OMB No. 0925-0001 and 0925-0002 (Rev. 10/2021 Approved Through 09/30/2024)

BIOGRAPHICAL SKETCH

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NAME: Fred Chang

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

POSITION TITLE: Professor

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
Princeton University, NJ	A.B.	06/1984	Biology
University of California, San Francisco, CA	Ph.D.	06/1991	Genetics, Biochemistry
University of California, San Francisco, CA	M.D.	06/1992	Medicine
Imperial Cancer Research Fund, London, UK	postdoctoral	09/1994	Genetics
University of California, Berkeley, CA	postdoctoral	12/1996	Biochemistry

A. Personal Statement

My lab studies fundamental mechanisms of cell morphogenesis. I received my training in yeast genetics and cell biology. As a PhD student with Ira Herskowitz, I studied cell cycle regulation in budding yeast and identified the first cell cycle kinase inhibitor Far1. As a postdoctoral fellow with Paul Nurse and David Drubin, I helped to establish fission yeast as a molecular genetic model for cytokinesis. I started my laboratory at Columbia Medical Center in 1997 and moved to UCSF in 2016. My lab has been NIH-funded since 1998 and is currently supported by an NIH R35 (MIRA), NSF, and UCSF Sandler PBBR grants. My lab has established many areas of study in fission yeast cell biology, including cytokinesis, actin and microtubule regulation, nuclear positioning, cell size and cell cycle regulation, polarized cell growth, and cell mechanics. I have longstanding interests in the dynamics of cellular structures and molecules in living cells, mechanical forces, regulation of cell size and scaling relationships, and effects of size and shape on cellular processes. In general, my work integrates physical biology with quantitative yeast cell biology and genetics. Many of our stories represent synergistic collaborations with physicists and modelers, and we gain inspiration from our scientific communities at UCSF and the Marine Biological Laboratories. I have established stellar interdisciplinary teams of collaborators who include: K.C. Huang, Julie Theriot, Liam Holt, Sophie Dumont, Thomas Fai, Gary Brouhard and Alexey Khodjakov.

Diversity: I am strongly committed to supporting diversity, equity and inclusivity in STEM. As an LGBTQ individual and an Asian-American, I am increasingly aware of the inequities and challenges that are faced by scientists and learners coming from underrepresented and disadvantaged groups. I believe that diversity is a critical component in the world of academic science and education, and thus there is a pressing need for equitably support the diverse representation of scientists at all levels including learners, staff, faculty and academic leadership. In my lab, I strive to create an inclusive climate where all members are valued and respected. Through my career, I have maintained research teams composed of individuals coming from diverse backgrounds, race/ethnicity, genders, sexual orientation, nationalities, family commitments etc. I believe that such diversity fosters innovative, creative science; for example, I have had the experience where the most junior member of my group transformed a colleague's project by simply expressing a different perspective.

I currently serve as the co-chair of the LGBTQ+ committee at the American Society of Cell Biology. With this committee, we are working on initiatives such as: 1) organizing multiple events at the Annual Meeting that honor and support LGBTQ+ scientists, learners, and their allies, 2) identifying the community through a speakers list and data collection, 3) building community through year-round online blogs and social media, and 4) advocating for public policy. Through such activities, we hope to build a supportive community of LGBTQ+ cell biologists. As an example of policy, I recently co-wrote a letter on behalf of ASCB asking the NIH to include LGBTQ+ groups in its DEI plan. I have been honored to speak at forums featuring LGBTQ+ scientists. I am a member of national LGBTQ+ organizations such as Out to Innovate and 500 Queer Scientists. I mentored many learners from underrepresented and disadvantaged groups. At UCSF, I served a term on the campus-wide LGBTQ committee and am currently on the Equal Opportunity committee that addresses issues pertaining to faculty equity. I also serve on DEI committees in my department and graduate program to improve the climate and support students from underrepresented and disadvantaged groups at UCSF. My long-term goals include advocating for national policy initiatives that support LGBTQ+ and other underrepresented groups in science.

Mentoring and Service: I have served on NIH cell biology grant study sections for two full terms. I served as an Associate Editor for Molecular Biology of the Cell journal for 15 years. I have also chaired two key Gordon Research Conferences which have impacted my field. My proudest achievements have been in the successful training of lab members. For example, 9 postdocs have gone on to build successful labs (at U. Penn, Inst. Curie, U. Lausanne. Jacob Monod etc.), many of whom have helped to establish the *S. pombe* cell biology/ biophysics community. I have mentored 8 PhD students in my lab, and currently supervise one PhD student in my lab. I am active in three graduate programs at UCSF (Biophysics, Tetrad, and Biomedical Sciences), in which I participate in teaching courses, journal clubs, mentor students, participate in qualifying exams and thesis committees, and participate in interviews and recruitment. I am committed towards empowering my lab members to be independent thinkers and enabling them to reach their own potential and obtain their life goals.

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

2016- present	Professor, UCSF, Dept. of Cell and Tissue Biology
2007-2015	Professor, Columbia University Medical Center, Dept. of Microbiology & Immunology
2004-2007	Associate Professor (with tenure). Columbia University Medical Center, Dept. Microbiology
2000- present	Whitman Summer Investigator, Marine Biological Laboratory.
1997-2004	Assistant Professor, Columbia University Medical Center, Department of Microbiology

Other Experience and Service

2022-	ASCB Awards Coordination Committee, member
2021-	UCSF Equal Opportunity Committee, Academic Senate
2021-	UCSF Biophysics Graduate Program DEI committee
2020-2021	ASCB Nominating Committee, member
2019-2021	LGBTQ Committee, UCSF
2017-	LGBTQ+ Committee, ASCB, 2021-present co-chair
2017-2021	Whitman Scientist Steering Committee member, Marine Biological Laboratories
2013-2015	Chair and Vice Chair of Gordon Research Conference on Motile and Contractile Systems2012-
2014	Chair and Vice Chair of Gordon Research Conference on Plant and Microbial Cytoskeleton
2012-2018	NIH NCSD study section, regular member
2011-	MBL Physiology Course Lecturer
2005-2020	Associate Editorial Board *Molecular Biology of the Cell*
2005-	Co-organizer of Cytoskeleton Seminar series, Marine Biological Laboratories
2005-2009	NIH NBT study section, Regular Member

Honors

2022	ASCB President nominee
2017	Featured speaker at LGBTQ+ session, ASCB meeting
2016-	Erph Gil Endowed Professorship, UCSF
2009	Ellison Senior Scholar Award
2003	Lamport Award for Excellence in Basic Research, Columbia U.

2002 Universal Imaging Corporation Fellow, Marine Biological Laboratories, MA
2001 Nikon Fellow, Marine Biological Laboratories, MA
2000 Irma T. Hirschl Career Scientist Award
1998 March of Dimes Basil O'Connor Starter Scholar Award
1992 Helen Hay Whitney Postdoctoral Fellow
1986 Dean's Prize for Medical Student Research, University of California, San Francisco

C. Contributions to Science

PhD Thesis - Cell Cycle Regulation

As a graduate student at UCSF, I worked in the lab of Ira Herskowitz where I identified Far1 through a genetic screen as a factor in budding yeast that mediated cell cycle arrest in response to pheromone by inhibiting CDK/G1 cyclins (Chang and Herskowitz, 1990); this was the first CDK inhibitor identified.

Cytokinesis and Formins

In my early career, I helped to establish fission yeast as a leading eukaryotic model for cytokinesis. As a postdoc with Paul Nuse and David Drubin, I conducted a forward genetic screen for cytokinesis genes, and cloned Cdc12 as one of the founding members of formin class of actin nucleators. This work identified a conserved set of cytokinesis genes that have since been shown to be generally implicated in cytokinesis in eukaryotes. We provided a critical finding that formin proteins are essential for forming specific actin structures (cytokinesis ring and actin cables) *in vivo* (Chang et al, 1997; Pelham and Chang, 2002). We also elucidated mechanisms for positioning the division plane. While the mitotic spindle sets the position of the cleavage furrow in mammalian cells, in the fission yeast, the nucleus dictates the position of the subsequent plane of division, by positioning Mid1 nodes on the plasma membrane (Daga and Chang, 2005).

- Chang F., Woollard A. and Nurse P. Isolation and characterization of fission yeast mutants defective in the assembly and placement of the contractile actin ring. J Cell Sci. 1996 Jan;109 (Pt 1):131-42
- Chang F., Drubin D. and Nurse P. cdc12p, a protein required for cytokinesis in fission yeast, is a component of the cell division ring and interacts with profilin. J Cell Biol. 1997 Apr 7;137(1):169-82
- Pelham R.J. and Chang F. Actin dynamics in the contractile ring during cytokinesis in fission yeast. Nature. 2002 Sep 5;419(6902):82-6.
- Daga R.R. and Chang F. Dynamic positioning of the fission yeast cell division plane. Proc Natl Acad Sci U S A. 2005 Jun 7;102(23):8228-32.

Positioning the Nucleus with Microtubules

We determined that in fission yeast the nucleus is positioned in the middle of the cell through a microtubule pushing-based mechanism (Tran et al., 2001). This is now a classic example of a MT pushing-based mechanism. By displacing the nucleus using cell centrifugation, we showed that MT bundles effectively can recenter the nucleus (Daga, 2006). We showed in sea urchin embryos how cell shape controls spindle orientation and division plane placement through nuclear positioning (Minc et al., 2011); we proposed a "universal law" that has now been used to predict division plane orientation in many contexts during development. In this work, we introduced a novel method of shaping cells by placing them into micro-fabricated wells of specified shapes, a method now used widely in investigations of cell geometry and synthetic biology. Another function of cytoplasmic MTs is to move chromosomes inside the nucleus, through links at the spindle pole body composed of the LINC complex and Csi1 (Hou et al, 2014). In Zhurinsky et al., 2019, we identified an unexpected function of interphase cytoplasmic MTs and the MT nucleation factor Mto1 in dsDNA break repair and cohesin loading possibly through chromosome movements.

- Tran PT, Marsh L, Doye V, Inoué S, Chang F. A mechanism for nuclear positioning in fission yeast based on microtubule pushing. J Cell Biol. 2001 Apr 16;153(2):397-411. PubMed Central PMCID: PMC216946
- Daga RR, Yonetani A, Chang F. Asymmetric microtubule pushing forces in nuclear centering. Curr Biol. 2006 Aug 8;16(15):1544-50. PubMed PMID: 16890530

- Minc N, Burgess D, Chang F. Influence of cell geometry on division-plane positioning. Cell. 2011 Feb 4;144(3):414-26. PubMed PMID: 21295701; PubMed Central PMCID: PMC3048034
- Zhurinsky J, Salas-Pino S, Iglesias-Romero AB, Torres-Mendez A, Knapp B, Flor-Parra I, Wang J, Bao K, Jia S, Chang F*, Daga RR. Effects of the microtubule nucleator Mto1 on chromosomal movement, DNA repair, and sister chromatid cohesion in fission yeast. Mol Biol Cell. 2019 Oct 1;30(21):2695-2708. PMC6761766. Supported by R01-GM115185. *Co- corresponding and co-senior author.

Regulation of Microtubules by TOG domain proteins

We established fission yeast as a model to study regulation of microtubule (MT) dynamics and organization (Tran and Chang, 2001). In recent years, we have focused on a class of MT regulators known as TOG-domain proteins: CLASP/ Cls1 and XMAP215/ Alp14 in collaboration with Jawdat Al Bassam. We established the function of CLASP as a MT rescue factor and XMAP215 as a MT polymerase that stimulates MT polymerization rates and MT nucleation (Bratman and Chang, 2007, Al-Bassam et al., 2012, Flor-Parra, 2018) With Jawdat Al-Bassam, we present crystal structures of two large complexes of Alp14 TOGs with tubulin, which suggest mechanisms for MT polymerase activity and MT plus end tracking (Nithianantham et al., 2018).

- Bratman SV, Chang F. Stabilization of overlapping microtubules by fission yeast CLASP. Dev Cell. 2007 Dec;13(6):812-27. PMCID: PMC2215317
- Al-Bassam J, Kim H, Flor-Parra I, Lal N, Velji H, Chang F. Fission yeast Alp14 is a dose-dependent plus end-tracking microtubule polymerase. Mol Biol Cell. 2012 Aug;23(15):2878-90. PMCID: PMC3408415.
- Flor-Parra I, Iglesias-Romero AB, Chang F. The XMAP215 Ortholog Alp14 Promotes Microtubule Nucleation in Fission Yeast. Curr Biol. 2018 Jun 4;28(11)1681-1691.PMID: 29779879. Supported by R01-GM115185
- Nithianantham S, Cook BD, Beans M, Guo F, Chang F, Al-Bassam J. Structural basis of tubulin recruitment and assembly by microtubule polymerases with tumor overexpressed gene (TOG) domain arrays. Elife. 2018 Nov 13;7. doi: 10.7554/eLife.38922. PMC6251626.

Cell Mechanics and Turgor Pressure.

My lab has made significant contributions in introducing physical factors such as cellular mechanics and osmotic pressure to our understanding of cell morphogenesis, division and endocytosis (Chang, 2017). We developed approaches to measure mechanical properties of fission yeast, showing that they have high turgor pressure of 1.5 MPa and a tough elastic cell wall that is expanded by this pressure (Atilgan et al., 2015; Minc et al., 2008). This high internal pressure impedes the ingression of the plasma membrane at the cytokinesis furrow (Proctor et al, 2012) and endocytic sites (Basu et al, 2014). In Proctor et al., 2012, we discovered that the actin contractile ring is actually dispensable for ingression, and propose that cell wall synthesis provides the primary force that drives ingression for cytokinesis. These results have led to a general reconsideration in the field of the contribution of contractile ring forces in cytokinesis across kingdoms. In Zhou et al, 2015 we showed that a function of the ring is to modulate cell wall synthesis to shape the septum. In this work, we developed an innovative method for imaging cytokinesis by positioning fission yeast cells vertically in micro-fabricated chambers. In Atilgan et al. 2015, we used experiments and modeling to show that turgor pressure inflates the elastic cell wall of the septum to form the rounded shape of “new” end of cell after cytokinesis. In general, these studies have high impact in elucidating the function of cell mechanics, turgor pressure and cell wall properties in the morphogenesis of walled cells.

- Chang F. Forces that shape fission yeast cells. Mol Biol Cell. 2017 Jul 7;28(14):1819-1824. PMCID: PMC5541833. Supported by R01-GM056836
- Zhou Z, Munteanu EL, He J, Ursell T, Bathe M, Huang KC, Chang F. The contractile ring coordinates curvature-dependent septum assembly during fission yeast cytokinesis. Mol Biol Cell. 2015 Jan 1;26(1):78-90. doi: PMCID: PMC4279231. Supported by R01-GM056836
- Atilgan E, Magidson V, Khodjakov A, Chang F. Morphogenesis of the Fission Yeast Cell through Cell Wall Expansion. Curr Biol. 2015 Aug 17;25(16):2150-7. Supported by R01-GM056836

Cell Growth: Control of Intracellular Density and Cell Size.

We have a longstanding interest in regulation of polarized growth, especially in microtubule- actin interactions through Tea proteins and formins (Chang and Martin, 2009). Knapp et al., 2019 served as the starting point for

our investigations into cell density. In proliferating cells, the rates of biosynthesis and volume growth must be coordinated in some way. In investigating the effects of turgor pressure on cell growth, we fortuitously discovered ways of uncoupling these processes. We found that inhibiting cell volume growth (by osmotic oscillations or secretion inhibition) caused the concentration of many proteins progressively increase. Upon removal of this inhibition, cells exhibit unusually rapid tip growth (supergrowth) for multiple cell cycles, during which density gradually decreases back to normal levels. The relationships between density and volume suggest a simple model for cell density homeostasis based upon regulation of volume growth rates. In Odermatt, et al., 2020, we used quantitative phase imaging to show variations of intracellular density in the fission yeast cell cycle. We show systematic variations in density in normal proliferating cells that arise from programmed changes in cell cycle regulated volume growth rates, again showing how volume growth and mass growth can be decoupled. In Molines et al. 2020 we show that the biophysical properties of the cytoplasm dampen microtubule dynamics predominantly through viscosity.

- Knapp BD, Odermatt P, Rojas ER, Cheng W, He X, Huang KC, Chang F. Decoupling of Rates of Protein Synthesis from Cell Expansion Leads to Supergrowth. Cell Syst. 2019 Nov 27;9(5):434-445.e6. PMC6911364. Supported by R01-GM056836
- Odermatt P, Bostan E, Huang K, Chang F. Variations of intracellular density during the cell cycle arise from tip-growth regulation in fission yeast. eLife 2021;10:e64901 DOI: 10.7554/eLife.64901
- Molines A.T, J. Lemière, C.H. Edrington, C-T. Hsu, I.E. Steinmark, K. Suhling, G. Goshima, L.J. Holt, G. J. Brouhard, F Chang. Physical properties of the cytoplasm modulate the rates of microtubule growth and shrinkage. Dev Cell 2022 57(4), 466-479.

Control of Cell and Nuclear Size

We study how cell size is regulated and maintained in proliferating cells. Fission yeast cells grow to a certain minimal threshold size before entering mitosis, using a “sizer” mechanism. We showed that fission yeast cells divide at a constant surface area, not their length or volume, suggesting that they somehow sense their surface area (Pan et al., 2014; Facchetti et al., 2019). Cell size sensing may involve a network of protein kinases that regulate mitotic entry (Cdr2, Pom1, Cdr1) that assemble into protein clusters on the plasma membrane. We have recently described how nuclear size is determined by a balance of osmotic forces produced by macromolecules present in the nucleus and cytoplasm (Lemiere et al., 2022).

- Pan K., Saunders T.E., Flor-Parra I., Howard M. and Chang F. Cortical regulation of cell size by a sizer Cdr2. eLife. 2014. 24642412. PMCID: PMC395629
- Facchetti G, Knapp B, Flor-Parra I, Chang F, Howard M. Reprogramming Cdr2-Dependent Geometry-Based Cell Size Control in Fission Yeast. Curr Biol. 2019 Jan 21;29(2):350-358.e4. PMC6345630. Supported by NSF/BIO MCB-1638195.
- Lemière J, Real-Calderon P, Holt LJ, Fai TG, Chang F. Control of nuclear size by osmotic forces in *Schizosaccharomyces pombe*. bioRxiv 2021**:** https://doi.org/10.1101/2021.12.05.4712

Bibliography

For complete list, see: https://www.ncbi.nlm.nih.gov/myncbi/fred.chang.1/bibliography/public/