CURRICULUM VITAE Brenda Jean Andrews

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BIOGRAPHICAL INFORMATION

1. Degrees:

Ph.D., 1986, University of Toronto, Medical Biophysics Thesis title: Site-specific Recombination of the 2-micron plasmid of yeast Advisor: Paul D. Sadowski B.Sc. (Honours), 1980; University of Toronto, Zoology

2. Employment:

University Professor, The Donnelly Centre, Department of Molecular Genetics, University of Toronto, May 2017-

Director, The Donnelly Centre for Cellular and Biomolecular Research, University of Toronto, July 2004-June 2020 [re-appointed July 2009 and July 2014]

Canada Research Chair (Tier 1) in Systems Genetics & Cell Biology, 2020-

Charles H Best Chair in Medical Research, University of Toronto, July 2011-2020 **Professor,** Department of Molecular Genetics, University of Toronto, July 2000-May 2017 **Director,** Program on Genetic Networks, Canadian Institute for Advanced Research (CIFAR), 2006-2016; Senior Fellow 2016-2020

Adjunct Professor, Joint Institute of Genetics and Genome Medicine Zhejiang University School of Medicine, 2015-

Chair, Banting & Best Department of Medical Research, July 2004-June 2014

Chair, Department of Medical Genetics and Microbiology, Graduate Department of Molecular and Medical Genetics, University of Toronto, Jan 1999-July 2004

Coordinator, Molecular Medicine Program, Faculty of Medicine, University of Toronto, March 1, 1999-December 2003

Associate Professor with tenure, Department of Medical Genetics and Microbiology; Full Member, Graduate Department of Molecular and Medical Genetics, University of Toronto, July 1996-June 2000

Assistant Professor, Department of Medical Genetics, Member-Limited Term, Graduate Department of Molecular and Medical Genetics, University of Toronto, December 1990-July 1996.

Assistant Specialist and Postdoctoral Fellow, Department of Biochemistry and Biophysics, University of California, San Francisco, 1986-1990. Sponsor: Ira Herskowitz.

3. Honours and Awards:

• Canada Research Chair (Tier 1) in Systems Genetics & Cell Biology, Nov 2020-

- International Member (elected), National Academy of Sciences, USA, 2020
- University Professor, University of Toronto, 2017
- Jeanne Manery Fisher Memorial Award, Canadian Society for Molecular Biosciences, 2017
- Companion, Order of Canada, 2016
- JJ Berry Smith Doctoral Supervision Award, 2013 (inaugural award) School of Graduate Studies, University of Toronto
- The Emil Christian Hansen Award for Microbiology, 2013, The Carlsburg Foundation, Copenhagen (with Charles Boone)
- Fellow, American Academy of Microbiology, USA, 2012
- Charles H. Best Chair in Medical Research, University of Toronto 2011-2020
- Fellow of the American Association for the Advancement of Science, 2011
- Ira Herskowitz Award, Genetics Society of America, 2010
- Women in Science and Engineering (WISE) "Breaking the Glass Ceiling" Award, University of Toronto, 2007
- Fellow, Royal Society of Canada (Academy of Science), 2005
- Director and Fellow, Program in Genetic Networks, Canadian Institute for Advanced Research, 2005-present
- Premiers Research Excellence Award (PREA), 1999-2002
- Medical Research Council of Canada Scientist, 1997-2002
- Medical Research Council of Canada Scholarship, 1991-1996.
- Medical Research Council of Canada Fellowship, 1986-1989.
- Medical Research Council of Canada Studentship, 1981-1986
- Ann Shephard Scholarship for Biological Sciences, University College, University of Toronto, 1980.
- Ann Shephard Memorial Gold Medal for Biological Sciences, University College, University of Toronto, 1980.
- C.L. Burton Open Scholarship, University College, University of Toronto, 1979.

4. Professional Affiliations and National/International Activities:

Editorial Boards

Member, Advisory Editorial Board, Molecular Systems Biology, 2022-

Co-Editor, FEMS Yeast Research, Special Issue on Computational and systems biology strategies to understand yeast evolution and adaptation, 2022-

Editor, Section on *Big Data Acquisition & Analysis,* Current Opinion in Systems Biology, 2023-Member, Editorial Board, *Cell Systems*, Elsevier Press 2015-

Founding Editor in Chief, *Genes, Genomes, Genetics* > G3, a Genetics Society of America journal, 2011-2022

Editor, Yeast Model System: A Methods Guidebook, edited by B. Andrews, C. Boone, T., Davis and S. Fields, *Cold Spring Harb Protoc* 2015-2016

Guest Editor, *Critical Reviews in Biochemistry and Molecular Biology*, focused on "Omics and Cell Biology" 2016

Member, Editorial Board, *BMC Biology* [formerly *Journal of Biology* (BioMed Central], Sept 2008-2021

Member, Editorial Board, *Molecular & Cellular Proteomics* (ASBMB), Aug 2009-Sept 2014 Member, Editorial Board, *Eukaryotic Cell* (ASM), Jan 2010-December 2012 **Associate Editor,** Editorial Board, *Genetics* (Journal of the Genetics Society of America), December 2000-2010

Editor (North American), Yeast (John Wiley Interscience), June 2005-2012 **Editor,** *Microbiology and Molecular Biology Reviews* (formerly "Microbiological Reviews", a journal of the American Society of Microbiology), June 2003-2010

Board of Directors, Advisory Boards and Committees

2021-present and Ongoing:

Member Committee to Assist Science Evaluation (CASE), Quantitative Cell Biology Program, Center for Genomic Regulation (CRG), Barcelona, Nov 2023

Member, 2024 NAS Award in Molecular Biology selection committee

Chair, Vice Chair, Elected Member, EMBL (European Molecular Biology Laboratory) Scientific Advisory Committee: 2023-Chair, 2021-2023- Vice-Chair; 2018-2021 member

Member, SickKids Research Institute Science and Innovation Advisory Board (SAIB), Hospital for Children, Toronto, 2023-

Member, External Review Committee, Biological Sciences Platform, Sunnybrook Hospital Research Institute, Toronto, Jan 23rd 2023

Chair, External Review Committee, Life Sciences Institute, University of British Columbia, Jan 10th-13th 2023

Chair, External Advisory Committee, search for Director of the VIB Center for Computational and Quantitative Life Science Research, 2022-23

Ad-hoc member, Scientific Advisory Board, Friedrich Miescher Institute for Biomedical Research, Sept 19th-22nd 2022, Grindelwald, Switzerland

Program Consultant, Cellular Senescence Program (SenNet), NIH Common Fund consortium, 2021-

Member, External Review Committee, Robarts Research Institute, Western University, July 12th-14th 2021 (virtual)

Member, Scientific Advisory Board, Cancer Research UK City of London (CRUK CoL) Centre 2020-

Member, Board of Directors, Burroughs Wellcome Fund, 2019-

Member, Governing Council, Canadian Institutes for Health Research (CIHR), 2018- [Governor in Council appointment, Government of Canada]

Member, External Advisory Committee, Montreal Clinical Research Institute (IRCM), 2019-

Member, Scientific Advisory Committee, DOE Joint Genome Institute, Walnut Creek, CA 2018-

Member, Scientific Advisory Board, Department of Excellence (Ministry of Research Award), Università degli Studi di Milano 2018-

Member, Advisory Council, Microscopy and Image Processing Activity, Allen Institute for Cell Science, Seattle, 2016-

Member, California Institute of Regenerative Medicine (CIRM) Working Group (program and grant review body), 2013-

Member, International Advisory Board, New York University Abu Dhabi, 2012-

Member, Board of Directors, Genetics Society of America, 2011-2022

Member, Finance and Policy Committee of the International Yeast Community, 2008-

Selected earlier activities:

Member, Scientific Advisory Board, Center for Genomic Regulation (CRG), Barcelona, Spain, 2017-2020

Member, 2019 Robert L. Metzenberg Award Selection Committee, Neurospora Genetics community

Member, Transdisciplinary Centers Advisory Committee, March of Dimes, USA, 2013-2018 **Member**, Board of Directors, Centre for Commercialization of Antibodies and Therapeutics, 2015-2018

Chair, External Review Committee, Program in Systems Biology, University of Massachusetts Medical School, Nov 29th 2017, Worcester, MA

Member, International Review Committee, External Review of the Department of Biology, ETH Zurich, Sept 18-21, 2017

Member, External Advisory Board (EAB) for the San Diego Center for Systems Biology (SDCSB; <u>http://sdcsb.ucsd.edu/</u>), 2015-2018

Member, Joint Genome Institute (JGI) User Meeting Committee 2015-2017

Invited participant, Workshop on Peer Review Reforms, Canadian Institutes of Health Research, July 13, 2016, Ottawa, ON

Member, Site Visit committee, March of Dimes Prematurity Research Centre at Washington University St. Louis, Oct 1st 2015, Sept 29 2016, St. Louis MO

Invited participant, Strategic Planning Retreat, Joint Genome Institute (JGI), Lawrence Berkeley National Laboratory, Pacifica, California, Apr 13-14, 2015

Member, Expert Review Panel, Science for Life Laboratory (SciLifeLab), Stockholm, Sweden, 2015

Invited Participant and speaker, Workshop on "From Genome Function to Biomedical Insight: ENCODE and Beyond", NHGRI, March 10-11, 2015, Bethesda

Member, External Review Committee, McGill Life Sciences Complex, January 2015

Member, Site Visit for Investigator Award, Science Foundation Ireland (SFI), Dec 3-4 2015, Dublin, Ireland

Member, External Advisory Committee, Lewis-Sigler Institute, Princeton University, 2012-2015 **Member**, Scientific Advisory Board, March of Dimes, USA, 2012-2018

Member, External Review Committee, Program in Functional and Structural Genomics, German Cancer Research Center (DKFZ), Heidelberg, Dec 2-3 2013

Member, External Review Committee, Program in Genetics, Genomics and Bioinformatics, SUNY Buffalo, Sept 2012

Chair, External Review Committee, High Through-put Biology (HiT) Center, Johns Hopkins Medical School, April 2011

Member, Expert Evaluation Committee, Research Evaluation for Development of Research 2010 (RED10), University of Gothenburg, Sweden

Member, External Review Committee, Department of Molecular Microbiology, VIB, Flanders, Belgium, 2010

Ad-hoc Member, Scientific Advisory Board, Keystone Symposia, Jan 2010

Member and Chair, Institute Advisory Board, Institute of Genetics, Canadian Institutes of Health Research, 2005-2011

Member, Alberta Heritage Fund for Medical Research Scientific Advisory Council, 2009-2010 **Member,** Scientific Advisory Committee, National Research Council Biotechnology Research Institute (BRI), Montreal, Sept 2008-2011

Member, Science & Industry Advisory Committee (SIAC), Genome Canada, January 2004-(appointed co-Chair 2006)-2009

Chair, Presidential Task Force on Career Support, Canadian Institutes of Health Research (report Nov_04)

Chair, Scientific Advisory committee, Ontario Genomics Institute, 2002-2004 **Member**, Organizing committee, Cold Spring Harbor meeting on *Yeast Cell Biology*, August 1999, August 2001, August 2003

Vice-Chair, FASEB summer conference on Yeast Chromosome Structure, Replication and Segregation, 2002 (Chair, Ted Weinert, U. of Arizona; Co-Chair, Joachim Li, UCSF) Co-Chair, Medical Review Committee, The Gairdner Foundation, 2002-2006 Member, Medical Review Panel, The Gairdner Foundation, Sept. 1998-2002 Member, Science and Research Committee, MRC (1997-99)

Grant and Program Review Committees (ongoing and past 10 years)

Member, Life Sciences panel, Irish Research Council Laureate Advanced Awards (IRCLA) 2023 **Reviewer,** European Research Council (ERC) Synergy Grant applications (SyG2023), Jan 27th, 2023

Reviewer, RFA-RM-22-020: NIH Director's Transformative Research Awards, January 20th 2023 (anonymized review pilot)

Panel Member, LS2–Genetics, Genomics, Bioinformatics and Systems Biology, Advanced Grant evaluation, European Research Council, 2017, 2019, 2021, 2023 calls

Member, review committee for Genomics of ASD: pathways to biological convergence and genetic therapies RFA, Simons Foundation Autism Research Initiative (SFARI), Dec 1-2nd 2022 (zoom video)

Expert reviewer, Internal Evaluation process for national Cluster of Excellence in Life Sciences, University of Heidelberg, Nov 2022

Member, Special Emphasis Panel – 2023/01 GNOM-G 1 – Center of Excellence in Genomics (CEGS), NIH, Nov 3rd 2022 (zoom video)

Member, Genomics Computational Biology and Technology (GCAT) study section, NIH, June 9-10 2022 (zoom video)

Chair, Special Emphasis Panel - RFA-RM-21-020 - Cutting Edge Informatics Tools for Illuminating the Druggable Genome, NIH, October 5th 2021 (zoom video)

Member, ZRG1 IMST-U (65) Special Emphasis grant review panel, NIH, August 13 2021, online **Member,** California Institute for Regenerative Medicine (CIRM) Bridges Grant Review Panel, June 21, 2021 (virtual meeting); August 12, 2021 (virtual meeting)

Member, Life Sciences sub-committee to review Centres of Excellence grants (Phase 1), Research Council of Norway, virtual meeting, March 1st-5th 2021

Member, ZRG1 CB-S (55) R - PAR-19-367: Maximizing Investigators' Research Award (MIRA) Grant Review Panel, NIH, Nov 16th-17th online meeting, 2020

Chair, Special Emphasis Panel – 2020/08 ZRG1 BST-T (50) R - RFA Panel: 4D Nucleome Data Integration, Modeling, Visualization, Coordination and Organizational Centers and Hubs, NIH, July 2020

Member, Jury to evaluate the Laboratoires d'excellence (Labex) program, Agence Nationale de la Recherche, France, 2018

Member, U54 funding program to support the establishment of Tissue Mapping Centers, NIH, June 2018

Member, Special Emphasis Panel – Early-Stage Investigator Maximizing Investigator's Research Award (ESI-MIRA), NIGMS, March 2018

Member, College of Reviewers, Canadian Institutes for Health Research, 2017-

Chair, National Institute of Aging study section – RFA on Systems Biology of Aging, Feb 16th, 2017 Bethesda

External Reviewer, Project grants (University of Gothenburg), Knut and Alice Wallenberg Foundation, Sweden, October 2016

Member, NIH Special Emphasis Panel; Fellowship in Cell Biology, Developmental Biology and Bioengineering (F05), October 2016

Member, Review Panel, Ontario Strategic Review Panel for the Ontario Research Fund -Research Data Infrastructure, Jan 2016

Member, NIGMS MIRA R35 award study section (Maximizing Investigators' Research Award), Nov 9th-10th, 2015 Bethesda

Member, AACR Clinical and Translational Cancer Research Grants Scientific Review Committee 2015-2016

External Reviewer, Marine Microbiology Initiative (MMI), Gordon and Betty Moore Foundation, Experimental Model Systems strategy, 2015

Member, Expert Review Committee, NIGMS <u>National Centers for Systems Biology</u> Program, NIH USA, December 2014

Member, Expert Review Committee (47). Canadian Foundation for Innovation, Innovation Fund 2015, Sept 2014.

Member, ZHG1 HGR-M Genomics of Gene Regulation (GGR U01) study section, NHGRI, NIH, April 2014

Member, Review Panel 'S', March of Dimes, USA, 2013-

Member, Genomics grant review panel, Canadian Institutes of Health Research, Sept 2008-2015

Member, Alberta Innovates – Health Solutions (AIHS) Translation Health Chairs Review Committee, Aug 2013-

Member, Jury to review grants submitted to the program for National Research Consortia on Systems Medicine, German Federal Ministry of Education and Research (BMBF), April 2013, Berlin Germany

Member, F05-R Fellowship Study Section, National Institutes of Health, U.S.A., November 2012 **Chair**, ENCODE RFA review panel, NHGRI, National Institutes of Health, U.S.A., March 2012 **Member**, ZGM1 NDIA-C NIH Director's New Innovator Award Panel, National Institutes of Health, U.S.A., February 2012

Chair, ZRG-1 GGG-F Special Emphasis review panel, Genomic Sciences, National Institutes of Health, U.S.A., March 2011

Member and Chair, Grants review panel (Committee C), March of Dimes Foundation, U.S.A. [five-year term beginning 2003] – reappointed Chair, 2008-2012

Meeting organization

Member, Allied Program Committee, The Allied Genetics Conference (TAGC24), Genetics Society of America, to be held March 5 – 10, 2024 Washington DC

Member, Organizing committee for Cold Spring Harbor Asia Meeting on Yeast and Life Sciences, Matsue, Japan – Oct 9th-13th 2023 (also June 2021 hybrid meeting)

Member, International Advisory Committee (IAC) for ISSY37, International Specialized Symposium on Yeasts, 2023 (to be held in Adelaide, Australia)

Member, Organizing committee for Workshop on Data Generation, Allen Institute for Cell Science, 2022

Member, Organizing committee, joint International Conference on Yeast Genetics and Molecular Biology (ICYGM) and International Conference on Yeasts (ICY15) (August 22nd-26th 2021 – virtual meeting) **Member**, Organizing committee for Cold Spring Harbor Asia Meeting on Yeast and Life Sciences, Suzhou China –hybrid meeting, June 21st-23 2021

Co-organizer, Workshop on Molecular Networks, 29th International Conference on Yeast Genetics and Molecular Biology, August 18-22 2019, Gothenburg, Sweden

Co-Organizer, Workshop on New Fluorescent Probes and High-Throughput Imaging Approaches, 2018 ASCB | EMBO Meeting, Dec 8-12, San Diego CA

Co-Organizer, 15th Annual BCI (Breast Cancer Informatics)-McGill Workshop on Genetic Networks, January 22nd 29th, 2016, Bellairs Research Institute, Holetown, Barbados **Member**, Scientific Program Committee, International Conference on Systems Biology (ICSB) 2016 (Barcelona)

Co-Chair, Organizing Committee, The Allied Genetics Conference (TAGC), Genetics Society of America, Yeast Community meeting (summer 2016)

Organizer and Chair, Workshop on "Tools in Yeast Genetics", 2015 27th International Conference on Yeast Genetics and Molecular Biology, Trento, Italy (Sept 2015)

Conference co-Chair, American Association of Cancer Research (AACR) Special Conference on 'Cancer Computational and Systems Biology' 2015 Feb 9-11, San Francisco

Member, 2015 Scientific Program Committee, American Association of Cancer Research (AACR)

Conference co-Chair, RECOMB/ISCB Conference on Regulatory and Systems Genomics, with DREAM challenges 2013, Nov 8-12, Toronto

"Co-President", Organizing committee, 13th International Conference on Systems Biology, University of Toronto, August 2012

Member and Chair, Organizing committee, 2008 Yeast Genetics and Molecular Biology meeting (Genetics Society of America) (Vice-Chair, 2006 meeting, Princeton University) **Co-organizer,** Systems Biology theme, American Society of Biochemistry & Molecular Biology (ASBMB) annual meeting, 2008 (with Fritz Roth)

Member, International Organizing committee, 9th International Conference on Systems Biology ICSB2008 [Gothenburg, Sweden, August 23-27, 2008]

Member, Organizing committee, Cold Spring Harbor meeting on *Yeast Cell Biology*, August 1999, August 2001, August 2003

Vice-Chair, FASEB summer conference on Yeast Chromosome Structure, Replication and Segregation, 2002 (Chair, Ted Weinert, U. of Arizona; Co-Chair, Joachim Li, UCSF)

5. University of Toronto Activities: (2020- and ongoing)

Member, Department of Molecular Genetics Professional Standards in Mentorship and Education Committee, 2022-2023

Member, Working Group on Curriculum Development, Centre for Graduate Mentorship and Supervision (CGMS), School of Graduate Studies, University of Toronto 2022

Member, University of Toronto Internal College of Reviewers for Research Awards and Honours, 2018-

Member, Department of Molecular Genetics Promotions Committee, 2014-

Member, Department of Molecular Genetics Graduate Admissions Committee, 2020-

Member, Graduate Advisory Team, Department of Molecular Genetics, 2020-

Member, Academic Appeals Committee, Department of Molecular Genetics, 2021-

Member, Committee for Honorary Degrees, 2018-2021

Member, Research Working Group, James and Louise Temerty Building (JLTB) project, Faculty of Medicine, 2020-2021

Member, Best Fellowship application review committee, The Donnelly Centre, 2020-2022 **Chair**, Interim Review Committee, Aaron Reinke, Department of Molecular Genetics. 2020 **Chair**, Tenure Review Committee, Karen Maxwell, Department of Biochemistry, 2021

Summary of Most Significant Contributions

These contributions are compiled from Dr. Andrews' entire career as an independent investigator. Citation counts were taken from Google Scholar, Sept 28 2023.

1. Mechanisms of cell cycle-regulated gene expression. After starting her lab at the University of Toronto, Dr. Andrews launched a program to follow up on her postdoctoral work involving the discovery and characterization of cell cycle transcription factors, SBF and MBF, which instigate gene expression at the G1-S phase transition in budding yeast [Andrews & Herskowitz, Cell 57, 21 (1989); 207 citations; Andrews & Herskowitz, Nature 342, 830 (1989); 279 citations]. First, Dr. Andrews' group was the first to report that key cell cycle regulators, the G1 cyclins, are controlled by SBF [Ogas et al, Cell 66, 1015 (1991); 397 citations], and that phosphorylation of SBF helps link cell cycle progression to signaling pathways [Madden et al, Science 275, 1781 (1997); 329 citations] Second, a productive collaboration with Mike Tyers' group revealed that the cell size regulator Whi5 inhibits SBF and MBF and that cyclin-dependent kinase (CDK)-dependent phosphorylation dissociates Whi5 from SBF/MBF and drives Whi5 from the nucleus [Costanzo et al, Cell (2004) 117, 899; 552 citations1. Third, a series of papers from Dr. Andrews' lab describe the use of reagents and methods for functional genomics developed in her group (see below), to discover new regulators of cell cycle transcription. For example, significant roles for chromatin remodelers in regulating histone gene expression were discovered [Fillingham et al, Mol Cell 35, 340 (2009); 1010 citations], including a conserved chromatin boundary protein, Yta7, which is a target of S-phase specific CDKs [Kurat et al, Genes & Dev 25, 2489 (2011); 48 citations]. This line of research has produced important insights into mechanisms of cell cycle regulation, a highly conserved biological process that is universally perturbed in human diseases such as cancer.

2. Exploration of protein kinase function, regulation and targets. In her first few years at the University of Toronto, Dr. Andrews positioned her lab as a leading venue for the study of protein kinases, key regulators of cell division and signaling, using a combined genetic and biochemical approach. Her group discovered a new class of G1-regulatory cyclin-dependent protein kinases (Cdks), Pcl1-Pho85 and Pcl2-Pho85 [Measday et al, Science 266, 1391 (1994); 236 citations]. A combination of yeast genetics and cell biology was used to establish a clear role for G1-specific Cdks, including Pho85, in cell morphogenesis - these results overturned previous models of the G1-S phase transition in yeast [Moffat and Andrews, Nature Cell Biol. 6, 59 (2004); 128 citations]. Two-hybrid and other methods were then used to identify a family of 10 cyclins that can activate Pho85 to perform a variety of cellular functions including aspects of metabolism, cell cycle regulation, cell polarity and gene expression [Measday et al, Mol. Cell. Biol. 17, 1212 (1997); 264 citations]. Dr. Andrews' group then developed and applied functional genomic approaches involving systematic gene overexpression to identify new targets of Pho85 involved in cell polarity and transcription [Sopko et al, Mol. Cell 21, 319 (2006); 793 citations]. The approach was then used to survey the yeast kinome, and network motif analysis enabled prediction of pathways regulated by protein kinases [Sharifpoor et al. Genome Research (2012) 22, 791; 82 citations].

3. Genetic interactions, genetic networks and systems biology. In a long-standing collaboration with Charlie Boone's group, the Andrews lab developed a method, called Synthetic Genetic Array (SGA) analysis, for systematic (automated) genetic analysis using high density arrays of yeast deletion mutants [Tong et al Science 294, 2364 (2001); 2528 citations: Tong et al Science 303, 808 (2004); 2494 citations]. This methodology was applied in combination with a novel analytical pipeline for measuring genetic interactions based on a colony size phenotype [Baryshnikova et al, Nature Methods 7, 1017 (2010); 397 citations], to produce the first large-scale genetic interaction map for any system [Costanzo et al, Science 327, 425 (2010); 2426 citations]. A few years later, the Andrews and Boone groups, together with their computational colleague Chad Myers, published the complete reference genetic interaction network for the budding yeast, the only map of its kind [Costanzo et al, Science 353, 1381 aaf1420 (2016); 1103 citations]. The number of citations of the 'suite' of SGA papers indicates the major impact of this work, which revealed the power of systematic genetics for understanding cellular function and the incredible potential for genetic interactions for determining the genotype to phenotype relationship [Costanzo et al., Cell 177, 85 (2019); 177 citations]

Together, the Andrews and Boone labs have also: (1) expanded the SGA platform to enable systematic analysis of genetic suppression, a type of genetic interaction that likely underlies the resiliency of subsets of people to genetic diseases [*van Leeuwen et al, Science 354, aag0839 (2016); 175 citations*]; (2) used SGA to explore more complex genetic interactions, including triple mutant phenotypes [*Kuzmin et al, Science 360, eaao1729 (2018); 228 citations: Kuzmin et al, Science 368 (6498) (2020); 69 citations*], and the effect of genetic network complexity on phenotypic expression [*Hou et al, PNAS 116, 5045 (2019); 44 citations*] and; (3) in collaboration with Jason Moffat, begun to leverage insights from the yeast global genetic network to map genetic interaction networks in human cells using CRISPR-based approaches [*Aregger et al, Nature Metabolism 2, 499 (2020); 58 citations: Mair et al., Curr Opin Genet Dev. 54, 64 (2019); 30 citations*]].

4. High content imaging and phenomics. The Andrews lab has developed methods that combine SGA with multi-dimensional phenotypic readouts, including transcriptional reporter genes (see above) and fluorescent markers of various subcellular compartments or of the entire yeast proteome [reviewed in Usaj et al, Trends in Cell Biol 26, 598 (2016), 258 citations; Grys et al, J. Cell Biol. 216, 65 (2017); 154 citations]. As part of this project, the Andrews group developed a computational framework to quantify changes in protein localization and abundance in an automated manner and applied these approaches to measure abundance and localization dynamics of the yeast proteome in response to genetic and environmental perturbations [Chong et al, Cell 161, 1413 (2015); 307 citations]. More recently, Dr. Andrews' lab developed a convolutional neural network for automated image analysis and demonstrated its utility for interpreting a variety of large-scale image-based datasets [Kraus et al, Mol Systems Biol 13, 924 (2017); 271 citations]. The lab is currently applying similar methods to quantify diverse cell biology phenotypes associated with nonessential deletion mutants and temperature sensitive alleles of essential genes as well as to assess cell cycle- and environment-dependent changes in protein dynamics and abundance [Usaj et al, Mol Systems Biol. 16, e9243 (2020); 38 citations].

5. Large scale exploration of gene function in yeast. Functional genomics efforts in the Andrews lab involve the construction of strain collections that serve as a resource for the yeast

community and enable systematic exploration of gene function. In particular, the Andrews and Boone labs have collaborated to assemble a pipeline for the efficient construction of collections of yeast strains for genome-wide analysis of genetic interactions and for systematic phenotypic analysis. These reagents include: (1) collections of strains temperature-sensitive alleles of essential genes [Li et al, Nature Biotech 29, 361 (2011); 422 citations]: (2) arrayed collections of strains overexpressing yeast genes [see above; and Douglas et al G3 2, 1279 (2012); 97 citations]; (3) collections of bar-coded plasmids expressing each yeast gene [Ho et al, Nat Biotech. 27, 369 (2009); 307 citations; Arita et al, Mol Syst Biol 17), e1020 (2021); 34 citations]: (4) a set of 'bar-coder' strains that facilitate the introduction of molecular barcodes into any collection of yeast strains [Yan et al, Nat Methods 5, 719 (2008); 117 citations]; (5) complete collections of viable haploid deletion mutants in the SGA guery strain background [Costanzo et al, 2010 see above] and in the sigma strain background which undergoes filamentous growth (Ryan et al, Science 337, 1353 (2012); 235 citations). Few groups in the world have made comparable collections, which are freely available, inspiring work in labs internationally and providing a roadmap for development of comparable collections in other systems. The collections have been widely used and have provided information about specific gene functions, and more general insights. For example, the conditional essential mutant collection enabled the systematic scrutiny of the function of this highly conserved gene set. The essential genes show functionally relevant profiles with ~5X more genetic interactions than nonessential genes, generating the fundamental scaffold of the global genetic network, a discovery is particularly important for future strategies to map analogous genetic networks in human cell models.