CURRICULUM VITAE

BRUCE A. HAY

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Cell death: One of our goals is to understand the genetic and molecular mechanisms that regulate cell death, neurodegeneration, and proliferation. Much of this work has as its ultimate goal the prevention of human diseases, particularly cancer and neurodegenerative diseases. We often use *Drosophila melanogaster* as a model system to identify genes that function to regulate these processes. Important cellular regulatory pathways are evolutionarily conserved; thus, molecules identified as regulators in *Drosophila* are likely to have counterparts in vertebrates, and the pathways that link these molecules are likely to be regulated similarly. Much of our work on neurodegeneration, particularly as it relates to defects in mitochondrial function, Alzheimer's disease and Parkinsons disease, occurs in collaboration with the lab of Ming Guo, MD, PhD, a practicing Neurologist and researcher at UCLA (http://guolab.neurology.ucla.edu/).

The composition and fate of populations: A second set of goal of our work addresses three questions in applied 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 so that all individuals express a trait of interest? With regard to this last aim, we are particularly interested in developing transgenic mosquitoes that will prevent transmission of the pathogens that cause malaria and dengue fever. 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.

Lifetime, single shot contraception: In a third project we are working to develop single shot, lifetime (but reversible) contraceptives for a variety of mammalian species. In brief, there is 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 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. We find that a single intramuscular injection of a recombinant adeno-associated virus (rAAV) designed to express an antibody that binds gonadotropin releasing hormone (GnRH), a master regulator of reproduction, 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 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.

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. Research Interests: Control of cell death in health and disease; manipulating composition or fate of wild insect populations; control of insect-borne diseases; very-long term, reversible, single-shot contraception in animals and humans

Honors/Awards:

1984-1985 UC Regents Graduate Fellowship
1991-1994 Helen Hay Whitney Foundation postdoctoral fellowship
1994-1996 Senior Postdoctorl 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.
2014 The Camille and Henry Dreyfus Foundation, Special Grant Program in the Chemical Sciences

Patents and applications:

1) Method for identifying proteases, protease target sites, and regulators of protease activity in cells. U.S.Patent 20020132327
2) Design of synthetic Maternal-effect selfish genetic elements that can drive population replacement in animals and plants. U.S. Application No. 60/873,648
3) Antibody-mediated immunocontraception. U.S. Application No. US 14/170,118
4) Repressible lethal system for regulating insect populations. U.S. Application No. US 14/206,011

Other Professional Activities:

-- Editorial board: Current Biology (2003-present)
-- 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

-- Ad hoc reviewer for multiple NSF proposals 2004-present.
-- Pierce's disease special review panel, 2012
-- 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.

Publications (all are available at our web site http://www.its.caltech.edu/~haylab/)

68) Marshall, J.M., and Hay, B.A. (2014). Medusa: a novel gene drive system for confined suppression of insect populations. PLoS One. Jul 23;9(7):e102694. doi: 10.1371/journal.pone.0102694.

67) Akbari, O.S., Papathanos, P.A., Sandler, J.E., Kennedy, K., and Hay, B.A. (2014). Identification of germline transcriptional regulatory elements in Aedes aegypti. Sci Rep. Feb 4;4:3954. doi: 10.1038/srep03954

66) Akbari, O.S., Antoshechkin, I., Hay, B.A., and Ferree, P.M. (2013). Transcriptome profiling of Nasonia vitripennis testis reveals novel transcripts expressed from the selfish B chromosome, paternal sex ratio. G3 (Bethesda). Sep 4;3(9):1597-605. doi: 10.1534/g3.113.007583

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

64) Lee, G., Kikuno, K., Sehgal, R., Wang, Z., Nair, S., Chen, C-H., Hay, B.A., and Park, J.H. (2012). Grim-led programmed cell death is essential for the establishment of Corazonin-producing peptidergic nervous system during embryogenesis and metamorphosis in *Drosophila melanogaster*. Biology Open. 2, 283-294.

63) Akbari, O.S., Matzen, K.D., Marshall, J.M., Huang, H., Ward, C.M., and Hay, B.A. (2012). A synthetic gene drive system for local, reversible modification and suppression of insect populations. Current Biology. 23, 671-7.

62) Akbari, O. S., Chen, C-H, Jarshall, J.M., Huang, H., Antoshechkin, I., and Hay, B.A. (2012). Novel synthetic *Medea* selfish genetic elements drive population replacement in *Drosophila*, and a theoretical exploration of Medea-dependent population suppression. ACS Synthetic Biology (DOI: 10.1021/sb300079h).

61) Rochet, J.C., Hay, B.A. and Guo, M. (2012) Molecular Insights into Parkinson's Disease, Progress in Molecular Biology and Translational Science 107, 125-88.

60) Marshall, J.M. and Hay, B.A. (2012). General principles of single-construct chromosomal gene drive. Evolution. 66,2150-66.

59) Hay, B.A. (2011) Synthetic Biology and Infectious disease: Challenges and Opportunities. In Institute on Science for Global Policy Proceedings: Emerging and Persistent Infectious Diseases: Focus on Prevention. George H. Atkinson (Editor) ISGP.

58) Marshall, J.M. and Hay, B.A. (2011). Confinement of gene drive systems to local populations: a comparative analysis. J. Theoretical Biology 294, 153-71

57) Marshall, J.M. and Hay, B.A. (2011). Inverse *Medea* as a novel gene drive system for local population replacement: a theoretical analysis. J. Heredity. 102, 336-41.

56) Marshall, J.M., Pittman, G.W., Buchman, A.B., and Hay, B.A. (2011). Semele: a killer-male, rescue-female system for suppression and replacement of insect disease vector populations. Genetics. 187, 535-51.

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.

54) Lee, G., Wang, Z., Sehgal, R., Chen, C.H., Kikuno, K., Hay, B., and Park, J.H. (2011). Drosophila caspases involved in developmentally regulated programmed cell death of peptidergic neurons during early metamorphosis. J. Comp. Neurol. 519, 34-48.

53) Hay, B.A., Chen, C.H., Ward, C.M., Huang, H., Su, J.T., and Guo, M. (2010) Engineering the genomes of wild insect populations: challenges, and opportunities provided by synthetic *Medea* elements. J. Insect Physiol. 56, 1402-13.

52) Siegrist, S.E., Haque, N.S., Chen, C.H., Hay, B.A., and Hariharan, I.K. (2010). Inactivation of both foxo and reaper promotes long-term adult neurogenesis in Drosophila. Curr Biol. 20, 643-648.

51) Ribaya, J.P., Ranmuthu, M., Copeland, J., Boyarskiy, S., Blain, A.P., Hay, B., and Laski, F.A. (2009). The deubiquitinase emperor's thumb is a regulator of apoptosis in *Drosophila*. Dev. Biol. 329, 25-35.

50) Sathyanarayanan, S., Zheng, X., Kumar, S., Chen, C-H., Chen, D., Hay, B.A., and Sehgal, A. (2008). Identification of novel genes involved in light-dependent CRY degradation through a genome-wide RNAi screen. *Genes and Development*. 22, 1522-33.

49) Yao J.-G., Weasner B.M., Wang L.-H., Jang C.-C., Tang C.-Y., Salzer C.L., Chen C.-H., Hay B.A., Sun Y.H., Justin P.(2008) Differential requirement of the Pax(5a) genes eyegone and twin of eyegone during eye development in Drosophila. *Developmental Biology*. 315, 535-551.

48) Shcherbata H.R., Ward E.J., Fischer K.A.,Yu J-A,Reynolds S.H., Chen CH, Xu P, Hay B.A., Ruohola-Baker H (2007). Stage-Specific Differences in the Requirements for Germline Stem Cell Maintenance in the Drosophila Ovary. *Cell Stem Cell*. 1, 698–709

47) Copeland, J.M., Bosdet, I., Freeman, J.D., Guo, M., Gorski, S.M., Hay, B.A. (2007). *echinus*, required for interommatidial cell sorting and cell death in the *Drosophila* pupal retina, encodes a protein with homology to ubiquitin-specific proteases. *BMC Developmental Biology*. (doi:10.1186/1471-213X-7-82).

45) 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.

44) Huh, J.R., Foe, I., Muro, I., Chen, C-H., Seol , J.H., Yoo, S.J., Guo, M., Park, J.M, and Hay, B.A. (2007). The *Drosophila* Inhibitor of Apoptosis DIAP2 is dispensable for cell survival, required for the innate immune response to Gram-negative bacterial infection, and can be negatively regulated by the reaper/hid/grim family of IAP-binding apoptosis inducers. *J. Biol. Chem*. 282, 2056-68.

43) Clark, I.E., Dodson, M.W., Jiang, C., Cao, J.H., Huh, J.R., Seol, J.H., Yoo, S.J., Hay, B.A., Guo, M. (2006). *Drosophil*a *pink1* is required for mitochondrial function and interacts genetically with *parkin*. *Nature*. 441, 1162-1166.

42) Muro, I., Berry, D.L., Huh, J.R., Chen, C.H., Huang, H., Yoo, S.J., Guo, M., Baehrecke, E.H., Hay, B.A. The *Drosophila* caspase Ice is important for many apoptotic cell deaths and for spermatid individualization, a nonapoptotic process. *Development*. 133, 3305-15.

41) Chen, C.H., Guo, M., Hay, B.A. (2006). Identifying microRNA regulators of cell death in Drosophila. *Methods in Molecular Biology*. 342, 229-240.

40) Hay, B.A. and Guo, M. (2006). Caspase-dependent cell death *in Drosophila*. *Annual Review of Cell and Developmental Biology*. 22, 623-50.

39) Yan, N., Huh, J.R., Schirf, V., Demeler, B., Hay, B.A., and Shi, Y. (2006). Structure and activation mechanism of the *Drosophila* initiator caspase Dronc. *J. Biol. Chem*. 281, 8667-74.

38) Hay, B.A., Huh, J.R., and Guo, M. (2004). The genetics of cell death: approaches, insights and opportunities in *Drosophila*. *Nature Reviews Genetics*. 5, 911-922.

37) Xu, P., Guo, M., and Hay, B.A. (2004). MicroRNAs and the regulation of cell death. Trends in Genetics. 20, 618-624.

36) Huh, J.R., Guo, M., and Hay, B.A. (2004). Compensatory proliferation induced by cell death in the *Drosophila* wing disc requires activity of the apical caspase Dronc in a nonapoptotic role. *Current Biology*. 14, 1262-1266.

35) Huh, J. R., Vernooy, S.Y., Yu, H., Yan, N., Shi, Y., Guo, M., and Hay, B. A. (2004). Multiple apoptotic caspase cascades are required in nonapoptotic roles for *Drosophila* spermatid individualization. *PLoS Biology* 2, 43-53.

34) Chai, J., Yan, N., Huh, J. R., Wu, J-W., Li, W., Hay, B. A., and Shi, Y. (2003). Molecular mechanism of Reaper/Grim/Hid-mediated suppression of DIAP1-dependent Dronc ubiquitination. *Nature Structural Biology*. 10, 892-898.

32) Hay, B. A., and Guo, M. (2003). Coupling cell growth, proliferation and death: Hippo weighs in. *Developmental Cell*. 5, 361-363.

31) Guo, M., Hong, E.J., Fernandez, J., Zipursky, S.L., and Hay, B.A. (2003). A reporter for Amyloid precursor protein g-secretase in living *Drosophila*. *Human Molecular Genetics* 12, 2669-78.

30) Xu, P., Vernooy, S.Y., Guo, M., and Hay, B.A. (2003). The *Drosophila* microRNA mir-14 suppresses cell death and is required for normal fat metabolism. *Current Biology*. 13, 790-795.

29) Olson, M.R., Holley, C.L., Yoo, S.J., Huh, J.R., Hay, B.A., and Kornbluth, S. (2003). Reaper is regulated by IAP mediated ubiquitination. *J. Biol. Chem* 278, 4028-4034.

28) Muro, I., Hay, B. A. and Clem, R. J. (2002). The *Drosophila* DIAP1 protein is required to prevent accumulation of a continuously generated, processed form of the apical caspase DRONC*. J. Biol. Chem*. 277, 49644-49650.

27) Huh, J. R. and Hay, B. A. (2002) Sculptures of a fly's head. *Nature*, 418, 926-927.

25) Dorstyn, L., Read, S., Cakouros, D., Huh, J. R., Hay, B. A., and Kumar, S. (2002). The role of cytochrome c in caspase activation in *Drosophila melanogaster* cells. *J. Cell Biol*. 156, 1089-1098.

24) Yoo, S. J., Huh, J. R., Muro, I., Yu, H., Wang, L., Wang, S. L., Feldman, R. M. R., Clem, R. J., Muller, H.-A. J., and Hay, B. A. (2002). Apoptosis inducers Hid, Rpr and Grim negatively regulate levels of the caspase inhibitor DIAP1 by distinct mechanisms. *Nature Cell Biol*. 4, 416-424.

23) Sun-Yun Yu, Yoo, S.J., Yang, L., Zapata, C., Srinivasan, A.,Hay, B. A. and Baker, N.E. (2002). A
pathway of signals regulating effector and initiator caspases in the developing *Drosophila* eye. *Development*. 129, 3269-3278.

22) 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 supress Rpr- and Grim-, but not Hid-dependent cell death. *Current Biol.* 12, 1164-1168.

21) Wu, J-W, Cocina, A.E., Chai, J., Hay, B. A., and Shi, Y. (2001). Structural analysis of a functional DIAP1 fragment bound to Grim and Hid peptides. *Mol. Cell* 8, 95-104.

20) Hawkins, C. J., Wang, S. L., and Hay, B. A. (2000). Monitoring the activity of caspases and their regulators in yeast. *Methods in Enzymology* 322, 162-174.

19) Hay, B. A. (2000) Understanding IAP function and regulation: a view from *Drosophila*. *Cell Death and Differentiation* 7, 1045-1056.

18) Vernooy, S. Y., Griffin, E. E., Ghaboosi, N., Copeland J., and Hay, B. A. (2000). Cell death in *Drosophila*: Conservation of mechanism and unique insights. *J. Cell Biol.* 150, F69-F75.

17) Hawkins, C. J., Yoo, S. J., Peterson, E. P., Wang, S. L., Vernooy, S. Y., and Hay, B. A. (2000). The *Drosophila* caspase DRONC cleaves following glutamate or aspartate and is regulated by DIAP1, HID and GRIM. *J. Biol. Chem.* 275, 27084-27093.

16) Rubin, G. M., et al., (2000). Comparative genomics of the eukaryotes. *Science*, 287, 2204-2215.

15) Guo, M, and Hay, B. A. (1999). Emerging links between cell proliferation and apoptosis. *Current Opinion in Cell Biology*, 11, 745-752.

14) Wang, S.L., Hawkins, C. J., Yoo, S. J., Muller, H.-A. J., and Hay, B. A. (1999). The *Drosophila* caspase inhibitor DIAP1 is essential for cell survival and is negatively regulated by HID. *Cell*, 98, 453-463.

13) Hawkins, C. J., Wang, S. L., and & Hay, B. A. (1999). A cloning method to identify caspases and their regulators in yeast: Identification of *Drosophila* IAP1 as an inhibitor of the *Drosophila* caspase DCP-1. *PNAS*, 96, 2885-2890.

12) Hay, B. A., Maile, R., and Rubin, G. M. P element insertion-dependent gene activation in the *Drosophila* eye. (1997). *PNAS* , 94, 5195-5200.

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. *Developmen*t 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. *Biochemsitry* 26, 8110-8115.

4) Hay, B. A., Barry, R.A., Liebergurg, 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 Ca^{2+}-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 meting 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 transgenisis 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 Alumni 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

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

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:

- Alejandra Olvera: Gene drive and long-term contraception
- 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, U. Mass. Worcester
- 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. Postdoctoral Fellow, Caltech

Current Postdoctoral Fellows:

Nikolai Kandul (2008-present). Mitochondrial quality control and gene drive
Omar Akbari (2009-present) Gene drive
Juan Li (2013-present) Long-term contraception
Danijela Markovic (2013-present) Long-term contraception

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) Assistant 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, U Massachusetts Worcester, Department of Immunology

Omar Akbari, Assistant Professor UC Riverside (Fall 2015)

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

Philippos Papathanos, Fellow, University of Perugia, Italy

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
3/14-3/15
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

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

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)

*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 supress 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 g-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