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INVESTIGATIONS AND AUTHOR SUMMARIES

- 379–386 **Strain Specific Genotype–Environment Interactions and Evolutionary Potential for Body Mass in Brook Charr (*Salvelinus fontinalis*)**
Amélie Crespel, Louis Bernatchez, Céline Audet, and Dany Garant
- In this study, the authors measured the genetic basis of body mass in three divergent strains of brook charr (*Salvelinus fontinalis*) in different rearing environments and time periods. They found that while body mass was a heritable trait in all strains, the level of heritability greatly differed among strains. Heritability estimates of each strain varied differently according to environmental rearing conditions and throughout ontogeny. These results highlight the significance of strain differences in genetic architecture as well as gene x environment interactions. The study also emphasizes the importance of considering strain-specific quantitative genetics characteristics in selective breeding programs.
- 387–397 **Accurate Identification and Analysis of Human mRNA Isoforms Using Deep Long Read Sequencing**
Hagen Tilgner, Debasish Raha, Lukas Habegger, Mohammed Mohiuddin, Mark Gerstein, and Michael Snyder
- Transcriptomes are currently analyzed by short-read (≤ 100 bps) sequencing of cDNAs, which allows the analysis of almost all (including lowly expressed) genes at low cost. These authors sequenced millions of long reads (> 500 bps) that often spanned 3, 4, 5 or more introns in the human ENCODE cell-lines HeLaS3 and K562. Their results indicate that short-read-derived exon-intron-structures can be improved considerably. Existing gene-structure annotations can also be improved, especially for lncRNAs. This analysis, as well as quantitative cell-type specific splicing analysis, can be performed independently of any prior annotation, making it ideal for the transcriptome analysis in newly sequenced genomes.
- 399–407 **On the Mutational Topology of the Bacterial Genome**
Patricia L. Foster, Andrew J. Hanson, Heewook Lee, Ellen M. Popodi, and Haixu Tang
- By sequencing the genomes of parallel lines of a high-mutating strain of *Escherichia coli*, the authors discovered that the mutations are not distributed at random but fall into a wave-like spatial pattern that is repeated in the two separately-replicating halves of the chromosome. The pattern is correlated to genomic features, with mutation densities highest in regions predicted to be highly structured. Superimposed upon this pattern are hotspots, some of which are located where replication forks may collide or be blocked. These results suggest that the two replication forks encounter parallel structural features that change the fidelity of DNA replication.

- 409–425 **A Mosaic Genetic Screen for Genes Involved in the Early Steps of *Drosophila* Oogenesis**
Marlène Jagut, Ludivine Mihaila-Bodart, Anahi Molla-Herman, Marie-Françoise Alin, Jean-Antoine Lepesant, and Jean-René Huynh
- Drosophila* oogenesis is a versatile model system to address many important questions of cell and developmental biology, such as stem cell regulation, cell polarization and differentiation, cell adhesion, and cell cycle regulation. To uncover novel genes involved during the early stages of oogenesis, the authors used the FLP/FRT-GFP system to perform a mosaic genetic screen for mutations causing an early arrest of development on the left arm of chromosome 2 (2L). They generated a collection of 73 EMS-induced mutants that affect oocyte determination, polarization, or localization. This collection of mutants will be useful in further investigations of the early steps of *Drosophila* oogenesis at a genetic level.
- 427–439 **Imputation of Unordered Markers and the Impact on Genomic Selection Accuracy**
Jessica E. Rutkoski, Jesse Poland, Jean-Luc Jannink, and Mark E. Sorrells
- Imputation methods suitable for markers of unknown order have not been rigorously evaluated in terms of imputation accuracy and impact on the genomic selection accuracy. In this study, the authors evaluated four such methods based on random forest regression, k-nearest neighbors, singular value decomposition, and expectation maximization algorithms. They compared each method to mean imputation and found that in some cases genomic selection accuracies can be improved when a method other than mean imputation is used prior to genomic selection model training.
- 441–450 **The Genetic Architecture of Degenerin/Epithelial Sodium Channels in *Drosophila***
Kathleen M. Zelle, Beika Lu, Sarah C. Pyfrom, and Yehuda Ben-Shahar
- In this article, the authors present detailed molecular and structural analyses of the Degenerin/epithelial sodium channel (DEG/ENaC) family in *Drosophila*. Members of the DEG/ENaC family of sodium channels have emerged recently as important players in diverse mammalian physiological processes. The data presented here will enable the use of *Drosophila* genetics to better understand the biology of DEG/ENaC proteins. Because it highlights the significant medical importance of this family of proteins, the authors anticipate that their work will have implications in diverse biological disciplines, including evolutionary genetics, behavioral and neurogenetics, ion channel biology, and sensory biology.
- 451–463 **Mature Microsatellites: Mechanisms Underlying Dinucleotide Microsatellite Mutational Biases in Human Cells**
Beverly A. Baptiste, Guruprasad Ananda, Noelle Strubczewski, Andrew Lutzkanin, Su Jen Khoo, Abhinaya Srikanth, Nari Kim, Kateryna D. Makova, Maria M. Krasilnikova, and Kristin A. Eckert
- Microsatellites are functional tandem repeat sequences that are abundantly distributed throughout the genome, including within genes. The authors identify over 350 human genes containing mature length dinucleotide repeats within exons. These dynamic DNA elements have the propensity for frameshift mutagenesis and pose an intrinsic threat to genomic stability. How do cells control the stability of these sequences? Using cellular and biochemical assays, the authors describe mechanisms of dinucleotide mutability. A bias towards expansions of dinucleotides, which has been reported for over 15 years, is here mechanistically ascribed to be a consequence of mismatch repair rather than of polymerase slippage errors.
- 465–480 **Unequal Recombination and Evolution of the Mating-Type (*MAT*) Loci in the Pathogenic Fungus *Grosmannia clavigera* and Relatives**
Clement K.-M. Tsui, Scott DiGiustini, Ye Wang, Nicolas Feau, Braham Dhillon, Jörg Bohlmann, and Richard C. Hamelin
- The mating-type (*MAT*) locus, with its two alleles *MAT1-1* or *MAT1-2*, is important in regulating the sexual reproduction of fungi. Recombination should be suppressed at the *MAT* locus. However, this study of the pine pathogen (*Grosmannia clavigera*) and its relatives inferred the presence of a genomic footprint indicative of a past recombination event. An ancient unequal recombination between opposite *MAT* alleles resulted in the ancestral *MAT1-1-1* gene integrating into the *MAT1-2* allele and surviving as the truncated *MAT1-1-1* gene. The truncated *MAT1-1-1* gene still expressed but was degenerated, leading to loss of the transcription factor with accelerated rate of amino acid substitutions.

- 481–491 **Resource Allocation for Maximizing Prediction Accuracy and Genetic Gain of Genomic Selection in Plant Breeding: A Simulation Experiment**
Aaron J. Lorenz
Allocating resources between population size and replication is critical to maximizing QTL detection power and prediction accuracy. In this article, the author shows that because genomic selection is able to achieve high prediction accuracy when population sizes are small, the resource allocation calculus differs between genomic selection and marker-assisted selection. Greater flexibility in experimental design exists for genomic selection.
- 493–503 **Genetic Interactions of *Arabidopsis thaliana* Damaged DNA Binding Protein 1B (DDB1B) With DDB1A, DET1, and COP1**
Ashwin L. Ganpudi and Dana F. Schroeder
Damaged DNA Binding protein 1 (DDB1) acts as a substrate adaptor for CUL4-based ubiquitin ligase complexes and is capable of interacting with a vast number of proteins. This study focuses on the genetic interactions between the two *Arabidopsis* DDB1 homologues: DDB1A and DDB1B. The authors used a reverse genetic approach to tease apart the redundant and distinct roles played by these two genes in overall growth and developmental response. By characterizing the genetic interactions of DDB1B with the negative regulators of photomorphogenesis DET1 and COP1, they also discovered unique and overlapping roles.
- 505–516 **A Genomic Survey of Reb Homologs Suggests Widespread Occurrence of R-Bodies in Proteobacteria**
Kasie Raymann, Louis-Marie Bobay, Thomas G. Doak, Michael Lynch, and Simonetta Gribaldo
R-bodies are puzzling intracellular structures produced by endosymbiont bacteria of *Paramecia*. The bacteria confer the R-bodies with a killing phenotype towards sensitive strains. The role and mechanism of action of the bacteria is still unclear. In this study, the authors show the presence of highly conserved Reb homologues in the genomes of a very large number of proteobacterial taxa displaying a wide variety of lifestyles, from free-living to association with eukaryotes. Phylogenomic analysis indicates a complex evolutionary history involving spread of entire reb loci across distantly related proteobacterial families along with species-specific reb gene duplications. These results allow the authors to propose a number of potential candidates for additional components of the R-body system.
- 517–525 **PolyCat: A Resource for Genome Categorization of Sequencing Reads From Allopolyploid Organisms**
Justin T. Page, Alan R. Gingle, and Joshua A. Udall
Read mapping is a fundamental part of next-generation genomic research and is complicated by genome duplication. Methods used to analyze diploid genomes can be extended to polyploid genomes if DNA sequencing reads can be properly categorized into their respective genomes. Here the authors present a pipeline for mapping and read categorization of sequence data produced from allopolyploid organisms including whole genome shotgun, RNA-seq, and bisulfite-treated reads. Their study demonstrates the functionality of this pipeline in allopolyploid *Gossypium hirsutum*. The pipeline output includes read-counts that are useful for downstream analyses such as differential expression, differential methylation, or differential DNA-protein binding sites from ChIP-seq experiments.
- 527–539 **Calcineurin Governs Thermotolerance and Virulence of *Cryptococcus gattii***
Ying-Lien Chen, Virginia N. Lehman, Yonathan Lewit, Anna F. Averette, and Joseph Heitman
Cryptococcus gattii is a human fungal pathogen that causes life-threatening pulmonary infections and meningoencephalitis in both healthy individuals and immunocompromised patients. It is the cause of an outbreak in the Pacific Northwest. These studies reveal that in *C. gattii* the phosphatase calcineurin functions in thermotolerance, virulence, fluconazole tolerance, and cation homeostasis. The authors' results illustrate both shared and divergent functions compared to those in *Cryptococcus neoformans*. The strongly attenuated virulence and increased fluconazole susceptibility of *C. gattii* calcineurin mutants suggest that a calcineurin inhibitor, alone or in combination with fluconazole, would be therapeutic against emerging *C. gattii* infections.

- 541–552 **Distinct 3-O-Sulfated Heparan Sulfate Modification Patterns Are Required for *kal-1*–Dependent Neurite Branching in a Context-Dependent Manner in *Caenorhabditis elegans***
Eillen Teclé, Carlos A. Diaz-Balzac, and Hannes E. Bülow
- Heparan sulfate is an extracellular glycan that is characterized by complex molecular modifications including sulfations of the sugar residues. These sugar polymers regulate intercellular communication by modulating protein-protein interactions. In this study, the authors found that 3-O-sulfation of heparan sulfate, the rarest of all modifications, is not required for viability. Instead, it is required for the formation of select neuronal branches. Additionally, HS 3-O-sulfation shows genetic interactions with the extracellular cell adhesion molecule *kal-1* that is mutant in Kallmann Syndrome, a neural targeting and migration defect. Thus, 3-O-sulfation of heparan sulfate is necessary for highly specific aspects of neuronal development.
- 553–561 **Actin Dosage Lethality Screening in Yeast Mediated by Selective Ploidy Ablation Reveals Links to Urmylation/Wobble Codon Recognition and Chromosome Stability**
Brian Haarer, Lei Mi-Mi, Jessica Cho, Matthew Cortese, Susan Viggiano, Daniel Burke, and David Amberg
- Changes in gene dosage for multiple genes are observed in many human genetic disorders, particularly cancer. The authors performed a whole genome screen in which they identified combinatorial changes in gene dosage that are deleterious to cells. The query for this screen was the gene for actin, a ubiquitous protein of the cytoskeleton that is centrally important for cell growth and division. The authors found that increases in actin gene dosage are deleterious when specific cellular functions including protein synthesis, chromosome stability, and cell growth are compromised by mutation. Their results also indicate that actin organization and protein synthesis are coordinated through a protein called EF1A, thus explaining the connection to protein synthesis and showing that actin has a role in chromosome inheritance.
- 563–572 **Fine-Mapping and Identification of a Candidate Gene Underlying the *d2* Dwarfing Phenotype in Pearl Millet, *Cenchrus americanus* (L.) Morrone**
Rajiv K. Parvathaneni, Vinod Jakkula, Francis K. Padi, Sebastien Faure, Nethra Nagarajappa, Ana C. Pontaroli, Xiaomei Wu, Jeffrey L. Bennetzen, and Katrien M. Devos
- The recessive *d2* dwarfing gene is widely used in pearl millet to reduce the height of commercial hybrids. Despite its economic importance, little research has gone into determining the identity of the *d2* gene. The authors used a combination of genetic mapping, comparative genomics, and haplotype analysis to identify *ABCBI*, a P-glycoprotein, as a likely candidate gene underlying *d2*. Mutations in *ABCBI*, which modulates auxin transport, have previously been shown to also cause dwarf phenotypes in sorghum and maize.
- 573–583 **Cell-Cycle Perturbations Suppress the Slow-Growth Defect of *spt10Δ* Mutants in *Saccharomyces cerevisiae***
Jennifer S. Chang and Fred Winston
- Spt10 of *Saccharomyces cerevisiae* is a putative acetyltransferase that activates transcription of histone genes. To understand Spt10 in greater depth, the authors screened for both enhancers and suppressors of the extremely poor growth caused by an *spt10* null mutation. Their results show that an *spt10* mutation causes lethality when combined with several classes of mutations, including those that impair the SAGA coactivator complex and other regulators of histone gene transcription. The authors also found that mutations or chemicals that slow the cell cycle partially suppress the *spt10* mutant growth defect.