

# Bin Z. HE, Ph.D.

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## A. EDUCATION AND TRAINING

- 2006-2012    **The University of Chicago**, Chicago, IL  
Ph.D. in Ecology and Evolution, Advisor: Martin Kreitman  
Thesis title: "Using *Drosophila* Natural Variation to Study the Role of Positive Selection in Cis-Regulatory Evolution and the Genetic Basis of a Complex Trait"
- 2002-2006    **Peking University**, Beijing, China  
B.S. , Advisor: Qi Ouyang  
Thesis title: "Using microfluidics device to investigate bacteria persistence phenomenon"

## B. PROFESSIONAL APPOINTMENT

- 2018-        **Assistant Professor**  
Biology Department, University of Iowa
- 2017-2018   **Associate research scholar**  
Lewis-Sigler Institute for Integrative Genomics, Department of Ecology and Evolutionary Biology, Princeton University  
Affiliation: Peter Andolfatto lab, Julien Ayroles lab  
Research: Evolution of gene regulatory networks controlling stress response in yeast
- 2012-2017   **Postdoctoral researcher**  
FAS Center for Systems Biology, Harvard University, HHMI  
Advisor: Erin O'Shea  
Research: Evolution of phosphate starvation response pathway in a commensal yeast

## C. HONORS, FELLOWSHIPS AND AWARDS

- 2016        The Allied Genetics Conference, GSA Trainee Travel Award (\$300)
- 2012        Sigma Xi Research-in-Aid Grant (\$950)
- 2012        BSD Women's Board Travel Fund, University of Chicago (\$400)
- 2011        1st Asia Pacific *Drosophila* Research Conference, Travel Fellowship (\$1000)
- 2011        Honorary mention, Harper Fellow for best Ph.D. thesis at The University of Chicago
- 2009-10    University of Chicago Hinds Fund (\$2000)

## D. CONTRIBUTION TO SCIENCE

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1. Acquired Stress Resistance (ASR) allows an organism to become more resilient to a severe stress after exposure to a primary stress. This phenomenon is likely an important mechanism for pathogenic yeasts adapting to the host environment. However, little is known about how ASR diverges between yeast pathogens and close relatives. We found a distinct ASR in the opportunistic yeast pathogen *C. glabrata* compared to the related *S. cerevisiae*. When subjected to a non-lethal phosphate starvation, *C. glabrata* activates over 15 oxidative stress genes, resulting in 3–10 times greater survival during a severe H<sub>2</sub>O<sub>2</sub> challenge.; the same treatment offers little protection in *S. cerevisiae*. Our investigation reveals a unique gene network for ASR, sharing key components with the canonical oxidative stress response but employing different regulatory mechanisms. Notably, we observed rapid inhibition of the Target-of-Rapamycin Complex 1 (TORC1) by phosphate limitation only in *C. glabrata*, uncovering a pivotal regulatory point underlying this divergent ASR. These findings offer insights into how ASR evolution may contribute to pathogenic yeasts' adaptation to their host environment.

- a. Liang J, Tang H, Snyder LF, Youngstrom CE, **He BZ** Divergence of TORC1-mediated Stress Response Leads to Novel Acquired Stress Resistance in a Pathogenic Yeast. PLoS Pathog 2023; 19(10): e1011748. PMID: 37871123

2. Very few fungal species are able to infect humans, and yet pathogenic fungi are spread across the phylogeny, raising the question of what genomic changes drove host adaptation and whether distinct pathogenic lineages evolved convergently. Building on my past experience in characterizing yeast gene family expansions, we turned our attention to another virulence-associated gene class, namely cell wall adhesins. Past research has suggested that expansion and diversification of adhesin families are associated with the rise of pathogens. However, careful phylogenetic studies of adhesin families are significantly lacking. We reconstructed the most comprehensive phylogeny for an adhesin family to date, and found it to be strongly enriched in pathogenic yeasts relative to the low-pathogenic relatives. This enrichment is due to repeated, independent duplication among different pathogenic lineages, followed by rapid divergence in their sequences, generating great diversity in protein length and  $\beta$ -aggregation potentials. We also found evidence of relaxed selective constraint and positive selection shaping the pattern of variations in the effect domain after gene duplication. Together, our results provide unprecedented details in the evolution of adhesin families in pathogenic yeasts.

- b. Nahas JV, Iosue CL, Shaik NF, Selhorst K, **He BZ**, and Wykoff DD. (2018) “Dynamic Changes in Yeast Phosphatase Families Allow for Specialization in Phosphate and Thiamine Starvation.” G3: Genes, Genomes, Genetics, g3.200303.2018.
- c. Smoak RA, Snyder FL, Fassler JS, and **He BZ**. Parallel Expansion and Divergence of an Adhesin Family in Pathogenic Yeasts. Genetics. 2023 iyad024. PMID: 36794645

3. Stress response regulation is most well-studied in model organisms that are evolutionarily distant. This leaves the question of how stress responses evolve among related organisms unattainable. Our comparative studies of the phosphate starvation response (PHO) network between the free-living baker's yeast and a related commensal and opportunistic pathogen, *C. glabrata*, uncovered a dramatic network expansion in the latter due to derived changes in its main transcription factor (TF) protein Pho4. Follow-up work identified three independent mechanisms driving the reduced Pho2 dependence involving divergence mainly in the Intrinsically Disordered Regions (IDRs). This work highlights the importance of TF protein evolution in gene regulatory network evolution, especially divergence in the IDRs, which make up a large proportion of most eukaryotic TFs.

- d. **He BZ**, Zhou X, O'Shea EK. Evolution of reduced co-activator dependence led to target expansion of a starvation response pathway. *Elife*. 2017 May 9;6. PMCID: PMC5446240.

## E. RESEARCH SUPPORT

- 2020-2025      “Evolution of Stress Response Gene Regulatory Network in Commensal Yeasts” (R35 GM137831), \$1,250,000, NIH / NIGMS, PI
- 2020-2021      “Iowa Biosciences Academy - supplementary for computational biology education” ( 3R25GM058939-19S1), \$80,000, NIH / NIGMS, co-PI (PI: Lori Adams, co-PI: Bin Z. He, Jan Fassler)

## F. PUBLICATIONS

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### *Preprint and manuscripts in preparation*

- [1] Snyder LF, O'Brien EM, Zhao J, Liang J, Zhang Y, Zhu W, Cassier T, Schnicker NJ, Zhou X, Gordan R, **He BZ** (2024) Evolution of a Eukaryotic Transcription Factor's co-TF Dependence Involves Multiple Intrinsically Disordered Regions Affecting Activation and Autoinhibition. *bioRxiv* 2024.04.20.590343; doi: <https://doi.org/10.1101/2024.04.20.590343>

### *Peer-reviewed journal articles*

- [2] Rocca SM, Saldana DN, Addemir M, Koenig JA, **He BZ**, Miakotina OL, and Eberl DF (2024). Reflective Environment Heightens Crayfish Aggressive and Fearful Behaviors. *microPublication Biology*, doi:10.17912/micropub.biology.001184.
- [3] Liang J, Tang H\*, Snyder LF\*, Youngstrom CE, **He BZ** (2023) Divergence of TORC1-mediated Stress Response Leads to Novel Acquired Stress Resistance in a Pathogenic Yeast. *PLoS Pathog* 19(10): e1011748. (\* equal contribution)
- [4] Smoak RA, Snyder LF, Fassler JS, **He BZ** (2023). Parallel Expansion and Divergence of an Adhesin Family in Pathogenic Yeasts. *Genetics* 223(4) doi:10.1093/genetics/iyad024
- [5] Shao Y\*, Chen C\*, Shen H^, **He BZ**^, Yu D., Jiang S, Zhao S, Gao Z, Zhu Z, Chen X, Fu Y, Chen H, Gao G, Long M, Zhang YE (2019). GenTree, an integrated resource for analyzing the evolution and function of primate-specific coding genes. *Genome Res.* doi:10.1101/gr.238733.118 (\* and ^ indicate equal contributions)
- [6] Nahas JV, Iosue CL, Shaik NF, Selhorst K, **He BZ**, and Wykoff DD. (2018) “Dynamic Changes in Yeast Phosphatase Families Allow for Specialization in Phosphate and Thiamine Starvation.” *G3: Genes, Genomes, Genetics*, g3.200303.2018. (He BZ performed all phylogenetic analyses)

- [7] **He BZ\***, Zhou X, and O'Shea EK\* (2017). Evolution of reduced co-activator dependence led to target expansion of a starvation response pathway. *eLife* 6, e25157. (\* co-corresponding authors)
- [8] Chen J-Y, Shen QS, Zhou W-Z, Peng J, **He BZ**, Li Y, Liu C-J, Luan X, Ding W, Li S, Chen C, Tan C-M, Zhang YE, He A, Li C-Y. (2015) Emergence, Retention and Selection: A Trilogy of Origination for Functional *De Novo* Proteins from Ancestral LncRNAs in Primates. *PLoS Genet* 11(7), e1005391.
- [9] Yang H\*, **He BZ\***, Ma H, Tsaour S-C, Ma C, Wu Y, Ting C-T, Zhang YE. (2014) Expression Profile and Gene Age Jointly Shaped the Genome-Wide Distribution of Premature Termination Codons in a *Drosophila Melanogaster* Population. *Mol Biol Evol*, 32 (1), 216-228 (\* co-first authors)
- [10] **He BZ\***, Ludwig MZ, Dickerson DA, Barse L, Arun B, Vilhjálmsdóttir BJ, Park SY, Tamarina NA, Selleck SB, Wittkopp PJ, Bell GI, Kreitman M\*. (2014) A *Drosophila* Model to Investigate Natural Variation Effect in Response to Expression of a Human Misfolded Protein. *Genetics* 196 (2), 557-567 (\* co-corresponding authors)
- [11] Park SY, Ludwig MZ, Tamarina NA, **He BZ**, Carl SH, Dickerson DA, Barse L, Arun B, Williams C, Miles CM, Philipson LH, Steiner DF, Bell GI, Kreitman M. (2014) Genetic Complexity in a *Drosophila* Model of Diabetes-Associated Misfolded Human Proinsulin. *Genetics* 196 (2), 539-555
- [12] **He BZ\***, Holloway AK, Maerkl JS, Kreitman M\*. (2011) Does positive selection drive transcription factor binding site turnover? A test with *Drosophila* cis-regulatory modules. *PLoS Genet* 7(4): e1002053. (\* co-corresponding authors)
- [13] Lu J, Shen Y, Wu Q, Kumar S, **He B**, Shi S, Carthew RW, Wang SM, Wu CI. (2008) The birth and death of microRNA genes in *drosophila*. *Nature Genetics* 40 (3), 351-355.
- [14] Lou C, Yang X, Liu X, **He B**, Ouyang Q. (2007) A quantitative study of  $\lambda$ -Phage SWITCH and its components. *Biophysical Journal* 92 (8), 2685-2693.

### Other publications

- [15] **He B**, Kreitman M. (2010) Evolution of Cis-Regulatory Modules. In: *Darwin's Heritage Today: Proceedings of the Darwin 200 Beijing International Conference*, Long M, et al., eds, Higher Education Press, Beijing, China

## G. INVITED ORAL PRESENTATION AND SCIENTIFIC ENGAGEMENT

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2024	Invited seminar speaker, CAS Institute of Zoology, Beijing, China
2024	Invited seminar speaker, Department of Genetics and Development, Shanghai JiaoTong University, Shanghai, China
2024	Invited seminar speaker, Department of Molecular Microbiology and Immunology, University of Texas, San Antonio, TX
2024	Invited seminar speaker, Department of Biology, University at Buffalo, Buffalo, NY
2022	Invited keynote speaker, SMBE Satellite Meeting on the Evolution of Fungal Pathogenesis, Québec, Canada
2021	Invited speaker and panel co-organizer, Asia Evolution Conference, virtual
2020	Instructor, Summer Scientific Coding Workshop, the University of Iowa, IA
2017	Invited seminar speaker, Laufer Center for Physical and Quantitative Biology, Stony Brook University, Stony Brook, NY

- 2017 Invited seminar speaker, CAS Institute of Zoology, Beijing, China
- 2016 Invited seminar speaker, Villanova University, PA

#### H. MAJOR CONFERENCE PRESENTATIONS (FIRST AUTHORED)

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- 2023 Oral presentation, “Evolution of Acquired Stress Resistance in a Pathogenic Yeast”, SMBE Satellite Meeting on Mechanisms of Cellular Evolution, Tempe, Arizona, US
- 2022 Oral presentation, “Parallel Expansion and Divergence of an Adhesin Family in Pathogenic Yeasts”, SMBE Everywhere Global Symposium 6: Evolution of Genes and Gene Families, hybrid
- 2021 Poster presentation, Candida and Candidiasis Meeting, “Evolution of An Adhesin Gene Family in *C. auris* and Independently Derived *Candida* Pathogens in the Ascomycetes”, Microbiology Society, Virtual
- 2019 Oral presentation, “Convergent evolution of specialized phosphatase genes in yeast”, ASBMB Special Symposium on Evolution and Core Processes in Gene Expression, East Lansing, Michigan, US
- 2017 Oral presentation, “Evolution of a Starvation Response Pathway in a Commensal Yeast”, ASBMB Special Symposium on Evolution and Core Processes in Gene Expression, Kansas City, Missouri, US
- 2016 Oral presentation, “Evolution of a Starvation Response Pathway in a Commensal Yeast” Beyond cerevisiae workshop, The Allied Genetics Conference, Orlando, Florida, US
- 2013 Oral presentation, “A Drosophila Model to Investigate Natural Variation Effect in Response to Expression of A Human Misfolded Protein”, The 54th Drosophila Research Conference, Washington DC, US
- 2011 Oral presentation, “Does positive selection drive transcription factor binding site turnover? A test with Drosophila cis-regulatory modules”, SMBE Annual conference, Kyoto, Japan
- 2010 Oral presentation, “Evolutionary turnover of transcription factor binding sites in Drosophila enhancers”, Midwest Ecology and Evolution Conference, Ames, Iowa, US

#### I. TEACHING EXPERIENCE

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- 2022-2024 Sole instructor, BIOL:3212 “Bioinformatics for Beginners”, the University of Iowa, 30 undergrad and graduate students, workshop-based
- 2021 Created “Summer Scientific Coding Workshop” at the University of Iowa, a summer immersion program supported by the NIH R25GM058939-19S1, taught Python or R to groups of 6 undergrad and high school students (50 total) on zoom for 7 weeks, virtual
- 2019-2023 Created and taught BIOL:4386 “Introduction to Scientific Computing”, the University of Iowa, 10-15 undergrad and graduate students, computational reproducibility
- 2019-2021 Co-instructor with Prof. Jan Fassler, BIOL:4213 “Bioinformatics”, the University of Iowa, ~20-25 undergrad and graduate students, lecture + lab
- 2019-2023 Guest lecturer, GENE:6150 “Genetic Analysis of Biological Systems”, University of Iowa, ~10 graduate students
- 2015 Teaching Fellow, “G1 Model Organism Jamboree”, Harvard University, ~20 students
- 2012 Teaching Assistant, “Biological Systems”, The University of Chicago, ~40 freshmen, *led discussions and taught R programming*

- 2008 Teaching Assistant, “Evolution of Gene Regulation”, The University of Chicago, ~20 undergrad and graduate students, *tutored in-class scientific presentations*
- 2007 Teaching Assistant, “Fundamentals of Molecular Evolution”, The University of Chicago, ~30 undergrad and graduate students, *gave one guest lecture, led discussions and tutored labs.*

## J. MENTORING

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### ***Postdoc advisor***

- 2023 - Present Anthony Pannullo
- 2022 - Present Christopher Younstrom
- 2021 - 2022 Vivek Kumar Srivastava

### ***PhD Advisor***

- 2023 - Present Baylee Bruce; In Progress
- 2023 - Present Varshu Saravanakumar; In Progress
- 2019 - Present Snyder, Lindsey; In Progress
- 2018 - Present Liang, Jinye; In Progress
- 2018 - 2019 Godthi, Abhishiktha; Pre-comp student in my lab from 2018/12 - 2019/08

### ***MS Advisor***

- 2022 - Present Tang, Hanxi; In Progress

### ***Thesis/Dissertation Committee***

- 2024 - Present Christian Weinrich; In progress
- 2023 - Present Jacob Wells; In progress
- 2022 - Present Tian (Thea) Hui; In progress
- 2022 - Present Jerzy Mateusz Twarowski; In progress
- 2021 - Present Yann Vanrobaeys; In Progress
- 2021 - Present Nicole Recka; In Progress
- 2018 - 2023 Pannullo, Anthony; Completed
- 2018 - 2023 Hippee, Alaine; Completed

### ***Undergraduate advisor***

average 5 each year, current trainees listed below

- 2021 - Present Shriya Magatapalli, Neurosciences major
- 2021 - Present Jessica Miller, Chemistry major
- 2021 - Present Frannie Murphy, Bioinformatics major
- 2022 - Present Cole Belcher, first-gen, Biology major
- 2022 - Present Conrad Gerhardt, Biology major
- 2023 - Present Kelsey Martin, Biology major

### ***REU - Interdisciplinary Evolutionary Sciences advising***

- 2023 summer Ava Gabrys, PSU, PA
- 2022 summer Sarai Badillo, UT Permian Basin, TX

2021 summer    Athena Aguiar, Coe College, IA

***High School mentor***

2022 - 2022    Sierra Frisvold, currently undergrad at William and Mary College, VA

2021 - 2021    Shenyuan Chen, currently undergrad at UCSD, CA

2020 - 2021    Ananya Albrecht-Buehler, currently undergrad at Cambridge University, UK

**K. SERVICE**

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***Departmental***

2018 - 2023    Graduate Recruitment and Admission Committee, member

2023 - Present    Seminar Committee, member

***University***

2019 - Present    Graduate Affairs Committee, Interdisciplinary Program in Genetics, member

2019 - 2020    Institutional Biosafety Committee, member

***Professional***

2023, 2024    Steering Committee Member for the Midwest Neglected Infectious Disease Meeting

2022    Chair of the organizing committee for the International Symposium on Molecular and Evolutionary Genetics, celebration of the career of Marty Kreitman, Chicago, IL

2021    Co-chair for the Evolutionary Genomics panel, 1st AsiaEvo Conference (Virtual)

2009 - Present    Reviewer for *Journal of Molecular Evolution*, *PLoS Genetics*, *PLoS Computational Biology*, *PLoS One*, *Genetics*, *Molecular Biology and Evolution*, *Genome Biology and Evolution*, *G3*, *Cell Reports*, *Genome Research*, *Science Advances*, *eLife*, average 5 reviews per year