ANIMESH RAY

Professor, Faculty Chair, Director of the PhD Program, and Director of the Center for Network Studies

AREAS OF EXPERTISE

Gene function, gene regulatory network, genomics, homologous recombination, gene targeting, microRNA, systems biology, epigenetic regulation, plant molecular biology, plant development, melanoma biology, synthetic biology, molecular computing

CONTACT INFORMATION

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Dr. Ray earned his PhD in microbial genetics from Monash University in Melbourne, Australia. His PhD research led to the identification of a gene for efficient plasmid maintenance in *Escherichia coli* and a method for generating a multi-copy infectious plasmid that is packageable inside a virus coat—an early example of synthetic biology. He subsequently conducted research at the Institute of Molecular Biology, University of Oregon, and the Department of Biology, Massachusetts Institute of Technology, in which he developed methods for precise *in vivo* chromosome engineering in yeast and in an experimental plant. He was an Assistant Professor from 1991 to 1995 and Associate Professor from 1996 to2001 of Biology at the University of Rochester, New York, and an adjunct faculty member at the University of California, San Diego from 2001 to 2004. He was a visiting professor at the University of Rochester from 2001 to 2004, Institute for Systems Biology in Seattle in 2009, and University of Hyderabad in 2009. Research in his laboratory led to the discovery of the first known maternal effect embryo pattern formation gene in plants. His student, Teresa Golden, cloned a plant gene (DCL1) that later became known as the first member of the Dicer group of genes required for microRNA biosynthesis. Another of his students, Stephen Schauer, identified the remaining known plant Dicer genes (DCL2-4). From 1999 to 2001, while on extended leave of absence from the University of Rochester, Dr. Ray directed research programs on regulation of gene expression and gene targeting at a plant biotechnology start-up company in San Diego.

In the late 1990s, Dr. Ray, along with a computer scientist colleague Dr. Mitsunori Ogihara, published a series of papers on experimental and theoretical investigations on designing massively parallel computing devices using solution phase DNA chemistry. Accounts of this research were featured in several news media including the *New York Times* and the *International Herald Tribune* and he and Dr. Ogihara were featured in the book *One Digital Day: How the Microchip is Changing Our World*.

He currently teaches courses on molecular systems biology that includes molecular mechanisms of human diseases and pharmacogenomics. He is the director of KGI's PhD program and also of the Center for Network Studies.

RESEARCH SYNOPSIS

Current research in Dr. Ray's laboratory uses yeast as a model system to address the basis of evolutionary robustness of the genome. In collaboration with colleagues at the University of Rochester, University of Toronto, and the Institute for Systems Biology in Seattle, Dr. Ray's laboratory has discovered a network of over 700 genes that can bypass the lethal effects of mutations in some forty other genes. These results have revealed a previously unappreciated view of the complex organization of a genome, which allows the cells to potentially bypass the deleterious effects of mutations by reshuffling and reorganizing their genomes. Dr. Ray's laboratory has also identified genes that cause chromosome instability. Chromosome instability is a hallmark of cancer and identifying such genes in a model organism would allow for better assessment of human cancer cell functions. Recent collaborative research in Dr. Ray's laboratory has also led to the discovery of a mechanism of chromosome break repair in plants, a human microRNA associated with melanoma, the development of a computational method for predicting protein-protein interaction pairs, the design of a systems biology computational platform (BiologicalNetworks.org), and a mathematical model that simulates the dynamics of gene expression in certain cancer cells in response to DNA damage.

KEY RESEARCH CAPABILITIES

The Ray laboratory is equipped for a variety of projects in molecular systems biology, microarray gene expression analysis, and chromatin immune-precipitation (ChIP-chip) analysis.

CURRENT RESEARCH PROJECTS

Genome-wide Bypass Network of Essential Gene Mutation (Dr. Biranchi Patra, postdoctoral researcher in Dr. Ray's laboratory and in collaboration with the University of Rochester Medical School and the University of Toronto): Mutation studies of each essential gene of *Saccharomyces cerevisiae* and selection for all possible genes in the genome which, if over-expressed, could potentially suppress the lethal effects of the original mutation. These collaborative studies have the potential to reduce the deleterious effects of drugs on normal cells while maximizing the lethal effects of the same drugs on diseased cells.

Genes That Induce Chromosome Instability by Gain-of-function: PhD student Jesse Frumkin is conducting a medium throughput screen for genes that cause high frequency chromosome instability when these genes are over-expressed. At least 24 such genes have been confirmed. The Ray lab anticipates that by using this information, it would be possible to identify human homologues, some of which might cause chromosome instability in cancer cells.

Evolutionary Games and Genome Evolution: The Ray lab is addressing whether evolutionary robustness through genetic bypass systems can be understood through the abstract model of evolutionary game theory using a hybrid experimental and theoretical approach.

FUTURE RESEARCH INTERESTS

Dr. Ray and the Center for Network Studies are looking for collaborators to extend their work on mutational bypass systems in yeast into chemotherapy bypass mechanisms in cancer cells under targeted chemotherapy. They would also like to collaborate to identify genes that cause chromosome instability in human systems.

SELECTED PATENTS

Ray A, Golden TA, inventors; University of Rochester, assignee. *Gene encoding short integuments and uses thereof*. Rochester, NY / USA patent 6,737,561. 2004 May 18.

Perera JR, Lu M, **Ray A**, inventors; *Polynucleotide sequences from rice*.6,544,783. 2003 Apr 8.

SELECTED PUBLICATIONS

Kozhenkov S, Sedova M, Dubinina Y, Gupta A, **Ray A**, Ponomarenko J, Baitaluk M. "BiologicalNetworks - tools enabling the integration of multi-scale data for the host-pathogen studies". *Bmc Systems Biology* 2011 Jan 14;5:7 doi:10.1186/1752-0509-5-7.

Mazar J, DeYoung K, Khaitan D, Meister E, Almodovar A, Goydos J, **Ray A**, Perera RJ. "The Regulation of miRNA-211 Expression and Its Role in Melanoma Cell Invasiveness". *Plos One* 2010;5(11):e13779.

Vallabhajosyula RR, Chakravarti D, Lutfeali S, **Ray A**, Raval A. "Identifying Hubs in Protein Interaction Networks". *Plos One* 2009;4(4):e5344.

Paladugu SR, Zhao S, **Ray A**, Raval A. "Mining protein networks for synthetic genetic interactions". *Bmc Bioinformatics* 2008;9(1):426.

Langer M, Sniderhan LF, Grossniklaus U, **Ray A**. "Transposon Excision from an Atypical Site: A Mechanism of Evolution of Novel Transposable Elements". *Plos One* 2007;2(10):e965.

Chickarmane V, **Ray A**, Sauro HM, Nadim A. "A model for p53 dynamics triggered by DNA damage". *Siam Journal on Applied Dynamical Systems* 2007;6(1):61-78.

Baitaluk M, Sedova M, **Ray A**, Gupta A. "BiologicalNetworks: visualization and analysis tool for systems biology". *Nucleic Acids Res*. 2006 Jul 1;34(supp_2):W466-W471.

Ray A. "Plant genetics - RNA cache genome trash?" *Nature* 2005 Sep 1;437(7055):E1-E2.

Mlotshwa S, Schauer SE, Smith TH, Mallory AC, Herr JM, Roth B, Merchant DS, **Ray A**, Bowman LH, Vance VB. "Ectopic DICER-LIKE1 expression in P1/HC-Pro Arabidopsis rescues phenotypic anomalies but not defects in microRNA and silencing pathways". *Plant Cell* 2005 Nov;17(11):2873-2885.

Ray A. "Displaced t-loop models and telomere maintenance in plants". *Nat Rev Genet* 2004 May;5(5)

Papp I, Mette MF, Aufsatz W, Daxinger L, Schauer SE, **Ray A**, van der Winden J, Matzke M, Matzke AJM. "Evidence for nuclear processing of plant micro RNA and short interfering RNA precursors". *Plant Physiol*. 2003;132(3):1382-1390.

Schauer SE, Jacobsen SE, Meinke DW, **Ray A**. "DICER-LIKE1: blind men and elephants in Arabidopsis development". *Trends in Plant Science* 2002 Nov;7(11):487-491.

Golden TA, Schauer SE, Lang JD, Pien S, Mushegian AR, Grossniklaus U, Meinke DW, **Ray A**. "Short Integuments1/Suspensor1/Carpel Factory, A Dicer Homolog, Is A Maternal Effect Gene Required for Embryo Development in Arabidopsis". *Plant Physiol*. 2002;130(2):808-822.

Ogihara M, **Ray A**. "Molecular computation: DNA computing on a chip". *Nature* 2000;403(6766):143-144.

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