:21918185. PMCID:PMC3190567.
    c. Li Q, Lu Q, Lu H, Tian S, **Lu Q.** Systemic autoimmunity in TAM triple knockout mice causes inflammatory brain damage and cell death. **PLoS One**. 2013 Jun 20;8(6):e64812. PMID:23840307. PMCID:PMC3688737.
    d. Ji R, Tian S, Lu HJ, Lu Q, Zheng Y, Wang X, Ding J, Li Q**, Lu Q**. TAM receptors affect adult brain neurogenesis by negative regulation of microglial cell activation. **J Immunol**. 2013 Dec 15;191(12):6165-77.

My scientific merit has also been directly reflected in my numerous collaborations (refer to my complete publication link). Collaboration not only lays a platform for me to contribute to the scientific fields and help other scientists, but is also beneficial for my own researches. Collaboration with Dr. Qiutang Li, we have collectively contributed to elucidation of the common and unique roles that the IKK1 or IKK2 play in regulation of NF-κB activation in innate and epithelial cells, and dissecting of YAP1 functions in corneal stem cells. In collaboration with Dr. Dean, we found that Taz/TEAD1 linked cell-cell contact to Zeb1 expression, and mediated proliferation of RPE cells; and repression of Zeb1 and hypoxia caused fibroblasts reprogramming.

    a. Gaddipati S, **Lu Q**, Kasetti RB, Miller MC, Lu Q, Trent JO, Kaplan HJ, Li Q. IKK2 inhibition using TPCA-1-loaded PLGA microparticles attenuates laser-induced choroidal neovascularization and macrophage recruitment. **PLoS One**. 2015 Mar 24;10(3):e0121185. doi: 10.1371/journal.pone.0121185. PMID: 25803615.
    b. Kasetti RB, Gaddipati S, Tian S, Xue L, Kao WW, **Lu Q**, Li Q. Study of corneal epithelial progenitor origin and the Yap1 requirement using keratin 12 lineage tracing transgenic mice. **Sci**

Rep. 2016 Oct 13;6:35202. doi: 10.1038/srep35202. PubMed PMID: 27734924; PubMed Central PMCID: PMC5062132.

c. Liu, Y., Xin, Y., Ye. F., Wang, W., **Lu, Q**, Kaplan, HJ, and Dean, DC. Taz-Tead1 Links Cell-Cell Contact to Zeb1 Expression, Proliferation and Dedifferentiation in Retinal Pigment Epithelial Cells. **Invest Ophthalmol Vis Sci** (2010) 51(7):3372-8. doi:10.1167/iovs. 09-4321; PMID: 20207963; PMCID: PMC2904003

d. Liu Y, Mukhopadhyay P, Pisano MM, Lu X, Huang L, **Lu Q**, Dean DC. Repression of Zeb1 and Hypoxia Cause Sequential MET and Induction of Aid, Oct4, and Dnmt1, Leading to Immortalization and Multipotential Reprogramming of Fibroblasts in Spheres. ***Stem Cells***. 2013 Jul;31(7):1350-62. doi: 10.1002/stem.1382. PMID: 23554223. PMCID: PMC4265806

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/qingxian.lu.1/bibliography/40347309/public/?sort=date&direction=descending