GENETICS, Vol. 214, March 2020, Copyright © 2020

A new polygenic model for nonfamilial colorectal cancer inheritance based on the genetic architecture of the azoxymethane-induced mouse model, pp. 691–702

Anika C. Bissahoyo, Yuying Xie, Lynda Yang, R. Scott Pearsall, Daekee Lee, Rosemary W. Elliott, Peter Demant, Leonard McMillan, Fernando Pardo-Manuel de Villena, Joe M. Angel, and David W. Threadgill

The azoxymethane carcinogen model of non-familial colorectal cancer has been used in mice to identify six new susceptibility loci and confirm 18 of 24 previous detected susceptibility loci. Using a population-based approach, the genetic architecture of colon cancer susceptibility was inherited in a genome-wide dominant fashion with the number of resistant alleles determining susceptibility. This suggests a new model of inheritance and has important implications on how cancer modifiers are detected and ultimately used in humans.

A microbe associated with sleep revealed by a novel systems genetic analysis of the microbiome in collaborative cross mice, pp. 719–733

Jason A. Bubier, Vivek M. Philip, Christopher Quince, James Campbell, Yanjiao Zhou, Tatiana Vishnivetskaya, Suman Duvvuru, Rachel Hageman Blair, Juliet Ndukum, Kevin D. Donohue, Carmen M. Foster, David J. Mellert, George Weinstock, Cymbeline T. Culiat, Bruce F. O'Hara, Anthony V. Palumbo, Mircea Podar, and Elissa J. Chesler

Host genetic diversity provides a variable selection environment and physiological context for microbiota and their interaction with host physiology. Using a highly diverse mouse population, Bubier *et al.* identified that Odoribacter abundance influences sleep architecture in a manner influenced by genetic variation in the Leptin pathway. Perturbation of the microbiome of $Lepr^{db}$ mutants altered sleep related behavior consistent with the prediction made from genetic analysis.

Impact of chromosome fusions on 3D genome organization and gene expression in budding yeast, pp. 651–667

Marco Di Stefano, Francesca Di Giovanni, Vasilisa Pozharskaia, Mercè Gomar-Alba, Davide Baù, Lucas B. Carey, Marc A. Marti-Renom, and Manuel Mendoza

In eukaryotic cells, the spatial organization of genes within the nucleus is correlated with their expression. However, correlation is not causation. To determine how nuclear spatial organization affects gene expression, Di Stefano *et al.* studied budding yeast cells with chromosome fusions that cause widespread changes in the spatial organization of the genome. They find that gene expression is largely unaffected by dramatic changes in chromosome location. However, proximity to chromosome ends and to the nuclear periphery has a mild effect in the expression of perinuclear genes, and moving these genes away from the periphery slightly increases their expression.

CNVmap: a method and software to detect and map copy number variants from segregation data, pp. 561–576

Matthieu Falque, Kamel Jebreen, Etienne Paux, Carsten Knaak, Sofiane Mezmouk, and Olivier C. Martin

Copy-number variants (CNVs) represent a large part of natural genetic diversity and contribute significantly to trait variation. As a complement to sequence-based approaches, Falque *et al.* propose an original method to both detect and map structural variations using genetic mapping panels. Specifically, they exploit the apparent heterozygous state of duplicated loci; peaks in the associated genome-wide allelic profiles provide highly specific signatures that identify the nature and position of the CNVs. They validate this approach on simulated and experimental data sets and provide a software that makes analyses straightforward given genetic mapping data.

Differential contributions of DNA-binding proteins to polycomb response element activity at the *Drosophila giant* gene, pp. 623–634

Elnaz Ghotbi, Kristina Lackey, Vicki Wong, Katie T. Thompson, Evan G. Caston, Minna Haddadi, Judith Benes, and Richard S. Jones

Polycomb-group (PcG) proteins utilize epigenetic mechanisms to maintain the transcriptional silence of target genes. Recruitment of *Drosophila* PcG proteins to target genes requires the presence of a Polycomb Response Element (PRE). Some PcG target genes, including the *giant* gene, have two PREs. In Ghotbi *et al.*, the different activities of three PRE binding proteins are examined, including their differential abilities to recruit other PcG complexes to a *giant* PRE. In addition, experimental evidence for the ability of PcG proteins to dampen the expression of an active gene is presented.

Cross-species complementation of nonessential yeast genes establishes platforms for testing inhibitors of human proteins, pp. 735–747

Akil Hamza, Maureen R. M. Driessen, Erik Tammpere, Nigel J. O'Neil, and Philip Hieter

Given the broad utility of humanized yeast to model and study human biology, a reference set of human genes that can replace cognate yeast genes and operate in yeast is needed. Hamza *et al.* present a systematic screen for human complementation of non-essential yeast genes implicated in chromosome instability (CIN), that produced a set of humanized yeast strains as a resource for cancer genetic studies. Complementation of single yeast mutants and 2-subunit protein complexes were assessed in conditional assays that test rescue of chemical sensitivity and/or CIN defects. The yeast-based platform was used to study chemical inhibitors of a human CIN protein that is a candidate target for anti-cancer therapeutics.

Sex chromosome pairing mediated by euchromatic homology in *Drosophila* male meiosis, pp. 605–616

Christopher A. Hylton, Katie Hansen, Andrew Bourgeois, and John E. Tomkiel Dean

Drosophila males have evolved a unique system of chromosome segregation in meiosis that lacks recombination. Chromosomes pair at selected sequences suggesting that early steps of meiosis may also differ in this organism. Using Y chromosomes carrying portions of X material, Hylton *et al.* show that pairing between sex chromosomes can be mediated by sequences other than the previously identified rDNA pairing sites. They propose that pairing may simply be homology-based and may not differ from canonical meiosis observed in females. The main difference in males may be that conjunctive mechanisms that join homologs in the absence of crossovers.

Mating-type-specific ribosomal proteins control aspects of sexual reproduction in *Cryptococcus neoformans*, pp. 635–649

Giuseppe Ianiri, Yufeng "Francis" Fang, Tim A. Dahlmann, Shelly Applen Clancey, Guilhem Janbon, Ulrich Kück, and Joseph Heitman

This study demonstrated that the ribosomal proteins Rpl22 and Rpl39 encoded by the *MAT* locus of *Cryptococcus neoformans* are essential. Focusing on the *RPL22***a** and *RPL22*α alleles, Ianiri *et al.* found differential expression of the two *RPL22* genes during mating, and an RNAi-dependent mechanism that contributes to control *RPL22***a** expression. Haploid *C. neoformans RPL22* gene exchange strains generated via CRISPR/Cas9 displayed morphological and genetic defects during bilateral mating. These results contribute to elucidate functions of *C. neoformans* essential mating-type genes that may constitute a type of imprinting system to promote inheritance of nuclei of both mating types during sexual reproduction.