ISSUE HIGHLIGHTS

The X chromosome in quantitative trait locus mapping, pp. 2151–2158

Karl W. Broman, Śaunak Sen, Sarah E. Owens, Ani Manichaikul, E. Michelle Southard-Smith and Gary A. Churchill

Most quantitative trait locus (QTL) mapping methods, including widely used computer packages, fail to account for the fact that the X chromosome requires special treatment in the mapping of QTL. In this article the authors develop a method for appropriate treatment of the X chromosome for QTL mapping in experimental crosses. They show that if the X chromosome is treated like an autosome, a sex difference in the phenotype can lead to spurious linkage on the X chromosome. Tests of significance need to be tailored to the X chromosome, and failure to do so can make the test too liberal. The methods are implemented in the R/qtl software package.

emb-4 is a conserved gene required for efficient germline-specific chromatin remodeling during *Caenorhabditis elegans* embryogenesis, pp. 1895–1906

Paula M. Checchi and William G. Kelly

and

EMB-4: A predicted ATPase that facilitates *lin-12* activity in *Caenorhabditis elegans*, pp. 1907–1915

Iskra Katic and Iva Greenwald

The establishment and maintenance of the embryonic germline is essential for fertility of the adult and hence maintenance of the species. Repressive mechanisms provide this maintenance in many organisms, including *Caenorhabditis elegans*. One mode of repression in *C. elegans* germ cells involves chromatin remodeling, and this requires the gene *emb-4*, which encodes a highly conserved protein with orthologs in fly, mouse, and human. The embryonic phenotype of *emb-4* mutants is consistent with a defect in the efficient and timely activation of developmental programs, including germline chromatin remodeling. The *emb-4* gene encodes a conserved nuclear-localized ATPase that functions cell autonomously to enhance LIN-12/Notch signaling.

roX RNAs are required for increased expression of X-linked genes in *Drosophila melanogaster* males, pp. 1859–1866

Xinxian Deng and Victoria H. Meller

The male-specific lethal (MSL) ribonucleoprotein complex is necessary for equalization of X:A expression levels in Drosophila males, which have a single X chromosome. The MSL complex binds selectively to the male X chromosome and directs acetylation of histone H4 at lysine 16. *roX1* and *roX2* noncoding RNAs are essential but redundant components of this complex. Simultaneous removal of both *roX* RNAs reduces X-localization of the MSL proteins and permits their ectopic binding to autosomal sites and the chromocenter. Microarray analysis revealed that the loss of the *roX1* and *roX2* RNAs resulted in a decrease in X chromosomal gene expression, but did not enhance gene expression at autosomal sites of MSL binding. These results indicate that it is the failure to compensate X-linked genes, rather than inappropriate upregulation of autosomal genes at ectopic sites of MSL binding, that is the primary cause of male lethality upon loss of *roX* RNAs.

Enhancer–promoter communication at the *yellow* gene of *Drosophila melanogaster*: Diverse promoters participate in and regulate *trans* interactions, pp. 1867–1880

Anne M. Lee and C.-ting Wu

The *yellow* locus of Drosophila is useful for investigating the mechanisms of *trans* interactions due to its ability to support transvection and the relative ease with which it can be altered by targeted gene replacement. Through the analysis of *yellow* alleles whose promoters have been replaced with wild type or altered promoters from other genes, the authors show that mutation of single core promoter elements of two of the three heterologous promoters tested can influence whether *yellow* enhancers act in *cis* or in *trans*. This finding parallels studies of the *yellow* promoter, suggesting that the manner in which *trans* interactions are controlled by core promoter elements describes a general mechanism. The authors further demonstrate that heterologous promoters can themselves be activated in *trans* as well as participate in pairing-mediated insulator bypass. These results highlight the potential of diverse promoters to partake in many forms of *trans* interactions.

Unexpected high polymorphism at the FABP4 gene unveils a complex history for pig populations, pp. 2119–2127

Ana Ojeda, Julio Rozas, Josep M. Folch and Miguel Pérez-Enciso

Agriculturally important animals provide excellent models for genetic architecture of important traits. Fatty acid binding protein 4 (FABP4) plays a key role in fat regulation in mammals. Resequencing of FABP4 identified exceptional nucleotide diversity for a mammal (0.01) and a gene genealogy that did not show any geographical or breed clustering. Additional genotyping showed that distant breeds often share similar haplotypes and that some of the most inbred breeds had high levels of heterozygosity. The coalescence time for FABP4 is older than the estimated time of domestication of pig, suggesting an exceptional duration of maintenance of high variability in the face of inbreeding.

Structure–function analysis of Delta trafficking, receptor binding and signaling in Drosophila, pp. 1947–1961

Annette L. Parks, Jane R. Stout, Scott B. Shepard, Kristin M. Klueg, Ana A. Dos Santos, Todd R. Parody, Martina Vaskova and Marc A. T. Muskavitch

The transmembrane proteins Delta and Notch act as ligand and receptor in a conserved signaling pathway required for a variety of cell fate specification events in many organisms. The binding of Delta to Notch results in a proteolytic cascade that releases the Notch intracellular domain, allowing it to participate in transcriptional activation in the nucleus. While the Delta N-terminal domain is necessary and sufficient for binding to Notch, the integrity of epidermal growth factor-like repeat (ELR) 2 is also required for Notch binding. Screening of 117 *Delta* mutant lines for proteins that exhibit aberrant subcellular trafficking has led to the identification of 18 *Delta* alleles, most of which result from missense mutations in ELRs within the Delta extracellular domain that encode "trafficking-defective" Delta proteins. However, the authors also find that two Dl^{ITD} alleles contain lysine missense mutations within the Delta intracellular domain (DeltaICD) that may identify residues important for Delta endocytosis and signaling.

Centromere-proximal crossovers are associated with precocious separation of sister chromatids during meiosis in *Saccharomyces cerevisiae*, pp. 1745–1754

Beth Rockmill, Karen Voelkel-Meiman and G. Shirleen Roeder

In virtually all eukaryotes, the frequency of recombination is reduced near the centromere, as might be expected if centromere-associated crossovers have deleterious effects on meiotic chromosome segregation. Indeed, studies in humans and Drosophila demonstrate that centromere-associated crossovers predispose chromosomes toward meiotic missegregation events that are the equivalent of meiosis II nondisjunction. In budding yeast, centromere-associated meiotic crossovers are also associated with meiotic chromosome missegregation, in this case with premature separation of sister chromatids (PSSC). The authors propose an elegant model in which crossovers disrupt structures that are essential for meiotic centromere function. This model can account for the differing meiotic defects caused by centromere-associated crossovers in different species.

Chemical inactivation of Cdc7 kinase in budding yeast results in a reversible arrest that allows efficient cell synchronization prior to meiotic recombination, pp. 1767–1774

Lihong Wan, Chao Zhang, Kevan M. Shokat and Nancy M. Hollingsworth

A chemical genetic approach was used to create a novel conditional allele of the highly conserved protein kinase Cdc7 (*cdc7-as3*) that enables cells to be synchronized immediately prior to recombination. When Cdc7-as3 is inactivated by addition of inhibitor to sporulation medium, cells undergo a delayed premeiotic S phase, then arrest in prophase before double-strand break (DSB) formation. The arrest is easily reversed by removal of the inhibitor, after which cells rapidly and synchronously proceed through meiosis. Using the synchrony resulting from the *cdc7-as3* system, DSB-dependent phosphorylation of the meiosis-specific chromosomal core protein, Hop1, was shown to occur after DSBs. The *cdc7-as3* mutant provides a valuable tool both for understanding the role of Cdc7 in meiosis and for facilitating studies of recombination.