**BIOGRAPHICAL SKETCH**

| NAME | POSITION TITLE |
|---|---|
| Mark A. Krasnow, M.D., Ph.D. | Professor of Biochemistry |
| eRA COMMONS USER NAME (credential, e.g., agency login)<br>KRASNOW.MARK | |

EDUCATION/TRAINING

| INSTITUTION AND LOCATION | DEGREE | YEAR(s) | FIELD OF STUDY |
|---|---|---|---|
| University of Illinois (Urbana, IL) | B.S. | 1978 | Biology, Chemistry |
| University of Chicago (Chicago, IL) | Ph.D. | 1983 | Biochemistry |
| University of Chicago (Chicago, IL) | M.D. | 1985 | Medicine |
| Stanford University (Stanford, CA) | Postdoc | 1985-1988 | Biochemistry |

**A. Personal Statement**

Our lab uses genetic and genomic approaches to elucidate the cellular and molecular basis of lung development and stem cells and the neural circuit of breathing, using Drosophila and mouse as model systems. We are interested in understanding the normal processes and how they go awry in human diseases such as lung cancer, pulmonary fibrosis, pulmonary hypertension and Sudden Infant Death Syndrome.

**B. Positions and Honors**

**Positions and Employment**

1983-1985 Lecturer, Department of Biochemistry, University of Chicago
1988-1994 Assistant Professor of Biochemistry, Stanford Univ. School of Medicine
1995-2000 Associate Professor of Biochemistry, Stanford Univ. School of Medicine
1996-2002 Director, Medical Scientist Training Program, Stanford Univ. School of Medicine
1997-2002 Associate Investigator, Howard Hughes Medical Institute
2000-2006 Associate Chair, Department of Biochemistry, Stanford Univ. School of Medicine
2001-pres Professor of Biochemistry, Stanford Univ. School of Medicine
2006-2013 Chair, Department of Biochemistry, Stanford Univ. School of Medicine
2003-pres Investigator, Howard Hughes Medical Institute
2010-pres Exec. Director, Wall Center for Pulmonary Vascular Disease, Stanford Univ. School of Medicine

**Other Experience and Professional Memberships**

1998 NIH Genetics Study Section
1999 NIH Cell Development & Function Study Section
2001 Co-chair, Developmental Biology Gordon Conference
2001 Co-chair, Cold Spring Harbor/Banbury Meeting on Tube Morphogenesis
2002-2014 Founding Editorial Board, Public Library of Science Journals
2004-2008 President Elect, President and Past-President, North American Drosophila Board of Directors
2009-2010 Distinguished Editorial Panel, NIH Challenge Grants
2009-pres Scientific Advisory Board, Vesalius Research Center
2010-pres Founder and Organizer, International Workshop and Initiative on Mouse Lemur Genetics
2010-2012 Scientific Advisory Board, Fate Therapeutics
2013-pres Scientific Advisory Board, Pediatric Research Center, Hannover Medical School
2013-pres Scientific Advisory Board, Centre ValBio Research Station, Madagascar

**Honors**

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|---|---|
| 1978 | B.S. summa cum laude and Phi Beta Kappa |
| 1978-1985 | MSTP Predoctoral Fellowship |
| 1985 | Univ. of Chicago Medical Alumni Prize |
| 1985-1987 | Helen Hay Whitney Postdoctoral Fellowship |
| 1987-1993 | Lucille P. Markey Scholar Award |
| 1991-1997 | NSF Presidential Young Investigator Award |
| 1998 | Fellow, American Association for the Advancement of Science |
| 2009 | Fellow, American Academy of Arts & Sciences |
| 2012 | Kaiser Family Foundation Award for Preclinical Teaching |

**C. Contributions to Science**

1. As a graduate (MD/PhD) student with Dr. Nicholas Cozzarelli, I established one of the first in vitro site specific recombination systems, purified the recombinase, and pioneered the application of DNA topology to elucidating the dynamics of recombination mechanisms including the structure of the synaptic complex and rearrangement of the DNA ends during the recombination event. As a postdoctoral fellow with Dr. David Hogness, and continuing in my own lab as an Assistant Professor at Stanford, Liz Gavis and I purified Drosophila Ultrabithorax protein, the protein product of the first developmental control gene to be cloned, and showed with Phil Beachy that it is a sequence-specific DNA binding protein. I showed it functions as a transcription factor that can positively-autoregulate to maintain its own expression and downregulate the transcription of other homeotic genes to select and maintain segment identity during development. This demonstrated how a developmental control gene functions at the biochemical level and helped open the biochemical era of developmental biology.

a. **Krasnow, M.A.** and Cozzarelli, N.R. (1983) Site-specific relaxation and recombination by the Tn3 resolvase: recognition of the DNA path between oriented res sites. *Cell* 32, 1313-1324.
b. **Krasnow, M.A.**, Stasiak, A., Spengler, S.J., Dean, F., Koller, T., and Cozzarelli, N.R. (1983) Determination of the absolute handedness of knots and catenanes of DNA. *Nature* 304, 559-560.
c. **Krasnow, M.A**., Saffman, E.E., Kornfeld, K. and Hogness, D.S. (1989) Transcriptional activation and repression by *Ultrabithorax* proteins in cultured Drosophila cells. *Cell* 57, 1031-43.
d. Johnson, F.B. and **Krasnow, M.A.** (1990) Stimulation of transcription by an Ultrabithorax protein in vitro. *Genes and Development* 4, 1044-52.

2. My lab and I pioneered the genetic dissection of organ development and stem cells. We established the first tractable genetic system to elucidate an organogenesis program by mapping the events of Drosophila respiratory (tracheal) system development at single cell resolution, and then carrying out systematic mutant screens that identified hundreds of genes that define the molecular pathways that control each of the fundamental steps in organogenesis, including branch budding and outgrowth, tubulogenesis, tube fusion, tube size control, cell rearrangement, cell fate selection, and oxygen control of branching. The Drosophila tracheal system is now the best understood organogenesis program, and serves as a paradigm for the study and understanding of all organogenesis programs.

a. Sutherland, D., Samakovlis, C., and **Krasnow, M.A.** (1996) *branchless* encodes a Drosophila FGF homolog that controls tracheal cell migration and the pattern of branching. *Cell* 87, 1091-1101.
b. Ghabrial, A. and **Krasnow, M.A.** (2006) Social interactions among epithelial cells during tracheal branching morphogenesis. *Nature* 441, 746-749.
c. Chen, F. and **Krasnow, M.A.** (2014) Progenitor outgrowth from the niche in Drosophila trachea is guided by FGF from decaying branches. *Science* 343,186-189.
d. Peterson, S.J. and **Krasnow, M.A.** (2015) Subcellular trafficking of FGF controls tracheal invasion of Drosophila flight muscle. *Cell* 160, 313-323.

3. We are applying the same systematic genetic and genomic approaches that we used to elucidate the Drosophila tracheal program (see above) to mammalian organs, and have used it to elucidate the complete branching program of lung development and to characterize at single cell resolution the progenitors and stem cells for many important cell types of the lung and to define how they go awry in disease. We showed that full developmental programs can be reconstructed by single cell RNAseq of dozens of developmental intermediates, and applied the approach to alveolar development. Through the characterization of the unusual, fully differentiated stem cells that maintain alveoli, we discovered that the pathway that controls alveolar stem cell renewal is genetically hijacked to cause lung adenocarcinoma, defining the cellular and molecular basis of the most deadly cancer.

a. Metzger, R., Klein, O.D., Martin, G.R., and **Krasnow, M.A.** (2008) The branching programme of mouse lung development. *Nature* 453, 745-750.
b. Desai, T., Brownfield, D.G., and **Krasnow, M.A.** (2014) Alveolar progenitor and stem cells in lung development, renewal and cancer. *Nature* 507, 190-194.
c. Treutlein, B., Brownfield, D.G., Wu, A.R., Neff, N.F., Mantalas, G.L., Espinoza, F.H., Desai, T.J.*, **Krasnow, M.A.***, and Quake, S.R.* (2014) Reconstructing lineage hierarchies of the distal lung epithelium using single cell RNA-seq. *Nature* 509, 371-375. (*, corresponding authors)
d. Kumar, M.E., Bogard, P.E., Espinoza, F.H., Menke, D.B., Kingsley, D.M., **Krasnow, M.A.** (2014) Defining a mesenchymal progenitor niche at single cell resolution. *Science* 346,1-9.
e. Kuo, C.S. and **Krasnow, M.A.** (2015) Formation of a neurosensory organ by epithelial cell slithering. *Cell*, in press.

4. We have applied the same systematic genetic and genomic approaches to mammalian blood vessel development, and used it to identify the progenitors and cellular and molecular events of vessel wall development including the control of wall thickness, a critical process that goes awry in the most prominent vascular diseases. Our studies of coronary arteries showed that they form from venous cells that undergo deprogramming and then reprogramming to arterial identity, overturning the longstanding textbook model of how these important vessels originate and with important implications for coronary artery disease and for inducing and engineering new vessels for therapy.

a. Red-Horse, K., Ueno, H., Weissman, I.L., and **Krasnow, M.A.** (2010) Coronary arteries form by developmental reprogramming of venous cells. *Nature* 464, 549-553. PMCID: PMC2924433
b. Greif, D., Kumar, M, Lighthouse, J.K., Hum, J., An, A., Ding, L., Red-Horse, M.K., Espinoza, F.H., Olson, L., Offermanns, S., and **Krasnow, M.A.** (2012) Radial construction of an arterial wall. *Dev Cell* 23, 482-493.

5. We have recently begun applying the same systematic genetic and genomic approaches to elucidate the control of breathing. We identified the acute oxygen sensor in breathing. We also demonstrated a striking molecular and functional diversity of neurons in the preBotzinger Complex, the primary breathing pacemaker, with identified neuronal subtypes that dictate the specific pattern of breathing and that define a novel ascending circuit that regulates calm vs. arousal behavior.

a. Chang, A.J., Ortega F.E., Riegler, J., Madison, D.V., and **Krasnow, M.A.** (2015) Oxygen control of breathing by an olfactory receptor activated by lactate. Nature, accepted.
b. Li, P.$^{+}$, Janczewski, W.A.$^{+}$, Yackle, K.$^{+}$, Kam, K., Pagliardini, S., **Krasnow, M.A.***, and Feldman, J.L.* (2015) The central control circuit of sighing. Nature, in revision. ($^{+}$, co-first authors; *, corresponding authors)
c. Yackle, K., Schwarz, L.A., Luo, L., and Krasnow, M.A. (2015) Breathing pacemaker neurons that promote arousal in mice. Submitted.

**Complete List of Published Work in MyBibliography:**
http://www.ncbi.nlm.nih.gov/myncbi/browse/collection/43645686/?sort=date&direction=ascending