OMB No. 0925-0001/0002 (Rev. 09/17 Approved Through 3/31/2020)

BIOGRAPHICAL SKETCH

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NAME: Shaw, Peter Xiao

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

POSITION TITLE: Assistant Professor of Ophthalmology

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 |
| --- | --- | --- | --- |
| Sichuan University, Chengdu, China | B.S | 02/1982 | Biochemistry |
| West China University of Medical Sciences | M.S. | 05/1985 | Biochemistry |
| McMaster University, Canada | Ph.D. | 05/1996 | Biochemistry/Molecular Biology |
| University of California, San Diego | Postdoctoral | 01/2000 | Endocrinology/lipid metabolism |

# A. Personal Statement

Prior to my research in the eye field, I had spent years of study towards the intricacies of the innate or adaptive immune response to oxidation-specific epitopes on oxidized phospholipids (oxPLs) and their impact on atherogenesis. Through these studies, I have built up a strong background in biochemistry, molecular biology, genetics, and immunology as well as animal studies. At Shiley Eye Institute, I have transitioned my research to focus on genetic and environmental risks of eye diseases and the underlying molecular mechanisms. As a principal investigator, I have dedicated my lab to further characterize the unexplored mechanisms underlying age-related macular degeneration (AMD) and focused on finding novel intervention approaches that may be exploited for therapeutic benefit and vision preservation.

With experience as a PI on several private and NIH-funded grants, I have extensively investigated the interplay of genetic risk and oxidative stress on molecular signaling leading to retinal degeneration and AMD progression. I have been working on the impact of genetic polymorphisms of ARMS2-HTRA1 and CFH loci on AMD pathogenesis for a decade. My academic achievement and dedication are demonstrated by my publication record, which has gathered with 7000 citations and through conducting and managing independent research.

**B. Positions and Employment**

1987-1989 Research Fellow, Dept. Pathology, University of California, San Francisco

Supervisor: Dr. Benedict TS. Yen

1989-1995 Teaching/Research Assistant, Dept. Biochemistry, McMaster University, Hamilton, Canada. Supervisor: Dr. John P. Capone

1996-2000 Postgraduate Biochemist, Dept. Medicine, University of California, San Diego

Supervisor: Dr. Joseph L. Witztum

2000-2006 Assistant Research Biochemist, Dept. Medicine, University of California, San Diego

2006-2015 Associate Project Scientist, Dept. Medicine/Ophthalmology, University of California, San Diego

2015-pres Assistant Professor, Dept. Ophthalmology, University of California, San Diego

## Other Experience and Professional Memberships

## 1997-2010 Council on Arteriosclerosis, Thrombosis and Vascular Biology (ATVB), Amer Heart Assoc

## 2004 Secretary General, Asian Pacific Conference on Tumor Biology and Medicine

## 2005 Steering Committee Member, Pacific Health Summit

## 2012-pres ARVO

## Honors

## 1987-1989 Chen Scholarship (Hong Kong), awarded to outstanding young medical researchers to conduct biomedical studies in the US. 8 to 10 annually;

## 1989-1991 Ontario differential fee waiver, awarded to outstanding foreign students, who pay tuition as residents (over $10,000 cash value);

## 1990, 1995 Grants from International Herpesvirus Workshops;

## 1998-1999 Research Grant, American Association of Clinical Chemistry;

## 1998-2000 Startup Grant, Stein Research Institute on Aging;

## 1998-2000, Postdoctoral fellowship, American Heart Association;

## 2000-2004 Beginning Grand-in-Aid, American Heart Association;

## 2004-2007 Scientist Development Award, American Heart Association.

# C. Contribution to Science

I have published more than 70 papers, which have gathered total of 7000+ citations (2314 since 2015); h-index of 34 and i10-index of 50.

1. My lab focuses on investigating biochemical bases and molecular mechanisms of genetic polymorphisms associated with AMD pathogenesis, particularly, the interactions of their related gene products with oxidative stress. We demonstrated that the AMD risk genotypes of complement factor H (e.g. CFH Y402H) results in differential binding affinity with oxidized phospholipids (oxPLs). This property of the AMD associated CFH variant may contribute to the disease pathogenesis by impairing the removal of oxidative damaged materials leading to inflammation and lipids accumulation. I also demonstrated that the disease haplotype of single nucleotide polymorphism (SNP) rs11200638/rs10490924 on HTRA1 promoter results in increased expression of HTRA1 and decreased expression of growth differentiation factor 6 (GDF6), a member of TGF-β superfamily, in AMD patients. Using HTRA1 knockout (*htra1*-/-) mice, I have shown that the removal of HTRA1 correlates with down-regulation of vascular endothelial growth factor (VEGF) and decreased retinal vasculature. This finding led to my novel approach to therapeutically target HTRA1 via engineering a functional, single-chain variable fragment (scFv) derived from anti-HTRA1 mAbs. Combining gene therapy technology, the development of RPE expressing viral vectors would set a predecessor in applying genetically engineered antibody of anti-angiogenic potential as an effective therapeutic approach in eye disease models.
2. **Shaw PX**, Zhang L, Zhang M, Du H, Zhao L, Lee C, Grob S, Lim SL, Hughes G, Lee J, Bedell M, Nelson MH, Lu F, Krupa M, Luo J, Ouyang H, Tu Z, Su Z, Zhu J, Wei X, Feng Z, Duan Y, Yang Z, Ferreyra H, Bartsch DU, Kozak I, Zhang L, Lin F, Sun H, Feng H, Zhang K. (2012) *Complement factor H genotypes impact risk of age-related macular degeneration by interaction with oxidized phospholipids.* ***Proc Natl Acad Sci USA***. 109(34):13757-62. doi: 10.1073/pnas.1121309109. PMID: 22875704 (Citation 101)
3. **Shaw PX\***, Stiles T, Douglas C, Ho D, Fan W, Du H, Xiao X. **(2016)** *Oxidative stress, innate immunity, and age-related macular degeneration.* ***AIMS Mol Sci.*** 2016;3(2):196-221. Epub 2016 May 11. \*Corresponding author. (Citation 94)
4. Zhang, L., Lim, SL, Du, H., Zhang, M., Kozak, I., Hannum, G., Wang, X., Ouyang, H., Hughes, G., Zhao, L., Zhu, X., Lee, C., Su, Z., Zhou, X., Shaw, R., Ideker, T., Oka, C., Wang, N., Yang, Z., **Shaw, PX.** and Zhang K. **(2012)** *HTRA1 regulates angiogenesis through TGF-β family member GDF6*. ***J Biol Chem.*** 25;286(12):10210-5 (co-corresponding author). doi: 10.1074/jbc.M111.275990. PMID: 22049084 (Citation 68)
5. Lu Z, Lin V, May A, Che B, Xiao X, Shaw DH, Su F, Wang Z, Du H, **Shaw PX.** **(2019)** *HTRA1 synergizes with oxidized phospholipids in promoting inflammation and macrophage infiltration essential for ocular VEGF expression.* ***PLoS One.*** 2019 May 17;14(5):e0216808. doi: 10.1371/journal.pone.0216808. eCollection 2019. PMID: 31100080
6. During my post-doc training, I have made significant contribution on the immunological property of oxidized phospholipids. We revealed a critical character of natural antibodies that specifically bind to oxPLs and their immune-biological roles in physiological and pathological conditions. These antibodies are produced by distinct sets of innate-like B cells, which arise early in development to become the sources of "natural immune memory". Due to their interactions with a variety of pathogenic microbes, natural antibodies have previously been postulated to play roles of providing first line of protection against bacterial and viral infections before the adaptive immunity kicks in. My work demonstrated that oxidation-derived epitopes on apoptotic cells and oxidized low-density lipoproteins can also be recognized by such germline encoded B-1 cell natural antibody, e.g. T15, which provide important "house-keeping" functions to remove or shield the oxidation damage. Since the oxidation-epitopes recognized by those antibodies reflect the internal oxidation status, I have recently developed oxidized phospholipids as a plasma biomarker in combination with genetic profile for pre-symptomatic diagnosis of Age-related Macular Degeneration (AMD).
7. **Shaw PX**, Hörkkö S, Chang MK, Curtiss LK, Palinski W, Silverman GJ, Witztum JL. (2000) *Natural antibodies with the T15 idiotype may act in atherosclerosis, apoptotic clearance, and protective immunity*. ***J Clin Invest.*** 105(12):1731-40. PMID: 10862788 (Comment in Immune recognition of OxLDL in atherosclerosis. [J Clin Invest. 2000]) (Citation 689)
8. Binder CJ, Chang MK, **Shaw PX**, Miller YI, Hartvigsen K, Dewan A, Witztum JL. (2002) *Innate and acquired immunity in atherogenesis.* ***Nature Medecine***. 8(11):1218-26. PMID: 12411948 (Citation 822)
9. Binder CJ, Hörkkö S, Dewan A, Chang MK, Kieu EP, Goodyear CS, **Shaw PX**, Palinski W, Witztum JL, Silverman GJ. (2002) *Pneumococcal vaccination decreases atherosclerotic lesion formation: molecular mimicry between Streptococcus pneumoniae and oxidized LDL*. ***Nature Medecine*** 9(6):736-43. PMID: 12740573 (Citation 752)
10. **Shaw PX**, Goodyear CS, Chang MK, Witztum JL, Silverman GJ. (2003) *The autoreactivity of anti-phosphorylcholine antibodies for atherosclerosis-associated neo-antigens and apoptotic cells*. ***J Immunol.*** 170(12):6151-7. PMID: 12794145 (Citation 116)
11. I have generated several human phage display libraries and cloned a panel of monoclonal antibodies to the oxidation-specific epitopes. These mAbs have been characterized for their immunological properties, genetic structures (VH and VL gene alignment with germline genes, VDJ recombination and CDRs), as well as their biological functions. One of the stable and high yield secretor, named IK17, recognizes specific ligands on OxLDL and apoptotic cells, which mediate LDL uptake by macrophage scavenger receptors and phagocytosis. In vitro study has shown that IK17 can block the uptake of OxLDL indicating the therapeutic potential of this human antibody. Using 125I-labeled IK17 to image rabbit aorta have demonstrated its association with the lesion plaque (Cover story of ATVB). I have also developed an approach using 99mTc-labeled IK17 as a reagent for non-invasive imaging of atherosclerotic lesions.
    1. **Shaw PX**, Hörkkö S, Tsimikas S, Chang MK, Palinski W, Silverman GJ, Chen PP, Witztum JL. (2001) *Human-derived anti-oxidized LDL autoantibody blocks uptake of oxidized LDL by macrophages and localizes to atherosclerotic lesions in vivo.* ***Arterioscler Thromb Vasc Biol.*** 21(8):1333-9. PMID: 11498462 (The Issue’s cover story with an Editorial) (Citation 249)
    2. Torzewski M, **Shaw PX**, Han KR, Shortal B, Lackner KJ, Witztum JL, Palinski W, Tsimikas S. (2004) *Reduced in vivo aortic uptake of radiolabeled oxidation-specific antibodies reflects changes in plaque composition consistent with plaque stabilization.* ***Arterioscler Thromb Vasc Biol.*** 24(12):2307-12. PMID: 15528482 (Citation 98)
    3. Briley-Saebo KC, **Shaw PX**, Mulder WJ, Choi SH, Vucic E, Aguinaldo JG, Witztum JL, Fuster V, Tsimikas S, Fayad ZA. (2008) *Targeted molecular probes for imaging atherosclerotic lesions with magnetic resonance using antibodies that recognize oxidation-specific epitopes*. ***Circulation.*** 117(25):3206-15. doi: 10.1161/CIRCULATIONAHA.107.757120. PMID: 18541740 (Citation 188)
    4. Tsimikas S, **Shaw PX.** (2003) *Non-invasive imaging of vulnerable plaques by molecular targeting of oxidized LDL with tagged oxidation-specific antibodies*. ***J Cell Biochem.*** Suppl 39:138-46. PMID: 12552613 (Citation 33)
12. During my time working at Shiley Eye Institute I have transitioned my research to focus on genetics and molecular mechanisms of eye diseases. I have studied the interaction of genetic and environment factors, such as smoking and unhealthy diet, and their impact on developing eye diseases, including AMD, Familial Exudative Vitreoretinopathy (FEVR), Primary Open Angle Glaucoma (POAG), Proliferative Diabetic Retinopathy (PDR), as well as their underlying molecular mechanisms.
13. Du H, Sun X, Guma M, Luo J, Ouyang H, Zhang X, Zeng J, Quach J, Nguyen DH, **Shaw** **PX**, Karin M, Zhang K. **(2013)** *JNK inhibition reduces apoptosis and neovascularization in a murine model of age-related macular degeneration*. ***Proc Natl Acad Sci USA.*** 110(6):2377-82. doi: 10.1073/pnas.1221729110. PMID: 23341606 (Citation 62)
14. Zhang K, Harada Y, Wei X, Shukla D, Rajendran A, Tawansy K, Bedell M, Lim S, **Shaw PX**, He X, Yang Z. **(2011)** *An essential role of the cysteine-rich domain of FZD4 in norrin/WNT signaling and familial exudative vitreoretinopathy*. ***J Biol Chem.*** 25;286(12):10210-5 (Citation 27)
15. Luo J, Zhao L, Chen AY, Zhang X, Zhu J, Zhao J, Ouyang H, Luo H, Song Y, Lee J, Patel SH, **Shaw PX**, Sadda S, Zhuo Y, Rosenfeld MG, Zhang K. *TCF7L2 variation and proliferative diabetic retinopathy.* ***Diabetes***. 2013 Jul;62(7):2613-7. (Citation 29).
16. Sommer JR, Estrada JL, Collins EB, Bedell M, Alexander CA, Yang Z, Hughes G, Mir B, Gilger BC, Grob S, Wei X, Piedrahita JA, **Shaw PX**, Petters RM, Zhang K. (2011*) Production of ELOVL4 transgenic pigs: a large animal model for Stargardt-like macular degeneration.* ***Br J Ophthalmol.*** 95(12):1749-54. doi: 10.1136/bjophthalmol-2011-300417. PMID: 21873315 (Citation 58)
17. I have also involved in investigation of the molecular mechanistic insights of intrinsic and extracellular signaling in retinal progenitor cell (RPC) differentiation and retinal ganglion cell (RGC) specification. We have found that the transforming growth factor-beta (TGF-β) superfamily, through differential SMAD phosphorylation, modulate both Math5 and Sox C transcriptional factors that are critical for RGC specification and maturation during development. I am also interested in delivering antagonists of Krüppel-like transcription factors (KLFs) that inhibit RGC axon regeneration after injury in different animal models. I have organized and conducted the experiment to study the topical application of Rhe associated protein kinase (ROCK) inhibitor in in protection of RGC and promoting optic nerve regeneration after injury.
18. Fang, J\*., **Shaw, PX\***., Wang, Y. and Goldberg, JL (2016) "*Krüppel-like factor 4 (KLF4) is not required for retinal cell differentiation"* ***eNeuro***, accepted for publication. \* Co-first author. (citation 10)
19. **Shaw, PX**, Fang, J, Sang A, Wang, Y. Kapiloff, M and Goldberg, JL (2016) *"Soluble adenylyl cyclase is required for retinal ganglion cell and photoreceptor differentiation"* ***Invest Ophthalmol Vis Sci.*** 1;57(11):5083-5092. doi: 10.1167/iovs.16-19465. (Citation 7)
20. **Shaw, PX**, A Sang, Y Wang, D Ho, C Douglas, L Dia, JL Goldberg **(2016)** *“Topical administration of a Rock/Net inhibitor promotes retinal ganglion cell survival and axon regeneration after optic nerve injury.* ***Experimental Eye Research***. 2016 Jul 18. pii: S0014-4835(16)30181-6. doi: 10.1016/j.exer.2016.07.006. (Citation 20)
21. Kroeger H, Grimsey N, Paxman R, Chiang WC, Plate L, Jones Y, **Shaw PX**, Trejo J, Tsang SH, Powers E, Kelly JW, Wiseman RL, Lin JH. **(2018)** *The unfolded protein response regulator ATF6 promotes mesodermal differentiation* Sci Signal. 2018 Feb 13;11(517). pii: eaan5785. doi: 10.1126/scisignal.aan5785. PMID: 29440509 (Citation 20)

Complete List of Published Work in My Bibliography:

<https://www.ncbi.nlm.nih.gov/sites/myncbi/peter.shaw.1/bibliography/49089751/public/?sortby=pubDate&sdirection=descending>

**EXTRA CURRICULARS AND SPECIALTIES:**

**Project Leader**, (2012-2013) (with Dr. Michael Young, Harvard Department of Ophthalmology) Retinal Transplantation of Human Retinal Progenitor Cells in RCS Rats to Preserve Vision. The study’s objective was to investigate the therapeutic potential of injection of each of two separate human Retinal Progenitor Cells (hRPC) cell lines into subretinal space of RCS rat to rescue the damaged photoreceptor phenotypes and visual function assayed by ERG and optokinetic response (OKN).

**Secretary-General**, (2004-2006) Asian-Pacific Conference on Tumor Biology and Medicine. As a major organizer, Dr. Shaw contributed to successful organization of “Asian pacific Conference on Tumor Biology and Medicine 2004 & 21st International Association of Tumor Marker Oncology Conference”. This was a four-day international conference on tumor marker oncology held in Xi’An, China. There were about 700 participants from all parts of the world. This conference covered a variety of topics regarding microarray analysis, genomic and proteomic studies to look for new tumor markers and therapeutic targets etc.

**Steering Committee Member**, 2005 Pacific Health Summit, (2005-2006) the first-ever gathering of the best minds in science, policy, medical practice, research and public health from around the Pacific Rim. The mission of the Pacific Health Summit is “By exploring emerging technologies, new collaborations and innovative strategies, Summit participants will develop effective and sustainable approaches to the study and management of global health. The participants included the then WHO Chief, the NIH director Elias Zerhouni, the Chinese Minister of Health, Dr. Zhu Chen, the President of Chinese Academy of Medical Sciences, the Director of Canadian Medical Research Consul, and etc.

**Academic Committee Member**, (2003-pre.) Cell Engineering Research Center/Cell Engineering Base of Hi-tech Research and Development Program of China. The center has developed into a prominent teaching, researching and producing base. Dr. Shaw provides the strategic and technological advice to the center.

**Lead Guest Editor**, (2016) Oxidative Medicine and Cellular Longevity

**Editorial Board Member,** (2017-pre.) Journal of Reactive Oxygen Species (ROS)

**Grant reviewer**

2016: Research and Development Grant, Foundation Fighting Blindness

2016: Research Grant, Fight for Sight

**Invited Reviewer**:

2002 – 2009: Journal of Internal Medicine

2002 – Present: Molecular Nutrition and Food Research

2002 – Present: Nature Cardiovascular Biology

2009 – Present: Archives of Biochemistry and Biophysics

2010-Present: Cell Biology International

2010-Present: Bone Marrow Transplantation (nature group)

2012-Present: Lead Guest Editor, Oxidative Medicine and Cellular Longevity

2014-Present: Mechanism of Aging and Development

2015-Present: Ophthalmology Research

2016-present: Journal of Reactive Oxygen Species (ROS)

2016-present: Journal of Human Hypertension (Nature Group)

2016-present: International Journal of Ophthalmic Pathology

2016-present: Archives of Biochemistry and Biophysics.

2016-present: Clinical and Experimental Ophthalmology

2017-present: Scientific Report (Nature Group)

2018-present: Invest. Ophthal. and Vis. Research (IOVS)

2019-present: Pharmacology

**TEACHING AND SUPERVISORY ACTIVITIES**

**Classroom teaching**: 2012-present, instructor to teach medical student course “Gene Therapy” (MED 271). Teaching subject “Gene therapy for the eye”

**Graduate Student supervisor:** Student name:Victor Lin, Degree Master of Science (2017-2019)

Dr. Shaw has been a supervisor for the lab technicians, graduate students and medical students during their research activities in the lab, as well as undergraduate trainees since his appointment in Ophthalmology.

**Lab Technicians and Students supervised and role:**

2011-2013 Kristin Rauscher (Technician), supervisor

2011-2013 John Quach (Technician), supervisor

2010-2011 Siok Lam Lim (post-doc), research advisor

2010-2011 Bin Lin (undergraduate student), research advisor

2010-2011 Matthew Bedell (medical student, 4th year), research advisor

2010-2011 Ye Wang (Visiting Graduate student, 4th year), research advisor

2010-2011 Xinrong Zhou (Visiting Graduate student, 4th year), research advisor

2010-2012 Clara Lee (undergraduate student), research advisor, mentor

2010-2012 Xumei Zhou (post-doc), research advisor

2010-2012 Guy Hughes (undergraduate student), research advisor

2010-2012 Martin Krupa (medical student, 3rd and 4th year), research advisor

2010-2012 Li Zhang (post-doc), research advisor

2011-2012 Jing Luo (post-doc), research advisor

2011-2012 Jing Zhu (Visiting graduate student), research advisor

2011-2012 Jing Zeng (post-doc), research advisor

2011-2012 Hong Ouyang (post-doc), research advisor

2011-2012 Janet Lee (medical student, 3rd year), research advisor

2012-2012 Duy Nguyen (medical student, 3rd year), research advisor

2012-2012 Yang Yang (post-doc), research advisor

2012-2012 Ke Ma (post-doc), research advisor

2012-2012 Jun Kong (post-doc), research advisor

2012-2012 Jin Zhu (graduate student, 1st year), research advisor

2012-2012 Juliet Yuan (undergraduate student), research advisor, mentor

2012-2012 Jeiran Javaherian (undergraduate student), research advisor, mentor

2012-2012 Jessica Lu (High school volunteer), research advisor, mentor

2012-2012 Yaojun Song (High school volunteer), research advisor, mentor

2012-2012 Honrong Luo (post-doc), research advisor, mentor

2013-2015 Praseeda Venugopalan (graduate student), research advisor.

2014-2015 Alan Sang (undergraduate student), research advisor, mentor

2014-2015 Daisy Ho (undergraduate student), research advisor, mentor

2014-2016 Christopher Douglas (undergraduate student), research advisor, mentor

2014-2015 Lara Dia (undergraduate student), research advisor, mentor

2014-2015 Edward Nillo (undergraduate student), research advisor, mentor.

2015-2016 Travis Stiles (Post-doct), research advisor, mentor

2016-2017 Adam May (undergraduate student), research advisor, mentor

2016-2017 Theodore Chin (undergraduate student), research advisor, mentor

2016-2017 Mike Matsumoto (undergraduate student), research advisor, mentor

2016-2017 Jingyao Chen (undergraduate student), research advisor, mentor

2016-2017 Briana Che (undergraduate student), research advisor, mentor

2016-2017 Kyle Tran (undergraduate student), research advisor, mentor

2016-2017 Victor Lin (undergraduate student), research advisor, mentor

2016-2017 Jiancheng Zhang (Visiting Scientist), research advisor, mentor

2016-2017 Zhigang Lu (Post-doc), research advisor, mentor.

2017-2019 Adam May (undergraduate student), research advisor, mentor

2017-2019 Zhihao Wang (undergraduate student), research advisor, mentor

2018-2019 Rachael Ehlen (undergraduate student), research advisor, mentor

2018-2019 Brian Dinh (undergraduate student), research advisor, mentor

2018-2019 Nan Hu (undergraduate student), research advisor, mentor