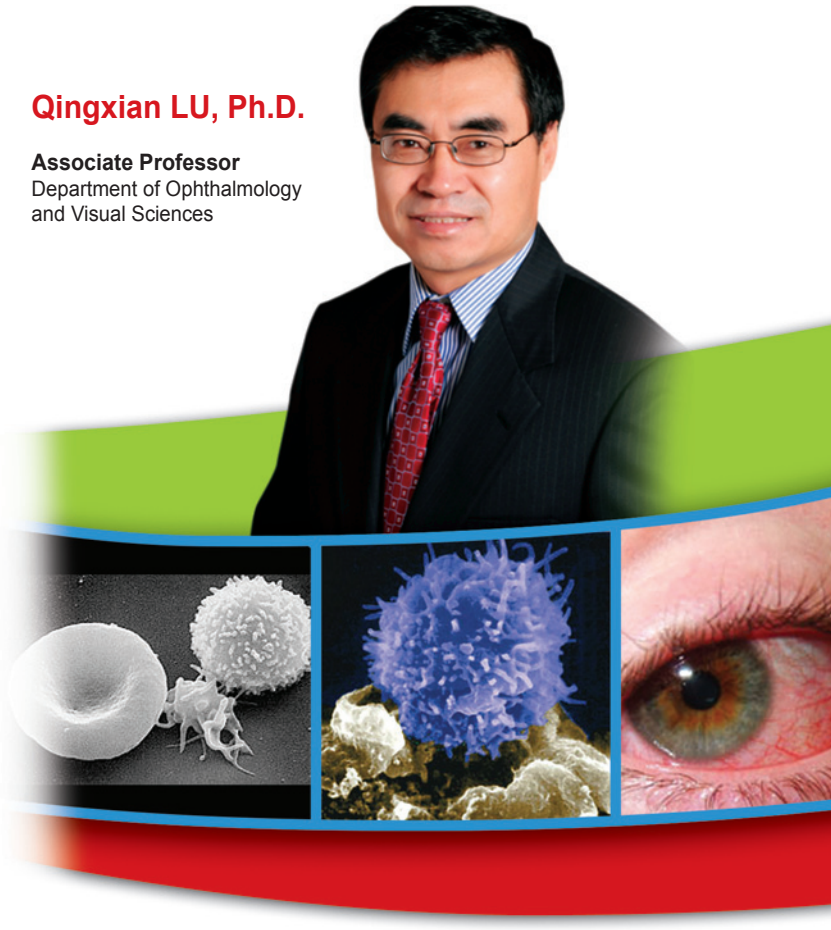
Qingxian LU, Ph.D.

Associate Professor
Department of Ophthalmology
and Visual Sciences



Scholarly Activities:

My research interests are focused on investigation of the functional roles of three closely-related receptor tyrosine kinases, named TYRO3, AXL and MERTK (TAM) in regulation of immune response by antigen-presenting cells (APC). Hyperactivation of APCs causes increased expression of antigen presentation molecules on the cell surface and enhanced production of proinflammatory cytokines, which drive an unrestrained and overactive T helper cell response, in many cases, attaching self-tissues and causing autoimmune diseases such as uveitis in human.

Uveitis is a T cell-mediated inflammation of the eye, and it is the second leading cause of human blindness accounting for approximate 10% of cases of legal blindness in the United States. The goal of our research is to understand how APCs become hyperactivated in uveitis. We have demonstrated that TAM family receptor tyrosine kinases are responsible for controlling APC activity. Triple knockout mice lacking all three TAM genes (TKO mice) develop autoimmune disease in multiple organs including kidney, liver, lung, central nerve system and eye. These mice also, spontaneously produce retinal autoantigen-specific CD4+ T cells. Some of these T cells convert to resting, long-lived retinal autoantigen-specific memory T cells that render the TKO mice more susceptible to retinal autoantigen stimulation. Immunization with retinal specific autoantigen, mimicking relapse in recurrent uveitis, such as Behcet's, Ocular sarcoidosis and Vogt-Koyanagi-Harada diseases, elicits a dominant T helper mediated inflammatory response in eye, which we link to hyperactivation of APCs and generation of antigen-specific memory T cells in TKO mice. Our studies suggest that TAM receptors play a negatively role in regulating APC activation, which in turn limit APC-mediated hyperactivation of the naïve T cell. The degree of initial T cell activation has been linked to conversion to autoantigen specific memory T cells. Recruitment of these long-lived memory T cells is thought to be linked to relapse seen in uveitis and other autoimmune diseases. researches in our laboratory aim to examine roles of TAM receptors in APC activation, and subsequent the generation of ocular tissue-specific T cells and recruitment of the memory T cells that cause disease relapses, and have a better understanding how the TAM deficient APCs affect generation, activation of the retinal specific memory T cells in recurrent uveitis, so that the novel therapeutic targets will be discovered and new medication approaches will be proposed for prevention and cue of uveitis, and other autoimmune diseases as well.

Grants:

Role: Co-PI
Title: Role of 14-3-3sigma in development and repair of corneal epithelium R01-Ey019891 (PI, Dr. Qiutang Li) NIH/NEI 09/01/2010-08/31/2014
Direct Cost: $250,000.00 per year
The goal of this project is to investigate the functional role of 14-3-3sigma in regulation of Notch signaling in development and repair of corneal epithelial cells.

Role: Co-P
Title: 14-3-3s and epithelial differentiation in the eye and other tissues
1R21EY021584-01 (PI: Qiutang Li), NIH/NEI 09/01/2011 – 08/31/2013
Direct Cost: $275,000
The goal for this project to study the roles of 14-3-3sigma in the corneal and other stratified squamous epithelium development and differentiation

Role: Principal Investigator
Title: MerTK regulation of the PTTG and RPE phagocytosis
R01-EY018830 (PI: Lu, Q), 09/30/2008-08/31/2013 NIH/NEI
Direct Cost: $240,000.00 per year
The goal of this project is to elucidate the molecular functions of the MerTK and its downstream targets in RPE phagocytosis.

Publications (2013-2014):

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

Li Q., Lu Q-J., Lv H-Y, Tian S., and **Lu Q**. Systemic autoimmunity in TAM triple knockout mice causes inflammatory brain damage and cell death. PlosOne, 2013 June 20, 8(6):e64812; doi:10.1371/journal.pone.0064812
Hajrasouliha AR, Jiang G, Lu Q, Lu H, Kaplan HJ, Zhang HG, Shao H.. Exosomes from retinal astrocytes contain anti-angiogenic components that inhibit laser-induced choroidal neovascularization. 2013 Sep 27;288(39):28058-67. doi: 10.1074/jbc.M113.470765 PMID:23926109. PMCID: PMC3784718.

Ji R., Tian S., Lu H.J., Lu Q-J., Zheng Y., Wang X., Ding J., Li Q. and **Lu Q**. TAM receptors affect adult brain neurogenesis by negative regulation of microglial cell activation. *Journal of Immunology*, (2013), December 15, 191 (12):6165-6177. PMID: 24244024; PMCID: PMC3870476.

Jiang G., Sun D., Yang H., **Lu Q**., Kaplan HJ., and Shao H. HMGB1 is an early and critical mediator in an animal model of uveitis induced by IRBP-specific T cells. Journal of Leukocyte Biology. 2014, 95(4): 599-607.

Lv H., **Lu Q**., Gaddipati S., Kasetti RB, Wang W, Pasparakis M, Kaplan H J and Li Q. (2014) IKK2 Inhibition Attenuates Laser-Induced Choroidal Neovascularization. PLoS One. e87530. 10.1371/journal.pone.0087530.
Jin JZ, Warner DR, Lu Q, Pisano MM, Greene RM, Ding J. Deciphering TGF-β3 function in medial edge epithelium specification and fusion during mouse secondary palate development. Developmental dynamics (2014), Dec;243(12):1536-43. PMID: 25104574. doi:10.1002/dvdy.24177.

Ji R., Meng L, Jiang X, CVM NK, Ding J, Li Q, and **Lu Q**. TAM receptors support neural stem cell survival, proliferation and neuronal differentiation. PlosOne, (2014). DOI: 10.1371/journal.pone.0115140 December 16, 2014
Ji R, Meng L, Li Q, and **Lu Q**. TAM receptor deficiency affects adult hippocampal neurogenesis. Metabolic Brian Disease, (2014). DOI 10.1007/s11011-014-9636-y, December 10, 2014