Genetic analysis of zinc-finger nuclease-induced gene targeting in Drosophila, pp. 641–651

Ana Bozas, Kelly J. Beumer, Jonathan K. Trautman and Dana Carroll

Zinc-finger nucleases can be designed to cleave arbitrary genomic sequences, which stimulates localized mutagenesis and targeted gene replacement. Both outcomes depend on normal cellular processes of DNA repair, and this study examines the pathways responsible. Gene replacement by homologous recombination depends on the activity of the Rad51 protein. Much of local mutagenesis depends on DNA ligase IV, lig4. In the absence of Rad51, repair is biased toward mutagenesis; in the absence of lig4, a strong shift toward gene replacement is seen.

Genome-wide analysis reveals novel pathways affecting endoplasmic reticulum homeostasis, protein modification and quality control, pp. 757–769

Alenka Čopić, Mariana Dorrington, Silvere Pagant, Justine Barry, Marcus C. S. Lee, Indira Singh, John L. Hartman, IV and Elizabeth A. Miller

Managing the repertoire of resident and client proteins is an integral part of organelle homeostasis. The authors of this article systematically screen for mutants of yeast with defects in retention of a resident chaperone of the endoplasmic reticulum. They discover known and novel components of protein biosynthesis, trafficking and quality control pathways.

Quantitative trait loci for aggressive behavior in Drosophila melanogaster, pp. 889–897

Alexis C. Edwards and Trudy F. C. Mackay

Aggressive behavior is important for survival and reproduction, and is near universal among animals, but little is known about its genetic architecture in natural populations. The authors map five quantitative trait loci (QTLs) affecting the difference in aggressive behavior between two Drosophila melanogaster wild-type strains in an initial genome scan. At least three, and possibly all five, of these QTLs interact epistatically. One small region containing two linked, epistatic QTLs fractionated into at least six QTLs affecting aggressive behavior. Extensive epistasis poses a serious challenge for understanding the genetic basis of complex traits.

Evolution in Candida albicans populations during a single passage through a mouse host, pp. 799–811

Anja Forche, P. T. Magee,安娜 Selmecki, Judith Berman and Georgiana May

What limits the evolution of virulence in opportunistic pathogens such as the yeast Candida albicans? These authors address this question by evaluating rates of population growth and evolution in C. albicans during its propagation in a mouse host and in vitro. They observe slower rates of population growth and higher rates of genomic and phenotypic variation during passage through a mouse host than during growth in vitro. They suggest that the evolution of virulence in opportunistic pathogens is strongly limited by population bottlenecks coupled with the generation of variation that persists during infectious growth but is deleterious during commensal growth.

Transcriptional silencing and reactivation in transgenic zebrafish, pp. 747–755

Mary G. Goll, Ryan Anderson, Didier Y. R. Stainier, Allan C. Spradling and Marline E. Halpern

Epigenetic regulation of transcription is fundamental to the development of organisms, and how do individual cells and tissues respond to epigenetic marks on genes? These authors exploit transgenic strategies to track changes in expression of fluorescent reporters in living zebrafish across multiple generations. They find unexpected differences in gene silencing and reactivation among different cell populations. This study lays the groundwork for uncovering new mechanisms that underlie epigenetic phenomena during vertebrate development through genetic screens.

Drosophila ISWI regulates the assistance of histone H1 with interphase chromosomes in vivo, pp. 661–669

Giorgia Siria, Renate Deuring, Maria Cristina Chiorda, Peter B. Becker and John W. Tamkun

Biochemical studies have suggested that histone H1 plays a major role in regulating higher-order chromatin structure, but its function in vivo is not well understood. To address this issue, these authors investigate phenotypes resulting from the loss of histone H1 in Drosophila. They reveal that histone H1 is a major determinant of interphase chromosome structure. The researchers also demonstrate that histone H1 undergoes rapid, replication-independent exchange, and they present data that suggest that the ISWI chromatin-remodeling factor is required for this process.

Epigenetic inheritance and the missing heritability problem, pp. 845–850

Montgomery Slatkin

Although large genomewide association studies have found many SNPs correlated with elevated risk of complex inherited diseases in humans, these SNPs account for a small fraction of familial risk, raising the question: what factors account for the remaining risk—the “missing heritability”? Transgenerational epigenetic inheritance has been proposed as one possible solution to the problem of missing heritability. The analysis in this article shows that epigenetic modifications are a potential solution to the problem of missing causality of complex diseases but likely not to the problem of missing heritability.

Telomeric RNAs mark sex chromosomes in stem cells, pp. 685–698

Li-Feng Zhang, Yuya Ogawa, Janice Y. Ahn, Satoshi H. Namekawa, Susana S. Silva and Jeannie T. Lee

These authors propose that telomeric RNAs, which mark both the X and the Y chromosome and show highly specific and developmentally regulated patterns of expression during stem cell differentiation, are linked to cell differentiation and may be marks of pluripotency and disease.

This Month in Genetics Research

Gene ontology analysis of genomewide association studies datasets provide insight into the biology of bipolar disorder, Am. J. Hum. Genet. 84: 13–24

Peter Holmans, Elaine K. Green, Jaspreet Singh Palvia, Manuel A. R. Ferreira, Shaun M. Purcell, Pamela Sklar, The Wellcome Trust Case-Control Consortium, Michael J. Owen, Michael C. O’Donovan and Nick Craddock

Genomewide association studies (GWAS) of human populations are successfully identifying genes involved in complex disease, so an article by Houssa et al. (2009) published in the July issue of The American Journal of Human Genetics is timely. The article presents a method for identifying biological processes involved in disease based on gene ontology terms of loci linked to the disease. The authors mine GWAS data on Crohn’s disease and successfully identify biological processes previously implicated in that disorder. Their analysis of GWAS data for bipolar disorder implicates modulation of transcription and cellular activity, including by hormonal action, as important for pathogenesis of that disease.


Margaret W. Leigh, Jessica E. Pittman, Johnny L. Carson, Thomas W. Ferko1, Sharon D. Dell, Stephanie D. Davis, Michael R. Knowles and Maimoona A. Zariwala

A recent article in Genetics in Medicine (Leigh et al. 2009) describes another example of how studies of model organisms reveal genes responsible for a human disease. Primary ciliary dyskinesia is the result of abnormal motility of cilia in the respiratory tract, the middle ear, the fallopian tubes, and on sperm, which results in chronic bronchitis, ear infections, and male infertility. Because cilia are ancient, identification of genes encoding them in Chlamydomonas and zebrafish provide candidate genes that lead to identification of seven genes that explain 40% of this rare disease.