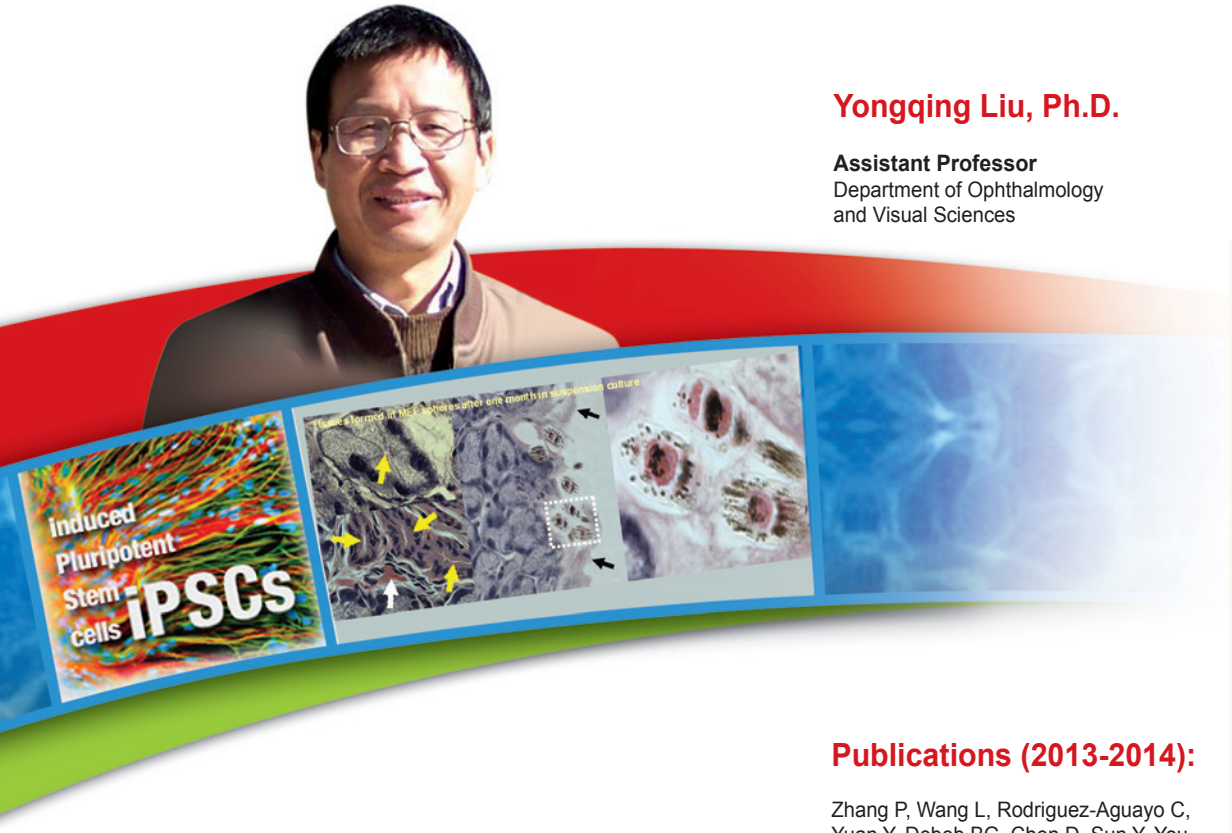

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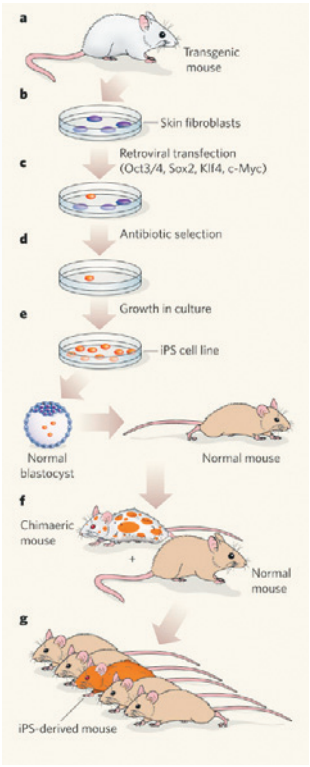

Scholarly Activities:

My research interest branches into two related areas: (1) reprogramming somatic differentiated mammalian cells into stem-like cells through sphere formation in vitro, and re-directing them to specifi c differentiation for tissue regeneration in vivo; (2) analyzing the effects of epithelial-to-mesenchymal transition (EMT) transcription factor Zeb1 on transition of fi broblasts to spherederived stem-like cells (SDSC).

Tissue damages or functional disorders due to trauma, aging, and inheritable diseases like retinitis pigmentosa (RP), and age-related macular degeneration (AMD), are diffi cult to treat. More and more hope now relies on advances in regenerative medicine in which stem cell application is part of the solution. Recently, we have developed a novel protocol for reprogramming fi broblasts to immortal multipotential adult stem-like cells. This reprogramming pathway involves sequential mesenchymal-to-epithelial transition (MET), hypoxic induction of Aid and in turn Oct4 and Dnmt1-dependent silencing of cdk inhibitors and Arf to cause immortalization. We are hoping that application of SDSC that are not tumorigenic in vivo though immortal in vitro will facilitate patient-specific cell therapies in the clinic.

Grants:

Role: Co-PI
Title: *Hypoxia-induced reprogramming to RPE stem cells.*
Funding Agency: NIH, 1 R21 EY024313 -01
Direct Costs Funded: $375,000

Role: PI
Title: *Sphere-induced transdifferentiation of mouse fibroblast into macrophage-like cells.*
Funding Agency: UofL School of Medicine
Direct Costs Funded: $25,000

Role: Co-PI
Title: *Reprogramming of somatic differentiated cells by initiating the endogenous stemness genes into sphere-derived pluripotent stem cell (sdSC) in vitro and their directed differentiation in the eye.*
Funding Agency: China NSF
Direct Costs Funded: ¥800,000

Publications (2013-2014):

Zhang P, Wang L, Rodriguez-Aguayo C, Yuan Y, Debeb BG, Chen D, Sun Y, You MJ, **Liu Y**, Dean DC, Woodward WA, Liang H, Yang X, Lopez-Berestein G, Sood AK, Hu Y, Ang KK, Chen J, Ma L. miR-205 acts as a tumour radiosensitizer by targeting ZEB1 and Ubc13. *Nat Commun.* 5:5671. doi: 10.1038/ ncomms6671 (2014)

Liu Y, Lu X, Huang L, Wang W, Jiang G, Dean KC, Clem B, Telang S, Jenson AB, Cuatrecasas M, Chesney J, Darling DS, Postigo A, Dean DC. Different thresholds of ZEB1 are required for Ras-mediated tumour initiation and metastasis. *Nat Commun.* 5:5660. doi: 10.1038/ncomms6660. PMID: 25434817 (2014)

Zhang P, Wei Y, Wang L, Debeb BG, Yuan Y, Zhang J, Yuan J, Wang M, Chen D, Sun Y, Woodward WA, **Liu Y**, Dean DC, Liang H, Hu Y, Ang KK, Hung MC, Chen J, Ma L. ATM-mediated stabilization of ZEB1 promotes DNA damage response and radioresistance through CHK1. *Nat Cell Biol.* 16(9):864-75 (2014)

Wang W, Zhou L, Lee SJ, **Liu Y**, Fernandez de Castro J, Emery D, Vukmanic E, Kaplan HJ, Dean DC. Swine cone and rod precursors arise sequentially and display sequential and transient integration and differentiation potential following transplantation. *Invest Ophthalmol Vis Sci.* 15;55(1):301-9 (2014)

Liu Y, Sanchez-Tillo E, Lu X, Huang L, Clem B, Telang S, Jenson AB, Cuatrecasas M, Chesney J, Postigo A, Dean DC. The ZEB1 Transcription Factor Acts in a Negative Feedback Loop with miR200 Downstream of Ras and Rb1 to Regulate Bmi1 Expression. *J Biol Chem.* 288(16):11572-80 (2013)

Liu Y, Sánchez-Tilló E, Lu X, Clem B, Telang S, Jenson AB, Cuatrecasas M, Chesney J, Postigo A, Dean DC. Rb1 family mutation is sufficient for sarcoma initiation. *Nat Commun.* 4:2650. doi: 10.1038/ ncomms3650 (2013)

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.* 31(7):1350-62 (2013)

Liu Y, Sanchez-Tillo E, Lu X, Huang L, Clem B, Telang S, Jenson AB, Cuatrecasas M, Chesney J, Postigo A, Dean DC. Sequential Inductions of the ZEB1 Transcription Factor Caused by Mutation of Rb and then Ras are required for Tumor Initiation and Progression. *J Biol Chem.* 288(16):11572-80 (2013)