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Place of Birth: Euless, TX

EDUCATION

2012 **Ph.D. Bioinformatics and Systems Biology**, University of California San Diego

Co-Advisors: Bernhard Ø. Palsson, Ph.D. and Philip E. Bourne, Ph.D.

Thesis: Structural Systems Biology Perspective on the Metabolic Impact of Physicochemical Stress

2005 **B.A. Molecular and Cell Biology** (genetics & development emphasis), University of California Berkeley

RESEARCH EXPERIENCE

Research associate and associate lab director, Harvard Medical School

2018-present

Primary Projects:

- Design of intrinsically disordered proteins (IDPs) to induce cryptobiosis in human cells: developed 5-year \$15M proposal, acted as project manager, performed computational analysis and design of IDPs

LSRF postdoctoral research fellow, Harvard Medical School

2013-2018

Advisor: Pamela A. Silver, Ph.D.

Primary Projects:

- Discovery of viral-encoded suppressors of innate immunity in humans: helped develop protein structure-based prediction method to identify immunosuppressors, developed automated gene expression construct design pipeline, advised on development of unsupervised learning analysis of high-throughput microscopy imaging data to establish immune response assay phenotypes, maintained human cell cultures and tested STAT1 nuclear localization assay for innate immune response
- Protein oxidation in *D. radiodurans*: modeled structural proteome, developed 3D feature analysis tools, developed machine learning predictor of protein carbonylation sites, conducted redox proteomic experiments
- Polyploidy in *D. radiodurans*: developed *in vivo* chromosome and plasma membrane fluorescent labeling technique, measured labeled cultures by flow cytometry and microscopy, performed clustering analysis
- RNA nanostructure engineering: developed design pipeline for RNA nanotubes, cloned expression constructs and expressed in *E. coli*, developed riboregulator and FISH tube assembly assays using flow cytometry and microscopy, helped develop super-resolution FISH-DNA-PAINT imaging technique

NSF IGERT & GK-12 graduate student research fellow, University of California San Diego 2007-2012

Co-Advisors: Bernhard Ø. Palsson, Ph.D. and Philip E. Bourne, Ph.D.

Primary Projects:

- Structural systems biology of *E. coli*: reconstructed protein structure-integrated metabolic network, analyzed proteome-wide enzyme thermostability, developed flux balance analysis predictor of thermotolerance, performed nutrient supplementation growth experiments, performed proteome-wide protein-antibacterial interaction prediction, simulated antibacterial mechanisms by flux balance analysis
- Simulation of drug mechanisms: developed model of human renal metabolism, simulated drug response phenotypes by integrating metabolic model with structure-based protein-drug interactions, analyzed clinical hypertensive genotypes in model and predicted genetic predisposition to adverse drug effects
- Modeling photosynthetic metabolism: annotated genome of eukaryotic alga *C. reinhardtii*, reconstructed genome-scale metabolic network of *C. reinhardtii*, devised flux balance scheme for simulating different light spectra

RESEARCH EXPERIENCE (continued)

NSF IGERT graduate student research fellow, The Scripps Research Institute 2008

Advisor: Stephen P. Mayfield, Ph.D.

Primary Projects:

- Gene silencing in *C. reinhardtii*: developed design software for gene-specific RNAi constructs, cloned constructs for carotenoid synthesis enzyme knock-downs, generated knock-down strains by chloroplast transformation, validated knock-downs by RT-PCR

Research technician, University of Texas Southwestern Medical Center 2006-2007

Advisor: Richard H. Scheuermann, Ph.D.

Primary Projects:

- Modular organization of biological networks: developed graph-theoretic algorithms for modularization of protein-protein interaction and genetic interaction networks, studied network sub-structure topology, performed Gene Ontology annotation analysis and helped develop ontology for concepts in network biology
- BioHealthBase Bioinformatics Resource Center: helped develop genomic database, web visualization and analysis tools, and user interface for genomic research of high public health risk pathogens

UCB BFP undergraduate student research fellow, University of California Berkeley 2003-2005

Advisors: Aziz Aboobaker, Ph.D. and Nipam Patel, Ph.D.

Projects:

- Hox gene evolution in nematodes: evaluated experimental tractability of a variety of nematode species, developed culturing, antibody staining, and RNAi protocols, cloned hox genes for use in RNAi constructs

FELLOWSHIPS AND AWARDS

2014-2017 Moore Foundation Fellow of Life Sciences Research Foundation (full support, postdoctoral)

2014 NIH NRSA F32 from NIGMS (full support, postdoctoral) (declined)

2011-2012 NSF GK-12 Socrates Teaching Fellow (full support)

2010 UCSD Bioinformatics Expo Best Poster Award

2008-2010 NSF IGERT Plant Systems Biology Fellow (full support)

2004-2005 UC Berkeley Biology Fellow

PUBLICATIONS

17. **Chang RL***, Robinson MC, Sher JW, Li Z, Chan YA, Omdahl AR, Wattiez R, Godzik A, Matallana-Surget S*. Unraveling oxidative stress resistance: molecular properties govern proteome vulnerability. (submitted). *Corresponding authors.

16. Brunk E, **Chang RL**, Xia J, Hefzi H, Yurkovich JT, Kim D, Buckmiller E, Wang HH, Cho BK, Yang C, Palsson BO, Church GM, Lewis NE. Characterizing posttranslational modifications in prokaryotic metabolism using a multiscale workflow. *Proc Natl Acad Sci U S A*. 2018 Oct 23;115(43):11096-11101.

15. Chaiboonchoe A, Ghamsari L, Dohai B, Ng P, Khraiwesh B, Jaiswal A, Jijakli K, Koussa J, Nelson DR, Cai H, Yang X, **Chang RL**, Papin J, Yu H, Balaji S, Salehi-Ashtiani K. Systems level analysis of the *Chlamydomonas reinhardtii* metabolic network reveals variability in evolutionary co-conservation. *Mol Biosyst*. 2016 Jul 19;12(8):2394-407. doi: 10.1039/c6mb00237d.

14. Brunk E, Mih N, Monk J, Zhang Z, O'Brien EJ, Bliven SE, Chen K, **Chang RL**, Bourne PE, Palsson BO. Systems biology of the structural proteome. *BMC Syst Biol*. 2016 Mar 11;10:26.

13. MacKellar D, Lieber L, Norman JS, Bolger A, Tobin C, Murray JW, Oksaksin M, **Chang RL**, Ford TJ, Nguyen PQ, Woodward J, Permingeat HR, Joshi NS, Silver PA, Usadel B, Rutherford AW, Friesen ML, Prell J. *Streptomyces thermoautotrophicus* does not fix nitrogen. *Sci Rep*. 2016 Feb 1;6:20086.

PUBLICATIONS (continued)

12. Ebrahim A, Almaas E, Bauer E, Bordbar A, Burgard AP, **Chang RL**, Dräger A, Famili I, Feist AM, Fleming RMT, Fong SS, Hatzimanikatis V, Herrgård MJ, Holder A, Hucka M, Hyduke D, Jamshidi N, Lee SY, Le Novère N, Lerman JA, Lewis NE, Ma D, Mahadevan R, Maranas C, Nagarajan H, Navid A, Nielsen J, Nielsen LK, Nogales J, Noronha A, Pal C, Palsson BØ, Papin JA, Patil KR, Price ND, Reed JL, Saunders M, Senger RS, Sonnenschein N, Sun Y, Thiele I. Do Genome-scale Models Need Exact Solvers or Clearer Standards? *Mol Syst Biol*. 2015 Oct 14;11(10):831.
11. Chen AH, Lubkowitz D, Yeong V, **Chang RL**, Silver PA. Transplantability of a circadian clock to a noncircadian organism. *Sci. Adv*. 2015 Jun 1;1(5):e1500358.
10. **Chang RL**, Xie L, Bourne PE, Palsson BØ. Antibacterial mechanisms identified through structural systems pharmacology. *BMC Syst Biol*. 2013 Oct 10;7:102.
9. O'Brien ET, Lerman JA, **Chang RL**, Hyduke DR, Palsson BØ. Genome-scale models of metabolism and gene expression extend and refine growth phenotype prediction. *Mol Syst Biol*. 2013 Oct 1;9:693.
8. **Chang RL**, Andrews K, Kim D, Li Z, Godzik A, Palsson BØ. Structural systems biology evaluation of metabolic thermotolerance in *Escherichia coli*. *Science*. 2013 Jun 7;340(6137):1220-1223. Selected by Faculty of 1000 (Aug. 2013).
7. Nam H, Lewis NE, Lerman JA, Lee D, **Chang RL**, Kim D, Palsson BO. Network context and selection in the evolution to enzyme specificity. *Science*. 2012, Aug 31;337(6098):1101-1104.
6. **Chang RL**, Ghamsari L, Manichaikul A, Hom EF, Balaji S, Fu W, Shen Y, Hao T, Palsson BØ, Salehi-Ashtiani K, Papin JA. Metabolic network reconstruction of *Chlamydomonas* offers insight into light-driven algal metabolism. *Mol Syst Biol*. 2011, Aug 2;7:518. doi: 10.1038/msb.2011.52. Thirty-day top downloaded MSB paper and highlighted in *Science* (August 2011).
5. **Chang RL**, Xie L, Xie L, Bourne PE, Palsson BØ. Drug off-target effects predicted using structural analysis in the context of a metabolic network model. *PLoS Comput Biol*. 2010, Sep 23;6(9):e1000938. Paper highlighted in *Journal of the American Medical Informatics* (July-August 2011), AMIA Summit on Translational Bioinformatics: Year in Review (March 2011), and selected by Faculty of 1000 (Jan. 2012).
4. **Chang RL**, Luo F, Johnson S, Scheuermann RH. Deterministic graph-theoretic algorithm for detecting modules in biological interaction networks. *Int J Bioinform Res Appl*. 2010;6(2):101-19.
3. Manichaikul A*, Ghamsari L*, Hom EFY*, Lin C*, Murray RR*, **Chang RL***, Balaji S, Hao T, Shen Y, Chavali AK, Thiele I, Yang X, Mello E, Hill DE, Vidal M, Salehi-Ashtiani K, Papin JA. Metabolic network analysis integrated with transcript verification for sequenced genomes. *Nat Methods* 2009, Aug;6(8):589-92. *Equal contribution.
2. Squires B, Macken C, Garcia-Sastre A, Godbole S, Noronha J, Hunt V, **Chang R**, Larsen CN, Klem E, Biersack K, Scheuermann RH. BioHealthBase: informatics support in the elucidation of influenza virus host pathogen interactions and virulence. *Nucleic Acids Res*. 2008, Jan;36(Database issue):D497-503.
1. Luo F, Yang Y, Chen CF, **Chang R**, Zhou J, Scheuermann RH. Modular organization of protein interaction networks. *Bioinformatics* 2007, Jan 15;23(2):207-214.

PRESENTATIONS

Chang RL. Structural Model of Vulnerability to Protein Oxidation in Bacteria. Invited talk at May 2018 Boston Aging Data Club, Boston, MA.

PRESENTATIONS (continued)

Chang RL. Understanding Vulnerability to Protein Oxidation in Bacteria. Invited talk at 2017 Virginia Tech Biocomplexity Institute – Beyond Sequence Alignment Symposium, Blacksburg, VA.

Chang RL, Robinson MC, Sher JW, Chan YA, Stork DA, Li Z, Silver PA, Matallana-Surget S. Bacterial Proteome Vulnerability to Oxidative Damage. **Poster** at 2017 11th Annual q-bio Conference, New Brunswick, NJ.

Chang RL. Proteome structure vulnerability to oxidative damage in *Deinococcus radiodurans*. **Talk** at 2016 Life Sciences Research Foundation Annual Meeting, Seattle, WA.

Chang RL, Sher JW, Stork D, Silver PA. Structural Analysis of Proteome Vulnerability to Oxidative Damage in *Deinococcus radiodurans*. **Poster** at 2016 ASM Microbe, Boston, MA.

Chang RL, Sher JW, Ren Z, Silver PA. Polyploidy and Proteome Vulnerability to Oxidative Damage in the Polyextremophile *Deinococcus radiodurans*. **Posters** at 2015 Life Sciences Research Foundation Annual Meeting, Baltimore, MD and 2015 6th Annual Life Sciences Undergraduate Research Fair, Cambridge, MA.

Chang RL. RNA nanotube scaffolds as synthetic *in vivo* macromolecular machines. **Posters** at 2014 Life Sciences Research Foundation Annual Meeting, Denver, CO and 2014 5th Annual Life Sciences Undergraduate Research Fair, Cambridge, MA.

Chang RL, Andrews K, Kim D, Li Z, Godzik A, Palsson BØ. Structural systems biology evaluation of metabolic thermotolerance in *Escherichia coli*. **Talk** at Feb. 5th, 2013 Wyss Institute Synthetic Biology Platform Meeting, Boston, MA.

Chang RL, Li Z, Godzik A, Palsson BØ. Structural Reconstruction of the metabolic network of *Escherichia coli* K12. **Poster** at 2011 5th IECA Conference, Riviera Maya, Mexico and 2012 UCSD Bioinformatics Expo, La Jolla, CA.

Lerman JA, O'Brien EJ, **Chang RL, Palsson BØ.** Genome-scale modeling in *E. coli*: M to ME. **Poster** at 2011 5th IECA Conference, Riviera Maya, Mexico.

Chang RL, Xie L, Xie L, Bourne PE, Palsson BØ. Drug off-target effects predicted using structural analysis in the context of a metabolic network model. **Talks** at 2011 UCSD Bioinformatics Expo and 2010 UCSD Dept. of Pharmacology Research Discussions, La Jolla, CA.

Chang RL, Ghamsari L, Manichaikul A, Hom EFY, Balaji S, Fu W, Shen Y, Palsson BØ, Salehi-Ashtiani K, Papin JA. Validated genome-scale reconstruction of *Chlamydomonas reinhardtii* illuminates light-driven metabolism. **Talk** at 2010 UCSD Plant Systems Biology IGERT Symposium, La Jolla, CA.

Chang RL, Manichaikul A, Santhanam B, Ghamsari L, Hom EFY, Salehi-Ashtiani K, Papin JA. Genome-wide Network Analysis of Metabolism in *Chlamydomonas reinhardtii*. **Posters** at 2010 UCSD Bioinformatics Expo, La Jolla, CA and 2010 DOE GTL meeting, Washington D.C.

Ghamsari L, Santhanam B, **Chang RL, Yu H, Shen Y, Yang X, Manichaikul A, Hom EFY, Balcha D, Vidal M, Papin JA, Salehi-Ashtiani K.** Identifying the metabolic potential of *Chlamydomonas reinhardtii* by large-scale annotation of its encoded open reading frames. **Poster** at 2010 DOE GTL meeting, Washington D.C.

Chang RL, Manichaikul A, Thiele I, Mayfield SP, Palsson BØ. Central metabolic network reconstruction and engineering of *Chlamydomonas reinhardtii* for biofuel production. **Posters** at 2009 UCSD Plant Systems Biology IGERT Symposium and 2009 UCSD Bioinformatics Expo, La Jolla, CA.

PRESENTATIONS (continued)

Chang RL, Luo F, Johnson S, Scheuermann RH. Deterministic graph-theoretic algorithm for detecting modules in biological interaction networks. **Talk** at BIOT-2008, Dallas, TX.

SELECTED GRANT WRITING

DARPA Design and Engineering of Biostasis Proteins (DARPA W911NF1920017) 2018

- PIs: Pamela A. Silver, Ph.D., Debora Marks, Ph.D.
- Conceived, wrote, budgeted, coordinated 7 co-investigators for grant, and managed project

DARPA Biological Robustness in Complex Settings (DARPA HR0011-15-C-0094) 2015

- PI: Pamela A. Silver, Ph.D.
- Contributed to portion of grant on computational modeling of bacterial consortia

DARPA Living Foundries - 1000 Molecules (funded for first phase, finalist for second) 2013-2014

- PI: Pamela A. Silver, Ph.D.
- Conceived and wrote portions of the grant
- Presented computational platform to DARPA in Washington D.C.

NIH R01 - Genome-scale *in silico* model for *E. coli* (funded) 2010

- PI: Bernhard Palsson, Ph.D.
- Wrote portions of the grant
- Ranked in 2nd percentile

NIH R21 - Computational drug development in the context of human metabolic network 2010

- PIs: Bernhard Palsson, Ph.D. & Philip Bourne, Ph.D.
- Conceived, wrote, and submitted entire grant

NIH SBIR for GT Life Sciences, Inc., San Diego, CA 2010

- Supervisors: Iman Famili, Ph.D. & Monica Mo, Ph.D.
- As consultant helped conceive, perform preliminary research for, and write grant

TEACHING AND MENTORSHIP EXPERIENCE

Harvard-Amgen Scholars Program 2017

- *Role*: research mentor
- *Activities*: trained an undergraduate research intern in computational systems biology, protein modeling and analysis, and viral genome analysis

Harvard FAS Center for Systems Biology Undergraduate Summer Research Program 2014-2016

- *Role*: research mentor
- *Activities*: trained undergraduate research interns in computational systems biology and bench experimental techniques for molecular biology and microbiology

Biology and Chemistry, Patrick Henry High School, San Diego 2011-2012

- *Role*: NSF GK-12 teaching fellow
- *Partner teacher*: Autumn Ross
- *Activities*: gave lectures, ran learning exercises, designed lessons introducing topics in bioinformatics, pharmacogenomics, structural biology, biochemistry, evolution, and bioethics
- *Published lesson plan*: Genomics, Bioinformatics, and Health
(<http://sciencebridge.ucsd.edu/programs/socrates/projects/biology/genomics-bioinformatics-health.html>)

TEACHING AND MENTORSHIP EXPERIENCE (continued)**Structural Bioinformatics Data & Analysis, University of California San Diego** 2009

- *Role:* graduate teaching assistant
- *Professor:* Philip Bourne
- *Topics:* macromolecular structure data, experimental techniques for structure determination, biological data classification, protein structure alignment, protein-protein and protein-ligand interactions
- *Activities:* prepared and graded homework assignments and exams, held regular office hours and individual tutoring sessions, aided in course redesign, guest lecturer (2010, 2011, 2012)

Systems Biology and Bioengineering, University of California San Diego 2009

- *Role:* graduate teaching assistant
- *Professor:* Bernhard Palsson
- *Topics:* network reconstruction, constraint-based modeling, linearization, singular value decomposition, omics data analysis
- *Activities:* developed slides, gave lectures, prepared and graded homework assignments and exams, held regular office hours and individual tutoring sessions, contributed to new textbook, maintained course website

ENTREPRENEURSHIP

- 2013 *Provisional patent:* Structural systems biology evaluation of metabolic thermotolerance
Inventors: **Chang RL**, Palsson BØ
- 2010 *Provisional patent:* Method for assessing physiological response to drug target inhibition
Inventors: **Chang RL**, Palsson BØ, Bourne PE
- 2009 *Business Plan Competition:* UCSD Entrepreneur Challenge Elevator Pitch Competition
Venture: Optibiotics *Team:* **Chang RL**, Lerman J, Nagarajan H, Udpa N

EDITORIAL ACTIVITIES

- Textbook contribution:
Palsson BO. Systems Biology: Constraint-based Reconstruction and Analysis
Cambridge University Press, 2015.
- Peer reviewer for ISMB Program Committee (2010)
- Peer reviewer for scientific journals:
The Plant Journal (2018-)
Scientific Reports (2016-)
ACS Synthetic Biology (2015-)
Molecular BioSystems (2013-)
Cell (2013-)
Nucleic Acids Research (2011-)
Nature Reviews Microbiology (2011-)
Cell Reports (2011-)
Metabolic Engineering (2010-)
Nature (2009-)
BioEssays (2009-)
PLoS Comp Biol (2009-)

COURSEWORK AND TECHNICAL SKILLS

- **Graduate Coursework:**
Molecular Biology
Structural Bioinformatics
Data for Systems Biology
Genome-scale Network Analysis
Dynamic Modeling of Networks
Sequence and Structure Analysis
Functional Genomics
Bioinformatics Statistics
Algorithm Design and Analysis
Plant Systems Biology

COURSEWORK AND TECHNICAL SKILLS (continued)

- **Undergraduate Coursework:**

Microbial Genomics/Bioinformatics
 Biochemistry
 Molecular Biology
 Cell Biology
 Genetics (lecture/lab)
 Biology (ecology, genetics, plant biology: lecture/lab)
 Developmental Biology
 Post-Genomic-Era Biology

Organic Chemistry (lecture/lab)
 Biophysical Chemistry
 Inorganic Chemistry (lecture/lab)
 Intro. Computing
 Calculus
 Physics (electricity, magnetism, mechanics, thermodynamics, optics, nuclear physics: lecture/lab)
 Psychology

- **Lab Techniques:**

sterile technique
 chemical reagent preparation
 bacteria/algae/nematode/human cell culture
 DNA/protein gel electrophoresis
 DNA/RNA blots
 molecular cloning
 PCR
 bacterial transformation

PPIs via yeast two-hybrid
 RNAi knock-downs
 DAPI and antibody staining
 fluorescence *in situ* hybridization
 spinning disk confocal microscopy
 flow cytometry
 protein extraction for proteomics
⁶⁰Co γ -irradiation

- **Computational Skills:**

constraint-based modeling
 flux balance analysis
 metabolic network reconstruction
 graph theoretic algorithms
 protein structure modeling/analysis
 DNA/RNA secondary structure
 design/analysis
 sequence analysis
 genome annotation

biostatistics
 machine learning
 signal processing
 Perl
 Python
 Java
 Unix/Bash
 Matlab
 R

REFERENCES

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 La Jolla, CA 92093-0412
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 858-534-5668

Philip E. Bourne (PhD co-advisor)
 Professor, Director of Data Science Institute
 University of Virginia
 Department of Biomedical Engineering
 Snyder Building PO Box 400229
 Charlottesville, Virginia 22908
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 434-924-6867

Richard H. Scheuermann (postbac advisor)
 Director, Professor
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REFERENCES (continued)

Debora S. Marks (collaborator)

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Jason A. Papin (collaborator)

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Kourosh Salehi-Ashtiani (collaborator)

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Adam Godzik (collaborator)

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University of California Riverside
Division of Biomedical Sciences
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Aziz Aboobaker (undergraduate mentor)

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