Qingxian LU, Ph.D.

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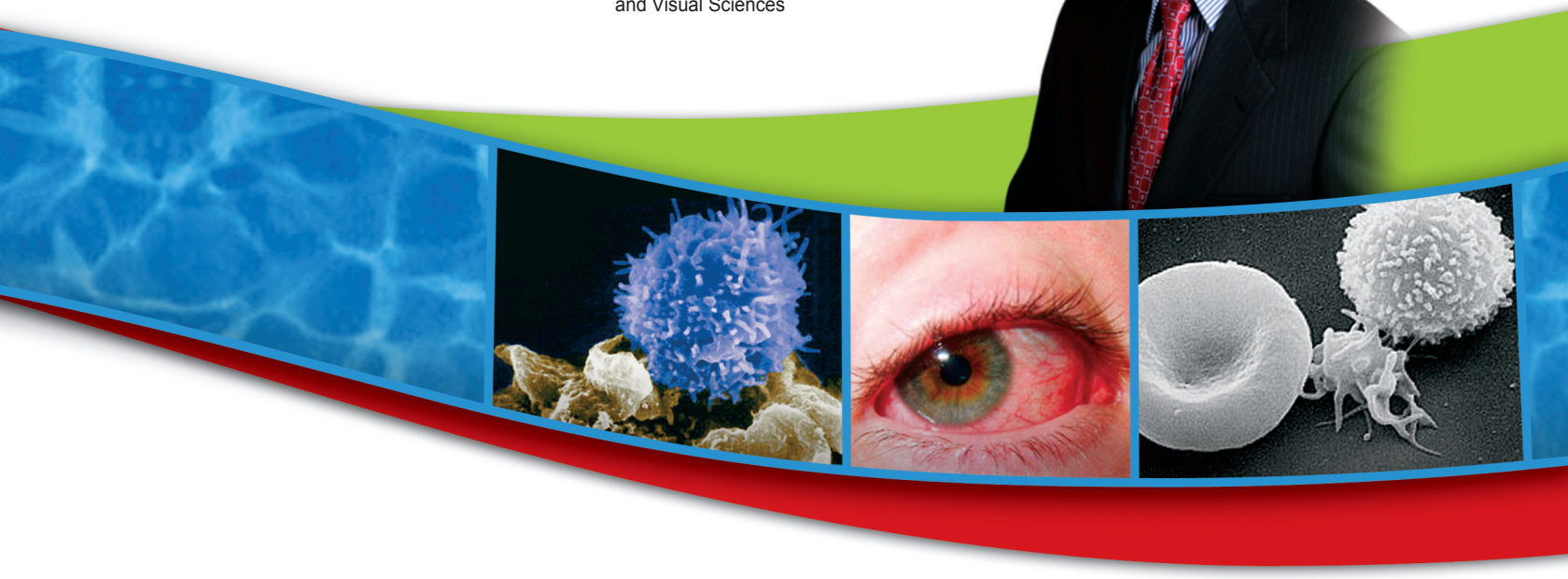

Uveitis is a T cell-mediated inflammation of the eye, and it is the second leading cause of human blindness accounting for approximate 10% of cases of legal blindness in the United States. Hyperactivation of antigen-presenting cells (APCs) leading to an overactive T helper cell response is able to cause autoimmunity including experimental autoimmune uveoretinitis (EAU). The goal of our research is to understand how APCs become hyperactivated in uveitis. We have demonstrated that Tyro3, Axl and MerTK (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. Mounting evidence suggests that TAM receptors play a negatively role in regulating APC activation, which in turn limit APC-mediated over activation of 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. The researches in our laboratory aim to examine roles of TAM receptors in APC activation and subsequent the generation and recruitment of the memory T cells that cause disease relapses, and have a better understanding how the TAM deficient APCs affect generation, long-term persistence and reactivation 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 relapse-remission types of uveitis.

Grants:

R01-EY018830 (PI: Lu, Q), 09/30/2008-08/31/2013 6 calendar
NIH/NEI $250,000.00 per year
Title: MerTK regulation of the PTTG and RPE phagocytosis
The goal of this project is to elucidate the molecular functions of the MerTK and its downstream targets in RPE phagocytosis.

R01-Ey019891 (Co-PI with 10% effort, PI, Dr. Qiutang Li) 1.2 Calendar
NIH/NEI 09/01/2010-08/31/2014 direct cost $250,000.00 per year
Title: Role of 14-3-3sigma in development and repair of corneal epithelium
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.

1R21EY021584-01 (Co-PI with 10% effort, PI: Qiutang Li), 0.72 calendar
NIH/NEI 09/01/2011 – 08/31/2013 direct cost $275,000
Title: 14-3-3sigma and epithelial differentiation in the eye and other tissues
The goal for this project to study the roles of 14-3-3sigma in the corneal and other stratified squamous epithelium development and differentiation

Publications

Lu Q, XinY, Ye F, Foulks G., and Li Q. 14-3-3σ controls corneal epithelium homeostasis and wound healing. Invest Ophthalmol Vis Sci. 52(5):2389-96 (2011) PMID: 21228373; PMCID: PMC3081250

Xin Y, **Lu Q**, Li Q. IKK1 control of epidermal differentiation is modulated by Notch signaling. American Journal of Pathology 178(4):1568-77 (2011). PMID: 20100467; PMCID: PMC3078471

Ren L, Jie D, Lu Q-J, Chen Z, and **Lu Q**. Regulation of HepG2 cell growth by Axl receptor tyrosine kinase. J. Hebei Medical University. 32(02):130-133, (2011), DOI:10.3969/j.issn.1007-3205.

Ye F, Li Q, Ke Y, Lu Q-J, Han L, Kaplan H, Shao H, and **Lu Q**. TAM receptor knockout mice are susceptible to retinal autoimmune induction. Invest Ophthalmol Vis Sci. 52(7):4239-46, (2011). PMID: 21467176; PMCID: PMC3175940

Ye, F., Han, L., Lu, Q-J., Dong, W., Shao, H., Kaplan, JK., Li, Q., and **Lu, Q.** Retinal self-antigen induces a predominantly Th1 effector response in Axl and Mertk double knockout mice. Journal of Immunology, 187:4178-4186, (2011). PMID:21918185; PMCID: PMC3190567

Li Q, Sambandam S, Lu HJ, Thomson A, Kim S, Lu H, Xin Y., and **Lu Q**. Opposing roles of 14-3-3σ and p63 in epidermal tumorigenesis. Carcinogenesis, 32(12):1782-1788, 2011. PMID 21926108; PMC3220605.

Huayi Lu, **Qingxian Lu,** Yajuan Zheng, and Qiutang Li. Notch signaling promotes the corneal epithelium wound healing. Molecular Vision 2012; 18:403-411. PMID:22355251; PMCID:PMC3283215