

CURRICULUM VITAE

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Cell death, neurodegenerative disease and mitochondrial quality control. One of our goals is to understand the genetic and molecular mechanisms that regulate cell death, neurodegeneration, and cancer. Much of our work on neurodegeneration, particularly as it relates to defects in mitochondrial function, Alzheimer's disease and Parkinson's disease, occurs in collaboration with the lab of Ming Guo, MD, PhD, a practicing Neurologist and researcher at UCLA (<http://guolab.neurology.ucla.edu/>). Expression from the mitochondrial genome (mtDNA) is required in almost all cells for respiration. Mutant mtDNA accumulates during adulthood and contributes to many diseases of aging, including Alzheimer's, Parkinson's, diabetes and muscle wasting. We are particularly interested in devising methods for selectively removing damaged mtDNA. We have developed a model of mtDNA mutation accumulation in muscle and are using this system to identify molecules that can promote the selective removal of mutant mtDNA, a form of quality control. In other work we have extended the system to the nervous system. In short, our goal is to engineer mtDNA "housecleaning" during adulthood. Our recently published results indicate that we can promote the removal of ~80% of mutant mtDNA in *Drosophila* muscle. We are, naturally, interested in expanding this work into human systems, and drug screens.

Engineering the mitochondrial genome, and movement of mitochondria between cells. Recent evidence from a number of labs suggests that mitochondria can move between cells. In some contexts mitochondria apparently move from healthy cells to cells that have been damaged or are under stress, helping to restore or maintain function. In other contexts, mitochondrial move into tumor cells, and there is evidence that this promotes their growth and/or survival. The idea that mitochondria might move between cells in physiological contexts is quite exciting but essentially unexplored. Such mitochondria could provide a localized source of energy production in the recipient cell. They could also be involved in a number of other local mitochondria-based metabolic activities. Finally, because mitochondria carry their own genome, such movement would also be associated with the long-term movement of self-replicating information between cells. Given the high frequency of heteroplasmysy for pathogenic mutations noted above, it also becomes interesting to determine the contexts in which mitochondria move between cells of the nervous system, and whether this acts to promote normal function and/or spread pathology. How a recipient cell signals need, and how the donor receives this signal and translates it into an act of donation is unknown. Nothing is known about what molecular pathways are important for transfer in vivo.

In order to address these questions, we need simple and quantitative methods for measuring mitochondrial donation, uptake and entry into the cytoplasmic compartment, in which mitochondria function. To this end we are working to create transgenic mitochondria, and to generate other methods of following the movement of mitochondria between cells that can be used in cell culture and in vivo-based screens.

Controlling the composition and fate of wild populations. A third set of projects address three questions in applied evolutionary population biology. 1) Can we bring about reproductive isolation (speciation) between populations of plants or animals that otherwise freely interbreed? Answers to this question have application to the growing number of situations in which plants and animals are engineered to show specific pharmaceutical or agricultural traits. In brief, we would like to be able to limit gene flow between engineered organisms and their wild counterparts. 2) Can we engineer the genetics of populations so that they drive themselves to local extinction? For example, invasive non-native plants and animals cause substantial economic losses and sometimes function as vectors of disease. A number also cause substantial environmental damage, leading in many cases to extensive range reduction and/or extinction of unique, endemic species. Our goal is to develop genetic tricks that drive local extinction of invasive species and disease vectors. 3) Can we drive genes into wild populations (population replacement) such that all individuals express a trait of interest? With regard to this last aim, we are also interested in developing transgenic mosquitoes that lack the ability to transmit pathogens such as malaria, dengue fever and chikungunya. We are also working with the citrus industry to develop population replacement-based strategies to prevent the citrus psyllid, an invasive insect, from transmitting *Candidatus Liberobacter*, the causative agent of the citrus disease HLB.

Engineering organismal physiology: Lifetime, single shot contraception as an example. In a third project we are working to develop single shot, lifetime (but reversible) contraceptives for a variety of mammalian species. In brief, there remains a need for very long-term or permanent, non-surgical methods of male and female contraception for humans that can be implemented in resource-poor settings in which access to health care may be sporadic. There is also a desire for non-lethal, humane, methods of population control for captive and free roaming animals. We have developed a technology, vectored contraception (VC), which can contribute to these goals. In VC an intramuscular injection is used to bring about transgene-mediated expression of a monoclonal antibody or other protein able to inhibit fertility through action on a specific target. In proof-of-principal experiments we recently showed that a single intramuscular injection of a replication defective, recombinant adeno-associated virus (rAAV) designed to express an antibody that binds gonadotropin releasing hormone (GnRH), a master regulator of reproduction in all vertebrates, results in long-term infertility in male and female mice. Female mice are also rendered infertile through rAAV-dependent expression of an antibody that binds the mouse zona pellucida (ZP), a glycoprotein matrix that surrounds the egg and serves as a critical sperm-binding site. Many proteins known or suspected to be important for reproduction can be targeted using VC, providing a new class of strategies for bringing about long-term inhibition of fertility in many species. We are working to implement several of these, along with strategies for bringing about reversal on demand.

Engineering antigen-specific tolerance. Antigen-specific tolerance is desired in autoimmunity, transplantation, allergy, type I diabetes and other diseases. It is also desirable in the context of

therapy with autologous proteins and non-autologous proteins. Such a method can be especially useful for those receiving recombinant proteins. There are a variety of recombinant proteins (RP) that are introduced into people on a chronic basis. Adverse reactions occur in some of these patients. In addition, induction of an anti-drug immune response can result in loss of RP efficacy. Antibodies generated against the RP are one important mechanism by which the abovementioned failures can occur. In some cases the RP is a foreign protein, and the RP is simply seen as non-self and eliminated through activation of an immune response. In other cases, antibodies are raised against therapeutic antibodies, which have undergone extensive "humanization" so as to be rendered as "self like" as possible. However, even in these cases anti-antibody responses are sometimes induced. More generally, autoimmunity arises when the immune system recognizes self-antigens as foreign. We are developing ways of tagging proteins that promote their being seen as self-antigens, thereby preventing an immune response, or eliminating an ongoing immune response. In brief, this strategy involves tagging the protein of interest with a phosphatidylserine-binding domain. Phosphatidylserine acts as an "eat me" signal on the surface of cells undergoing apoptosis (billions of cells each day in humans). When cells undergoing apoptosis are taken up by phagocytic cells, their proteins are presented on the phagocytic cell surface in a way that promotes immunological tolerance to them. By targeting antigens of interest to dying cells (through linkage with a phosphatidylserine-binding domain) we hope to leverage this normal tolerance-inducing process to induce tolerance to foreign proteins and self-antigens associated with autoimmunity.

Interactive learning and Community Science Academy. For a number of years I have been pioneering use of the SKIES learning system (<https://www.skieslearn.com/>) to enhance student participation in class, to provide new forums for asking questions, and to encourage students to add their own content to my lectures, in the form of links to scientific articles, in-class clarifications, in-depth explanations, and flashcards. More recently, a number of other Professors have begun using this system. An important goal going forward is to create links between classes so as to create a more general web of knowledge that students and others can use to explore.

In a second, related activity, I hosted the beginnings of The Community Science Academy at Caltech (CSA@Caltech) (<https://csa.caltech.edu/>). The goal of CSA, initiated by two Caltech alumni, James Maloney and Julius Su, is to develop curriculum and instrumentation to support low cost but high quality science relevant to community needs. CSA is currently hosted by the Caltech Center for Teaching, Learning and Outreach. I also served as PI on a grant from the Camille and Henry Dreyfus Foundation, Special Grant Program in the Chemical Sciences, 2014-2015. The goal of this grant is to foster High School community science and the design of portable custom molecular sensors.

Education:

1978-1982 Claremont McKenna College, Claremont CA. B.A. in Biology

1983-1989 University of California, San Francisco, San Francisco, CA. Ph.D. Neuroscience.
Thesis advisor Yuh Nung Jan

Research and Professional Experience:

- 1982-1983 Research Assistant with Dr. Daniel Alkon, Marine Biological labs, Woods Hole, MA. Research topic: Characterization of ionic currents in molluscan and vertebrate neurons
- 1983-1989 Graduate student Neuroscience Program with Dr. Yuh-Nung Jan, University of California, San Francisco. Ph.D, Neuroscience, 1989. PhD Thesis: Identification and characterization of genes required for germ cell specification in *Drosophila melanogaster*.
- 1990 Postdoctoral fellow with Dr. Yuh-Nung Jan, University of California, San Francisco, Departments of Physiology and Biochemistry. Research Topic: Identification and characterization of *germ cell-less*, a gene required for germ cell formation in *Drosophila melanogaster*.
- 1991-1996 Postdoctoral fellow with Dr. Gerald M. Rubin, University of California, Berkeley, Department of Molecular and Cell Biology. Research Topic: The molecular genetics of programmed cell death in *Drosophila melanogaster*.
- 1996-2002 Assistant Professor of Biology, California Institute of Technology. Research Interests: Control of cell death in health and disease.
- 2002-2008 Associate Professor of Biology, California Institute of Technology. Research Interests: Control of cell death in health and disease; spermatogenesis; microRNAs; selfish genetic elements; manipulating the composition or fate of wild insect populations; control of insect-borne diseases.
- 2008-present Professor of Biology and Biological Engineering. Research Interests: Control of cell death in health and disease in the nervous system; mitochondrial DNA quality control and neurodegenerative diseases; manipulating composition or fate of wild insect populations; control of insect-borne diseases; very-long term, reversible, manipulation of animal physiology (fertility as an example) using gene-therapy-based approaches

Honors/Awards:

- 1984-1985 UC Regents Graduate Fellowship
- 1991-1994 Helen Hay Whitney Foundation postdoctoral fellowship
- 1994-1996 Senior Postdoctoral Fellowship, American Cancer Society, California Division
- 1997-1999 Searle Scholar
- 1998-2001 Burroughs Wellcome New Investigator Award in the Pharmacological Sciences
- 1998-2002 Ellison Medical Foundation New Scholar, 1998-2002
- 1997-1999 Gustavus and Louise Pfeiffer Research Foundation. Identifying regulators of C-myc oncogene activity.
- 1998-1999 California Institute of Technology Keck Foundation (B. A Hay and J. L. Kirschvink co P. I.s) Molecular genetics of magnetite biomineralization in magnetotactic bacteria.

- 1999-2001 Amgen Inc. Identification of evolutionarily conserved regulators of cell death
2003 Margaret E. Early Medical Trust. Noncoding RNAs as cell death inhibitors and their role in oncogenesis.
2007 The popular science magazine Scientific American (January 2008 issue) chose the development of *Medea* for inclusion (#17) in their SCIENTIFIC AMERICAN 50, a list that highlights 50 individuals or groups demonstrating outstanding technological leadership in 2007.
2008 NIH Directors Pioneer Award (genetic strategies for spreading genes into wild mosquito populations that prevent human disease transmission). For details see <http://nihroadmap.nih.gov/pioneer/Recipients08.aspx>. The Pioneer award is NIH's most prestigious single investigator award.
2012 Ellison Medical Foundation Senior Scholars Award in Aging Research
2014 The Camille and Henry Dreyfus Foundation, Special Grant Program in the Chemical Sciences
2019-2020 Beaufort Visiting Fellow, St. John's College, University of Cambridge

Patents and applications:

- 1) Method for identifying proteases, protease target sites, and regulators of protease activity in cells. U.S. Patent 20020132327
- 2) Antibody-mediated immunocontraception U.S. Patent 10,570,200 B2
3. Population control using engineered translocations U.S. Application No. 15/164452 (allowance in progress)
4. Induction of antigen-specific tolerance U.S. Application No. 14/837941
5. DNA sequence modification based gene drive U.S. Application No. 15/970,728
6. 2-locus DNA sequence modification based gene drive U.S. Application No. 16/673,823

Other Professional Activities:

- Editorial board: Current Biology (2003-18)
- NIH Study Section (Special meeting for cell death grants from CDF-5) 1999; Ad hoc reviewer CDF-5 2002
- NIH study section regular member 2003-2009 DEV-1.
- NIH Study Section, Vector Biology 2012, 2020
- Ad hoc reviewer for multiple NSF proposals 2004-present.
- Reviewer for multiple Israeli Science Foundation (ISF) proposals.
- Reviewer for multiple US-Israel Agricultural Research and Development Fund (BARD) proposals
- Reviewer for multiple German Research Foundation (Deutsche Forschungsgemeinschaft) proposals
- Pierce's disease special review panel, 2012
- Advisory board for California Citrus Industry and insect borne disease
- Reviewer for numerous journals including Nature, Science, Journal of Cell Biology, Journal of Neuroscience, Nature Cell Biology, Cell, Molecular Cell, Developmental Cell, Development, Genes and Development, Embo Journal, Nature Biotechnology, Nature Methods, Current Biology, etc.
- Review panel member for members Center For Life Sciences (members of Tsinghua and Peking University), Beijing China 2015-present.

Publications <https://www.haylab.caltech.edu/publications/>

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- 80) Oberhofer, G., Ivy, T., and hay, B.A. (2020). Gene drive and resilience through renewal with next generation Cleave and Rescue selfish genetic elements. *PNAS*. 117: 9013-9021. doi: 10.1073/pnas.1921698117
- 79) Oberhofer, G., Ivy, T., and Hay, B.A. (2019). Cleave and Rescue, a novel selfish genetic element and general strategy for gene drive. *PNAS*. 116: 6250-6259. doi: 10.1073/pnas.1816928116
- 78) Oberhofer, G., Ivy, T., and Hay, B. A. (2018) Behavior of homing endonuclease gene drives targeting genes required for viability or female fertility with multiplexed guide RNAs. *PNAS* 115: E9343-E9352. doi: 10.1073/pnas.1805278115
- 77) Hay, Bruce A. and Li, Juan and Guo, Ming (2018) Vectored gene delivery for lifetime animal contraception: Overview and hurdles to implementation. *Theriogenology*, 112: 63-74. doi: 10.1016/j.theriogenology.2017.11.003
- 76) Buchman, Anna B. and Ivy, Tobin and Marshall, John M. and Akbari, Omar S. and Hay, Bruce A. (2018) Engineered Reciprocal Chromosome Translocations Drive High Threshold, Reversible Population Replacement in *Drosophila*. *ACS Synthetic Biology* . ISSN 2161-5063. doi: 10.1021/acssynbio.7b00451
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- 74) Kandul, Nikolay and Guo, Ming and Hay, Bruce A. (2017) A positive readout single transcript reporter for site-specific mRNA cleavage. *PeerJ*, 5 . Art. No. e3602. doi: 10.7717/peerj.3602
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- 72) Kandul, N.P., Zhang, T., *Hay, B.A. and *Guo M. (2016). Selective removal of deletion-bearing mitochondrial DNA in heteroplasmic *Drosophila*. *Nature communications*. ***Co-corresponding authors**. *Nature Communications*. 7: 13100. doi: 10.1038/ncomms13100
- 71) Choi, H.M. et al. (2016). Mapping a multiplexed zoo of mRNA expression. *Development*. 143:3632-3637. doi: 10.1242/dev.140137. doi: 10.1242/dev.140137
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- 11) Hay, B. A., Wassarman, D., and Rubin, G.M. (1995). *Drosophila* homologs of baculovirus inhibitors of apoptosis proteins function to block death. *Cell* 83, 1253-1262.
- 10) Hay, B. A., Wolff, T., and Rubin, G.M. (1994). Expression of baculovirus P35 prevents cell death in *Drosophila*. *Development* 120, 2121-2129.
- 9) Jongens, T.A., Hay, B. A., Jan, L.Y. and Jan, Y.N. (1992). The *germ cell-less* gene product: A posteriorly localized component necessary for germ cell development in *Drosophila*. *Cell* 70, 569-584.
- 8) Hay, B. A., Jan, L.Y. and Jan, Y.N. (1990). Localization of *vasa*, a component of *Drosophila* polar granules, in maternal-effect mutants that alter embryonic anteroposterior polarity. *Development*. 109, 425-433.
- 7) Hay, B. A., Jan, L.Y. and Jan, Y.N. (1988). A protein component of *Drosophila* polar granules is encoded by *vasa* and has extensive sequence similarity to ATP-dependent helicases. *Cell*. 55, 577-587.

- 6) Hay, B. A., Ackerman, L., Barbel, S.B., Jan, L.Y. and Jan, Y.N. (1988). Identification of a component of *Drosophila* polar granules. *Development* 103, 625-640.
- 5) Hay, B. A., Prusiner, S.B. and Lingappa, V.R. (1987b). Evidence for a secretory form of the cellular prion protein. *Biochemistry* 26, 8110-8115.
- 4) Hay, B. A., Barry, R.A., Lieberburg, I., Prusiner, S.B. and Lingappa, V. (1987a). Biogenesis and transmembrane orientation of the cellular isoform of the scrapie prion protein. *Mol.Cell.Biol.* 7, 914-920.
- 3) McKinley, M.P., Hay, B. A., Lingappa, V.L., Lieberburg, I. and Prusiner, S.B. (1987). Developmental expression of the prion protein in brain. *Dev. Biol.* 121: 105-110
- 2) Woody, C.D., Alkon, D.L., and Hay, B. A. (1984). Depolarization-induced effects of Ca²⁺-calmodulin-dependent protein kinase injection, in vivo, in single neurons of cat motor cortex. *Brain Res.* 321: 192-197
- 1) Alkon, D.L., Farley, J., Sakakibara, M. and Hay, B. A. (1984). Voltage-dependent calcium and calcium-activated potassium currents of a molluscan photoreceptor. *Biophys. J.* 46: 605-614

Speaker at the following meetings:

- 1996 Annual National Drosophila Research conference
- 1996 Fly eye development meeting. Asilomar CA
- 1997 Cold Spring Harbor meeting on Programmed cell death
- 1998 Fly eye Development meeting. Asilomar, CA
- 1999 Searle Scholars meeting
- 2000 ASBMB Satellite symposium on proteolysis.
- 2000 Gordon Research Conference on eye development
- 2000 Ellison Foundation symposium on Aging, MBL Woods Hole, MA
- 2001 ASBMB meeting Satellite symposium on proteolysis, and Session chair
- 2001 Gordon Research Conference on Development, New Hampshire
- 2001 Gordon conference on Cell Death, Oxford England
- 2001 Cold Spring Harbor meeting on Programmed Cell Death, and Session chair
- 2002 International Cell Death Society, Noosa Lake Australia
- 2002 Gordon Conference on Proteolysis, New Hampshire
- 2002 American Assn. for Cancer Research, Annual meeting, San Francisco
- 2002 American Assn. Cancer Research meeting: Ubiquitination in normal and cancer cells, NIH

2003 Cold Spring Harbor meeting on Programmed cell death
2003 Ellison Medical Foundation Symposium on Aging, MBL Mass.
2003 Gordon Research Conference on Development, New Hampshire
2003 Washington University, Department of Genetics Annual Retreat, Keynote speaker
2003 International Congress of Genetics, Melbourne Australia
2003 International Drosophila conference, Cairns, Australia
2004 March of Dimes Annual Meeting
2004 Keystone Symposium on Cell Death, Keystone Colorado
2004 University of Tokyo meeting on cell death and cell cycle
2005 Annual Drosophila Genetic Research Conference, San Diego
2007 EMBO meeting on Insect Disease Vectors, Crete
2007 Cold Spring Harbor meeting on Cell Death, and session chair
2007 UC Irvine, Southern California Drosophila Conference
2007 UC Irvine, Stop Dengue Now meeting
2007 National Evolutionary Synthesis Center, Selfish DNA and genetic control of disease
2008 49th Annual National Drosophila Research Conference
2008 GEANCO Foundation symposium on African Health
2008 Keynote speaker at International workshop on transgenesis and genomics of invertebrates
2008 American Society for Tropical Medicine and Hygiene
2009 Gordon Conference on molecular approaches for emergent/re-emergent tropical diseases
2009 Ecological and ethical issues in genetic approaches to pest management, NCSU.
2010 Entomological Society of America
2011 California Citrus Research Board annual meeting
2010 Caltech Seminar day
2011 Systems Biology meeting, UC Irvine
2011 Institute for Science and Global Policy
2011 EMBO meeting on Insect Disease Vectors, Crete
2012 Entomological Society of America
2013 Caltech Alumni Day
2013 Synthetic Biology@UW, Seattle WA
2015 Entomological Society of America

2016 University of Southern California Aging symposium
2016 Craig Venter Institute symposium on gene drive
2016 Bellagio Center Symposium on synthetic biology and conservation
2017 Caltech Seminar Day: Mitochondria and aging
2017 Leiden Lorentz symposium on Challenges for the regulation of gene drive technology
2017 ILSI Research Foundation: Symposium on Gene drive
2017 JASON Department of Defense analysis of Gene drive
2019 Keynote speaker IRCHLB conference
2021 Keystone conference on gene drive (scheduled)

Invited lectures:

1996 University of Southern California, Department of Genetics
1996 City of Hope Medical Center, Duarte, CA
1998 UCLA Childrens Hospital
1999 University of Southern California School of Medicine, Department of Neuro and Cell Biology
1999 Harbor UCLA Medical Center
1999 Salk Institute. Salk/Caltech symposium
1999 Kansas State University, Developmental Genetics Symposium
1999 MBL, Woods Hole, Ellison Medical Foundation Symposium of the Biology of Aging
2000 Amgen Inc.
2000 Duke University Medical Center. Program in Genetics
2000 UC San Francisco, Department of Biochemistry and Biophysics
2001 Kyoto University, Institute of Virology , Kyoto, Japan.
2001 Amgen, Inc
2002 Harbor UCLA Medical Center
2002 Dartmouth University, Genetics
2002 Rockefeller University, Physics and Biology colloquium
2002 Yale University, Department of Cell Biology
2002 University of Pennsylvania, Department of Genetics
2003 Salk Institute/EMBL joint meeting
2003 Columbia University

2003 Mayo Clinic, Rochester Minnesota, Departments of Transplantation Biology and Biochem.
2003 UCLA, Department of Human Genetics
2004 University of Washington, Department of Genetics
2004 Joint Sciences Center, Claremont Colleges
2005 Stowers Institute for Medical Research
2006 University of Miami School of Medicine, Department of Molecular and Cellular Pharmacology
2006 Purdue University, Department of Biology
2007 Kansas State University, Department of Biology
2007 Colorado State University, Microbiology, Immunology and Pathology
2007 Burnham Institute, San Diego
2007 North Carolina State University, Departments of Entomology and Genetics
2008 UC Riverside, Departments of Genetics and Entomology
2008 USC Department of Molecular and Cellular Biology
2008 UCLA, Department of Pharmacology
2008 UC San Francisco, Departments of Biochemistry and Neuroscience
2008 MD Anderson Cancer Center Blaffer Lecture
2008 Indiana University Department of Biology
2008 Purdue University
2009 Johns Hopkins School of Public Health
2009 University of Utah, Department of Biology
2009 Nanjing Model systems Institute, China
2010 University of Dundee, Scotland
2011 Joint Science Center, Claremont Colleges
2011 Pomona College
2012 UC Riverside
2015 UT Austin, Department of Integrative Biology
2016 UC Riverside
2016 USC Department of Genetics
2018 UCLA Department of Genetics
2019 Cambridge UK

Teaching Activities:

1997-present: Bi 122, Principles of Genetics. Bi 122 is a **9 unit** lecture and discussion course covering basic principles of Genetics. It is required for all Biology Majors. I give all the lectures and oversee all other aspects of this class.

1997-present: Bi 123, Genetics Laboratory. Bi 123 is a **12 unit** laboratory course that emphasizes modern approaches to genetic analysis and the study of development in the model organisms *Drosophila melanogaster* and *C. elegans*. Typically students carry out real research projects of interest to the fly and worm labs on campus. I lecture, give weekly demonstrations of *Drosophila* techniques, and oversee all aspects of this class.

1997-2005: Bi 226, Topics in Genetics; With Paul Sternberg and Ray Deshaies. Bi 226 was a graduate report and discussion course that covers a broad range of topics in genetic analysis. It is designed for students intending a major or minor specialization in genetics.

2000-2009. Bi/Ch113, Biochemistry of the Cell. Upper division Undergraduate course on cell biology. I lecture on cell death and its relationship to cancer and neurodegenerative diseases. David Chan runs the course.

Teaching awards

Biology Undergraduate Student Advisory Committee (BUSAC) annual award for excellence in undergraduate teaching (2001-2002).

Administrative duties:

- Biology Graduate Admissions Committee. 1997-present
- Co-chair of Biology Annual Retreat. 2001
- Member, Cell Biology Faculty Search Committee. 2000
- Member, Genetics of Development Faculty Search Committee 2001-2003
- Member, Cellular and Regulatory Biology Faculty Search Committee, 2005
- Chair, Cellular and Regulatory Biology Faculty Search Committee, 2006-2007
- Chair, Cellular and Regulatory Biology Faculty Search Committee, 2007-2008
- Chair, Cellular and Regulatory Biology Faculty Search Committee, 2008-2009
- Member, Cellular and Regulatory Biology Faculty Search Committee 2010-2011
- Biology Division Faculty representative for Safety 1997-present
- Member of Institute-wide Chemical and Hazardous waste Safety Committee 1997-present

- Biology Division Undergraduate Option (for Biology majors) representative 2004-present. I oversee the undergraduate Biology option: Provide guidance on requirements, course options, resolve conflicts, etc.

- Biology Division Graduate Option representative December 2007- present. I oversee all aspects of the daily function of the Biology Division Graduate option. This includes guidance on courses, requirements for advancement to candidacy and graduation, assignment of TAships, resolution of conflicts, etc.

Current Graduate Students:

- Tobin Ivy: Gene drive

Former Graduate Students:

- Susan L. Wang (PhD, 2000). Thesis title: Turning on cell death in the fly: Regulation of apoptosis in *Drosophila melanogaster*. Senior Corporate Council, Pfizer Pharmaceuticals

- Stephanie Y. Vernooy (PhD 2002). Thesis title: Identification of apoptotic regulators in *Drosophila* and their nonapoptotic roles in spermatogenesis: Implications for the existence of a "caspase cassette" which regulates diverse biological processes. Assistant Professor, Siena College

- Jun R. Huh (PhD 2005). Thesis title: To die or differentiate: apoptotic and non-apoptotic roles of death molecules in *Drosophila melanogaster*. Assistant Professor, Harvard Medical School

- Jeffrey M. Copeland (PhD 2005). Thesis title: Identification of novel cell death regulators in *C. elegans* and *Drosophila*. Assistant Professor, Eastern Mennonite University

- Catherine M. Ward (PhD 2010). Thesis title: *Medea* selfish genetic elements as tools for altering traits of wild populations: a theoretical analysis. Postdoctoral Fellow, NCSU

- Kelly D. Matzen (PhD 2012). Thesis title: Engineering of Dengue virus refractoriness in *Aedes aegypti* and development of an underdominant gene drive system in *Drosophila melanogaster*. Senior Scientist, Oxitec, Oxford England

- Anna Buchman (2010-2014). Engineering of underdominant gene drive and reproductive isolation. **Recipient of 2014 Ferguson Prize for outstanding thesis in Division of BBE, Caltech.** Postdoctoral Fellow, UCSD

Current Postdoctoral Fellows:

Danijela Markovic, Mitochondrial quality control

Marlene Biller, Mitochondrial quality control

Georg Oberhofer, Gene drive

Former Postdoctoral fellows:

Christine J. Hawkins (1997-1999). Group leader, Senior Research Fellow, Department of Biochemistry, La Trobe University, Melbourne Australia

Soon Ji Yoo (1998-2005). Associate Professor of Biology, College of Sciences, Kyung Hee University, Seoul, Korea

Peizhang Xu (2000-2004) Postdoctoral Fellow, UCSF

Cain Yam (2002-2004) President and CEO, Bestgene, Transgenesis Company in China.

Israel Muro (2004-2007) Postdoctoral Fellow, University of Wyoming

Chun-Hong Chen (2004-2008) Professor, Taiwan National University

Haixia Huang (2005-2010). Senior Technologist, Huntington Hospital

K.P. Arunkumar Group Leader, Department of Biotechnology, Ministry of Science and Technology, Hyderabad, India

Jun R. Huh. Assistant Professor, Harvard Medical School, Department of Immunology

Omar Akbari, Assistant Professor UC San Diego

Geoffrey Pittman (2008-2012). Science teacher, Australia

Philippos Papathanos, Assistant Professor, University of Jerusalem

Research Support:

NIH R01 GM57422-01 (1997-03). Regulation of cell death in *Drosophila*.

Ellison Medical Foundation New Scholar (1998-2002). Identification and characterization of proteases that regulate cell death in the aging brain.

Amgen Inc (1999-2001). Identification of evolutionarily conserved regulators of cell death

Gustavus and Louise Pfeiffer Research Foundation (1997-1999). Identifying regulators of C-myc oncogene activity.

Keck Foundation (B.A Hay and J.L. Kirschvink co P.I.s) (1998-1999). Molecular genetics of magnetite biomineralization in magnetotactic bacteria.

Burroughs Wellcome New Investigator Award in the Pharmacological Sciences (1998-2001).
Identification and characterization of regulators of caspase-dependent cell death signaling

Searle Scholar (1997-2000). Regulation of cell death in *Drosophila* by the IAP family of proteins

Margaret E. Early Medical Trust. (2003). Noncoding RNAs as cell death inhibitors and their role in oncogenesis.

GM057422

NIH

9/1/03-8/31/07

Regulation of Cell Death in *Drosophila*

The major goals of this project are: 1) to characterize mechanisms apoptotic stimuli use to disrupt the balance between levels of IAPs and the caspases they inhibit; 2) To identify new IAP pathway components through IAP-affinity purification and a genetic screen; and 3) To characterize the roles and mechanism of action of DIAP2.

GM070956

NIH

5/1/04-3/31/08

Characterization of MicroRNA Cell Death
Regulators

The major goals of this project are: 1) to identify evolutionarily conserved cell death-inhibiting miRNAs, and 2) to determine the mechanisms by which these miRNAs function—the identities of their mRNA targets—and the contexts in which they are important.

GM072879

NIH

2/1/05-12/31/09

Nonapoptotic roles for caspase proteases in
spermatogenesis

This project will 1) characterize the mechanisms that spermatids utilize to avoid apoptosis in the presence of activated caspase; 2) identify the mechanisms that mediate caspase activation in spermatids; and 3) characterize mutations derived from a recent large scale screen for male sterile flies, with the goal of identifying new regulators of caspase activity and function in spermatogenesis.

FNIH Research/Bill and Melinda Gates
Foundation

9/15/07-9/15/10

Creation of maternal-effect selfish genetic elements to drive Population replacement in wild populations of mosquitoes

The major goal of this project is to create maternal-effect selfish genetic elements in *Aedes* mosquitoes that can drive genes conferring disease refractoriness to fixation within wild populations.

Seymour Benzer NIH aging grant
2008-2009

Overseeing the completion of ongoing projects, and the movement of associated individuals to other jobs.

Weston Havens Foundation

9/1/08-9/1/10

Creation of maternal-effect selfish genetic elements to drive population replacement in wild populations of mosquitoes

Sanofi Bioengineering Award

6/1/12-10/1/13

Mitochondrial DNA quality control and age-related diseases: promoting selective removal of mutant mitochondrial genomes

NIH Director's Pioneer award

10/1/08-10/1/13

Creation of maternal-effect selfish genetic elements to drive population replacement in wild populations of mosquitoes; and any other topics we find interesting.

Ellison Medical Foundation Senior Scholar Award

10/1/12-9/30/16

Mitochondrial DNA quality control and age-related diseases: promoting selective removal of mutant mitochondrial genomes

USDA/CDRF NIFA award

10/1/12-9/30/17

Develop transgenic technologies to render citrus psyllids unable to transmit the bacterial disease HLB

DARPA
9/2013-2016
High threshold gene drive for insect vectors of disease.

California Cherry Board
3/14-3/18
Gene drive for population suppression in *Drosophila suzukii*

The Camille and Henry Dreyfus Foundation, Special Grant Program in the Chemical Sciences
2014-2015
High school community science and the design of portable custom molecular sensors

NIA R56 (Guo PI, Hay co-PI)
9/1/17-8/30/18
Identifying regulators of neurodegeneration due to defective mitochondrial DNA

DARPA
3/19/18-3/18/19
Engineering the plant mitochondrial genome

NIH R01 (Guo, PI; Hay, PI) 9/1/2018 –
8/31/2023

Identifying Regulators of Degeneration Due to Defective Mitochondrial DNA

The major goals of this project are to develop *Drosophila* transgenic heteroplasmy models and inducible systems together with UCLA, to discover how mitochondrial DNA damaged is sensed, and how cells work to remove defective genomes, or compensate for a loss of mitochondrial function. Systems biology approaches, including transcriptional profiling, tests for interactions with known regulators of neurodegeneration, and genetic screens using *Drosophila* eye and other tissues will be carried out to identify regulators of these processes.

Fellowships/awards to lab personnel:

- Human Frontiers Science Program fellowship to Christine J. Hawkins
- Jane Coffin Childs fellowship to Soon Ji Yoo
- Croucher Foundation of Hong Kong to Cain Yam.
- Host sponsor for Human Frontiers Foundation Short Term Fellowship 2001 to Professor H.-A.J. Muller, Heinrich Heine University, Dusseldorf, Germany.
- Gosney Postdoctoral Fellowship to Peizhang Xu.
- NSF predoctoral award to Catherine Ward
- Caltech Center for Biological Circuit Design postdoctoral award to Chun-Hong Chen.
- EMBO postdoctoral fellowship to Philippos Pappathanos
- Gosney Postdoctoral Fellowship to Nikolai Kandul
- German Research Foundation postdoctoral fellowship to Georg Oberhofer.
- Gosney postdoctoral fellowship to Georg Oberhofer

Undergraduate trainees and resulting publications (Caltech student unless noted otherwise)

Stavroula Otis
*Jennifer Yang
*Koen Verbrugghe
*Julius Su
*Vivian Chow
Jane Garrity
*Elizabeth J. Hong
Yile Ding
Greg Stachelek
Nguyen Nguyen (JPL Scholar)
Kimberly M. Walter (University of Virginia)
Jennifer Taggart
Yingding Xu
Sixin (Samantha) Lu
Yang Yang
*L. Schaeffer
*Jessica T. Su
Chieh Yu (Joy) Chen
Margaret Chiu
Kelly Guan
Annie Hong
Daniel Leighton
Ang (Alan) Li
Benjamin Steele
Shamili Allam
Kenneth Chan (Portland State)
Elizabeth Gilliam
Ran Yang
Mario Zubia
Shanon Mohler
Jennifer Hu
Gal Barak
Sharon Garrison (Rochester Polytechnic)
Michelle Bobrow
Philip Kong
*Race DeLoreto
Dustin Harris (UC San Diego)
Olga Tkachenko (Cambridge, UK)
Wen Min Chen
Albert Liu
Erin Wang
*Alexander Hsu
James Wagstaff (Oxford, UK)
Alex Sampson (Cambridge, UK)

- *23) Vernooy, S. Y., **Chow, V., Su, J., Verbrugghe, K., Yang, J.**, Cole, S., Olson, M. R., and Hay, B. A. (2002). *Drosophila* Bruce can potently suppress Rpr- and Grim-, but not Hid-dependent cell death. *Current Biol.* 12, 1164-1168.
- *26) Guo, M., **Hong, E.J.**, Fernandez, J., Zipursky, S.L., and Hay, B.A. (2003). A reporter for Amyloid precursor protein γ -secretase in living *Drosophila*. *Human Molecular Genetics.* 12, 2669-2778.
- *34) Chen, C-H., Huang, H., Ward, C. M., **Su, J.T., Schaeffer, L.**, Guo. M., Hay, B.A. (2007). A synthetic maternal-effect selfish genetic element drives population replacement in *Drosophila*. *Science.* 316, 597-600.
- *55) Ward, C.M., **Su, J.T.**, Huang, Y., Lloyd, A.L., Gould, F., and Hay, B.A. (2011). *Medea* selfish genetic elements as tools for altering traits of wild populations: a theoretical analysis. *Evolution.* 65, 1149-62.
- *65) Akbari, O.S., Aantoshechkin, I., Armhein, H., Williams, B., **Diloreto, R***, Sandler, J., and Hay, B.A. (2013). The developmental transcriptome of the mosquito *Aedes aegypti*, an invasive species and major arbovirus vector. *G3 (Bethesda)*. Sep 4;3(9):1493-509. doi: 10.1534/g3.113.006742
- *81) Kandul, N.P., Liu, J., **Hsu*, A.D.**, Hay, B.A., and Akbari, O.S. (2020). A drug-inducible sex-separation technique for insects. *Nature Communications.* 11: 2106. doi: 10.1038/s41467-020-16020-2