

Sheng-hong Chen, Ph.D.

Curriculum Vitae

Department of Systems Biology
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QUALIFICATIONS

- Accomplished Ph.D. scientist with 10+ years extensive interdisciplinary research experience in signaling, computation, biochemistry, proteomics and cancer biology.
- Proven scientist with an outstanding track record of high-quality publications.
- Significant contributions in revealing signaling mechanisms by integrating *in vitro* reconstitution assays, *in vivo* signaling profiling and quantitative proteomics.
- Successful efforts in identifying novel signaling dynamics for combinatorial cancer therapy by quantitative single-cell time-lapse imaging and computational modeling.
- Innovative life sciences professional with excellent communication and teamwork skills.

EDUCATION

2002-2008	Ph.D., Biological Sciences University of California, San Diego Department of Cellular and Molecular Medicine Mentor: Prof. Huilin Zhou	San Diego, CA, U.S.
2000-2001	M.Sc., Evolutionary and Adaptive System (Distinction) University of Sussex School of Informatics Mentor: Prof. Inman Harvey	Brighton, U.K.
1994-1998	B.Sc., Zoology National Taiwan University	Taipei, Taiwan

PROFESSIONAL EXPERIENCE

2011-present	Harvard Medical School Postdoctoral Research Fellow Mentor: Prof. Galit Lahav Department of Systems Biology Focus: <i>Single-cell signaling dynamics and combinatorial cancer therapy</i> <ul style="list-style-type: none">• Established a single-cell bi-phasic p53 dynamics after depletion of an oncogene Mdmx using long-term time-lapse single-cell imaging.• Examined effects of signaling dynamics on cellular response to DNA damage as a reference to design combinatorial therapies for cancers.	Boston, MA, U.S.
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- Constructed a mathematical model of Mdmx-Mdm2-p53 signaling system for the control of p53 dynamics using small molecules.
 - Industrial collaboration: leader of a collaborative project with the Novartis Institutes for Biomedical Research to develop screening assays for small molecule inhibitors of cancer using single-cell quantitative imaging.
- 2010-2011 University of California, San Francisco San Francisco, CA, U.S.
 Postdoctoral Research Fellow
 Mentor: Prof. Keith Yamamoto
 Department of Cellular and Molecular Pharmacology
 Focus: *Regulatory logic of glucocorticoid receptor mediated transcription*
- Identified cell-type specific target genes of glucocorticoid receptor and dissected regulatory mechanisms underlying their transcription.
 - Industrial collaboration: active participant of a collaborative team with Merck to characterize effects of agonistic and antagonistic ligands on transcriptional regulation.
- 2009 Ludwig Institute for Cancer Research San Diego, CA, U.S.
 Postdoctoral Research Fellow
 Mentor: Dr. Huilin Zhou
 Focus: *Phospho-proteomics approach to map kinase-substrate signaling networks*
- Developed phospho-proteomic technology to screen for substrates of DNA damage checkpoint kinases by combining stable isotope labeling by amino acids in cell culture (SILAC) method and multi-dimensional chromatography.
- 2002-2008 University of California, San Diego San Diego, CA, U.S.
 Ph.D. student
 Mentor: Dr. Huilin Zhou
 Focus: *Biochemical reconstitution and quantitative-proteomics of the DNA damage checkpoint*
- Reconstituted firstly the kinase-signaling cascade of the DNA damage checkpoint to determine the role of adaptor protein Mrc1 in activating downstream effector kinases.
 - Integrated *in vitro* reconstituted assay with *in vivo* quantitative phosphorylation mapping to identify conserved activation mechanism for Chk2 family kinases.
- 2001-2002 University of Sussex Brighton, U.K.
 M.Sc. student
 Mentor: Dr. Inman Harvey
 Focus: *Mathematical modeling and simulations of viral epidemics*
- Constructed an agent-based computational model to simulate the effects of human transportation on the viral epidemics and the evolution of virulence.

RESEARCH SUPPORT

- NIH/NIGMS F32-GM105205 Role: PI 02/01/2013 - 03/31/2016
The Combinatorial Effect of p53 Dynamics and Modifications on Cell Fate Decisions
 The aim is to control cell fate decision by dissecting the molecular mechanisms underlying p53 dynamics and post-translational modifications using interdisciplinary approaches including single-cell imaging, proteomics and mathematical modeling.

HONORS AND AWARDS

2013-2016	Ruth L. Kirschstein National Research Service Award - NIGMS (F32)
2015	Scholarship for the Cellular Dynamics & Models conference, Cold Spring Harbor Laboratory
2014	Travel Award for Evolution of Complex System workshop, OIST
2012	Genesis Travel Award, Asia Pacific Developmental Biology Conference
2011-2014	Ruth L. Kirschstein National Research Service Award - NIGMS (F32) (kindly declined due to relocation)
2010	Scholarship for Eukaryotic Gene Expression course, Cold Spring Harbor Laboratory
2009	Scholarship for Embryology course, Marine Biological Laboratory
2006	Graduate Travel Award, American Society for Biochemistry and Molecular Biology
2001	Distinction honor degree, M.Sc., Evolutionary and Adaptive System, University of Sussex

PUBLICATIONS

1. Lettman MM, Wong YL, Viscardi V, Niessen S, **Chen S.-H**, Shiao AK, Zhou H, Desai A, Oegema K. "Direct binding of SAS-6 to ZYG-1 recruits SAS-6 to the mother centriole for cartwheel assembly", *Dev Cell*. 2013 May 13; 25(3):284-98. [PMID: 23673331](#)
2. **Chen S.-H**, Masuno K, Cooper SB, Yamamoto R.K. "An Incoherent Feed-forward Regulatory Logic underpinning Glucocorticoid Receptor Action", *Proc Natl Acad Sci U S A*. 2013 Jan 29; 110(5):1964-9. [PMID: 23307810](#)
3. **Chen S.-H***, Albuquerque CP*, Liang J, Suhandynata R, Zhou H. "A proteome-wide analysis of kinase-substrate network in the DNA damage response", *J Biol Chem*, 2010 Apr 23; 285(17):12803-12. *equal contribution. [PMID: 20190278](#)
4. **Chen S.-H**, Zhou H. "Reconstitution of Rad53 activation by Mec1 through adaptor protein Mrc1", *J Biol Chem*, 2009 Jul 10; 284(28):18593-604. [PMID: 19457865](#)
5. Saito K, Chen M, Bard F, **Chen S.-H**, Zhou H, Woodley D, Polischuk R, Schekman R, Malhotra V. "TANGO1 facilitates cargo loading at Endoplasmic Reticulum exit sites", *Cell*, 2009 Mar 6; 136(5): 891-902. [PMID: 19269366](#)
6. Tang T, Zheng B, **Chen S.-H**, Murphy AN, Kudlicka K, Zhou H, Farquhar MG. "hNOA1 interacts with complex I and DAP3 and regulates mitochondrial respiration and apoptosis", *J Biol Chem*, 2009 Feb 20; 284(8):5414-24. [PMID: 19103604](#)
7. Smolka MB, Albuquerque CP, **Chen S.-H**, Zhou H. "Proteome-wide identification of in vivo targets of DNA damage checkpoint kinases", *Proc Natl Acad Sci U S A*, 2007 Jun 19; 104(25):10364-9. [PMID: 17563356](#)
8. **Chen S.-H**, Smolka MB, Zhou H. "Mechanism of Dun1 activation by Rad53 phosphorylation in *Saccharomyces cerevisiae*", *J Biol Chem*, 2007 Jan 12; 282(2):986-95. [PMID: 17114794](#)
9. Smolka MB, **Chen S.-H**, Maddox PS, Enserink JM, Albuquerque CP, Wei XX, Desai A., Kolodner RD, Zhou H. "An FHA domain mediated protein interaction network of Rad53 reveals its role in the regulation of

polarized cell growth", *J Cell Biol*, 2006 Dec 4; 175(5):743-53. PMID: 17130285

10. Su YH, **Chen S.-H**, Zhou H, Vacquier VD. "Tandem mass spectrometry identifies proteins phosphorylated by cyclic AMP-dependent protein kinase when sea urchin sperm undergo the acrosome reaction", *Dev Biol*, 2005 Sep 1; 285(1):116-25. PMID: 16038896
11. Smolka MB, Albuquerque SP, **Chen S.-H**, Schmidt KH, Wei XX, Kolodner RD, Zhou H. "Dynamic Changes in Protein-protein Interaction and Protein Phosphorylation Probed with Amine Reactive Isotope Tag", *Mol Cell Proteomics*, 2005, Sep; 4(9), 1357-1369. PMID: 15972895

PRESENTATIONS

1. Cellular Dynamics & Models, Cold Spring Harbor Laboratory (Cold Spring Harbor, NY, U.S., March, 2015)
Mdmx buffers against p53 oscillations that specifies temporal decisions on cell fate (Oral Presentation)
2. 6th LMU-Harvard Young Scientists' Forum (Cambridge, MA, U.S., July, 2014)
Controlling signaling dynamics and cell fate decisions (Oral Presentation)
3. Stochastic Physics in Biology, Gordon Research Conference (Ventura, CA, U.S., January 2011)
Dissecting the regulatory logic of GR mediated differential transcription (Poster Presentation)
4. Institute of Molecular Biology, Academia Sinica (Taipei, Taiwan, January 2009)
From Bottom up to Top down - study of DNA damage checkpoint signaling pathway (Invited talk)
5. Yeast Chromosome Structure, Replication and Segregation, FASEB Summer Research Conference (Carefree, Arizona, U.S., June 2008)
Reconstitution of DNA replication checkpoint (Poster Presentation)
6. Annual meeting of the American Society for Biochemistry and Molecular Biology (San Francisco, CA, U.S., April 2006)
An FHA domain-mediated protein interaction network reveals parallel targeting of two Chk2 family kinases, Rad53 and Dun1 (Oral Presentation)

TEACHING EXPERIENCE

2005	University of California, San Diego Teaching Assistant – BIBC100: Biochemistry
2004	University of California, San Diego Teaching Assistant – BIBC103: Biochemical Techniques Lab
2003	University of California, San Diego Teaching Assistant – BIEB154: Molecular Evolution

PROFESSIONAL SERVICES

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| 2012-present | Founding President and Board of Boston Taiwanese Biotechnology Association (BTBA) <ul style="list-style-type: none"> • Recruited and led 20 people to organize a symposium with 300 participants, two keynotes (President of Academia Sinica and Director of the Picower Institute for Learning and |
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- Memory), two panels (Academic and Industrial panels) and 15 contributed talks.
- BTBA is developing into a non-profit organization that holds monthly academic and industrial career events and annual symposiums.

2014

- Organizing committee of Future of Research conference (<http://futureofresearch.org/>)
- A conference organized by post-doctors in the Boston area with 300 participants, two panels and four workshops discussing the sustainability of the biomedical research enterprise.

SKILLS AND TECHNIQUES

Biochemistry

- Recombinant protein expression in bacteria, insect cells and mammalian cells.
- Epitope tagged protein purification.
- Generation of protein-coupled columns for affinity purification.
- Protein purification using open columns and the FPLC system (ion exchange, gel filtration and affinity columns).
- SDS-PAGE and Western blot analysis.
- Protein immunoprecipitation analysis.
- Protein synthesis through in vitro transcription and translation.
- *in vitro* reconstitution assay of kinase-signaling cascade using purified proteins.
- *in vitro* ubiquitination assay with recombinant E1, E2, E3 and substrates.
- *In vitro* cell-free system for kinase signaling and protein ubiquitination.

Computation and Imaging

- Simulations of dynamic systems (ODE models) using Matlab and Mathematica.
- Agent-based simulations using C programming.
- Bioinformatic analysis using Perl and Matlab.
- Image analysis for quantifying fluorescent signals at single cells using Matlab and ImageJ.
- Single cells long-term time-lapse imaging (Nikon Eclipse Ti).
- Confocal microscopy (Zeiss710 and Nikon C1si).

Mass spectrometry

- Quantitative mass spectrometry using chemical labeling and SILAC.
- Sample preparation for in-gel and in solution protein digestion for mass spectrometry.
- Phospho-peptide purification using immobilized metal ion affinity chromatography.

Molecular Biology

- Common cloning techniques and site-directed mutagenesis.
- Design CRISPR strategy for gene targeting in mammalian systems.
- Yeast (*Saccharomyces cerevisiae*) gene targeting and tetrad dissection.
- Gene expression knockdown with siRNA or shRNA.
- RNA isolation and Real-time RT-quantitative-PCR.
- Chromatin immunoprecipitation (ChIP) assay

Cell Biology

- Yeast, insect, and mammalian cell culture.

- Transcriptional reporter assay with luciferase substrates.
- Generation of cell lines stably expressing tagged proteins or reporters.
- Lentivirus production and infection.
- Cell growth and apoptosis assays.
- Flow cytometry and data analysis.