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SOFTWARE AND DATA RESOURCES

- 3839–3848 **ARSDA: A New Approach for Storing, Transmitting and Analyzing Transcriptomic Data**
Xuhua Xia

ARSDA is a software package for analyzing high-throughput sequencing (HTS) data. It aims to eliminate/alleviate two key problems in HTS storage, transmission and analysis. First, it reduces 1) the size of HTS files (typically gigabytes in size in FASTQ format) without losing sequence information, and 2) computation time in data analysis such as gene expression characterization. Second, it offers a new method for proper allocation of multiple-matched reads to paralogous genes which should increase the accuracy of data analysis. ARSDA is freely available for Windows, Macintosh and Linux computers at <http://dambe.bio.uottawa.ca/ARSDA/ARSDA.aspx>, together with source code. The source code is also available as a zipped supplemental file ARSDA.Src.zip in <https://github.com/xuhuxia/ARSDA>.

- 3849–3856 **rSalvador: An R Package for the Fluctuation Experiment**
Qi Zheng

For nearly 75 years, the fluctuation experiment has been the preferred method for measuring microbial mutation rates in the laboratory. Using the R package rSalvador as a vehicle for presenting concrete examples, this article discusses new developments and open problems in the analysis of data produced by fluctuation experiments. The article helps the reader make an informed decision about which computational method is the most appropriate for a given experiment.

INVESTIGATIONS

- 3857–3866 **Dissecting Nucleosome Function with a Comprehensive Histone H2A and H2B Mutant Library**
Shuangying Jiang, Yan Liu, Caiyue Xu, Yun Wang, Jianhui Gong, Yue Shen, Qingyu Wu, Jef D. Boeke, and Junbiao Dai

As highly conserved structural proteins, histones play pivotal roles in many DNA-related processes and are closely related to human diseases. Using two libraries of histone H2A and H2B mutants, a comprehensive analysis of phenotypes of each amino acid residue was carried out in various stress conditions. H2B N- and H2A C-termini were identified to be critical for maintaining nucleosome function and mutations in these regions led to pleiotropic phenotypes. This study not only demonstrates the applications of the versatile histone library, but also revealed many previously unknown functions of histone H2A and H2B.

- 3867–3873 **Transcriptomic Analysis of Octanoic Acid Response in *Drosophila sechellia* Using RNA-Sequencing**
Stephen M. Lanno, Sara M. Gregory, Serena J. Shimshak, Maximilian K. Alverson, Kenneth Chiu, Arden L. Feil, Morgan G. Findley, Taylor E. Forman, Julia T. Gordon, Josephine Ho, Joanna L. Krupp, Ivy Lam, Josh Lane, Samuel C. Linde, Ashley E. Morse, Serena Rusk, Robie Ryan, Avva Saniee, Ruchi B. Sheth, Jennifer J. Siranosian, Lalitpatr Sirichantaropart, Sonya R. Sternlieb, Christina M. Zaccardi, and Joseph D. Coolon

This study focused on a species of fruit fly called *Drosophila sechellia* that has evolved to be a specialist and eat the fruit of a toxin-producing plant called *Morinda citrifolia* or noni. *D. sechellia* is unique because all closely related species of fruit flies die within minutes after eating the toxic noni fruit. To identify the genes that may be responsible for evolved resistance to toxins in *D. sechellia*, we used RNA-seq to measure genome-wide gene expression response to octanoic acid, the primary toxin in noni fruit. Using this approach, we identified many new candidate genes for functional characterization.

- 3875–3885 ***Caenorhabditis elegans* BUB-3 and SAN-1/MAD3 Spindle Assembly Checkpoint Components Are Required for Genome Stability in Response to Treatment with Ionizing Radiation**
Simone Bertolini, Bin Wang, Bettina Meier, Ye Hong, and Anton Gartner
 The spindle assembly checkpoint delays anaphase progression when chromosomes are not attached to the spindle. Following an unbiased forward genetic screen we found the spindle assembly checkpoint components BUB-3 and SAN-1/MAD-3 are required to ensure viability after treatment with ionizing radiation. We provide evidence the spindle checkpoint is required during somatic development and in germ cells. Furthermore, we find that BUB-3 and SAN-1/MAD-3 act independently of the DNA repair pathways known to mend double-strand breaks caused by ionizing irradiation, possibly by changing cell cycle timing during development.
- 3887–3899 **SID-1 Domains Important for dsRNA Import in *Caenorhabditis elegans***
Jennifer S. Whangbo, Alexandra S. Weisman, Jeiwook Chae, and Craig P. Hunter
 SID-1 is a conserved *Caenorhabditis elegans* transmembrane protein that transports doublestranded (ds)RNA across membranes. Its activity supports systemic RNA interference (RNAi), the spread of silencing between cells, and environmental RNAi, RNAi triggered by ingested dsRNA. Through structure-function analysis, the authors identify SID-1 domains important for dsRNA transport. Most mutations in these domains partially disrupt systemic RNAi. Analysis of mutations in one particular domain provides evidence for SID-1-dependent dsRNA import into intestinal cells and shows that this import is important for subsequent export to other tissues. This is the first evidence that SID-1 functions in the intestine to support environmental RNAi.
- 3901–3912 **A Predictive Model for Time-to-Flowering in the Common Bean Based on QTL and Environmental Variables**
Mehul S. Bhakta, Salvador A. Gezan, Jose A. Clavijo Michelangeli, Melissa Carvalho, Li Zhang, James W. Jones, Kenneth J. Boote, Melanie J. Correll, James Beaver, Juan M. Osorno, Raphael Colbert, Idupulapati Rao, Stephen Beebe, Abiezer Gonzalez, Jaumer Ricaurte, and C. Eduardo Vallejos
 The common bean is a facultative short day plant that has expanded its habitat through domestication and modern breeding. A key to its wide adaptation is the control of the time to flower trait. To identify the major genetic and environmental determinants that control this trait, we analyzed a recombinant inbred family from an inter-gene pool cross. A mixed effects model was used to identify and characterize the quantitative contributions to this trait by the genetic, environmental, and GxE interaction components. The model ($r^2 = 0.89$) identified 12 QTLs, four environmental factors and seven specific GxE interactions controlling the time to flower.
- 3913–3924 **H⁺ and Pi Byproducts of Glycosylation Affect Ca²⁺ Homeostasis and Are Retrieved from the Golgi Complex by Homologs of TMEM165 and XPR1**
Nathan A. Snyder, Christopher P. Stefan, Camille T. Soroudi, Adam Kim, Carlos Evangelista, and Kyle W. Cunningham
 The Golgi complex is where sugars are linked to proteins and lipids prior to their secretion from the cell. These glycosylation reactions require calcium and result in production of byproducts (phosphate and protons) that must be eliminated to ensure proper functioning of the organelle. Using genetic approaches in baker's yeast, we identify a protein that promotes export of protons and import of calcium and we identify another protein that promotes recycling of phosphate for reuse in the cytoplasm. The findings shed light on related proteins in humans and on congenital disorders of glycosylation.
- 3925–3935 **A Horizontally Transferred Autonomous Helitron Became a Full Polydnavirus Segment in *Cotesia vestalis***
Pedro Heringer, Guilherme B. Dias, and Gustavo C. S. Kuhn
 Bracoviruses associate symbiotically with thousands of parasitoid wasp species, working as gene vectors that allow the development of wasp larvae within hosts. One of the segments of *Cotesia vestalis* bracovirus contains a gene previously described as a helicase of unknown origin. We demonstrate that this gene belongs to a transposable element that covers the viral segment almost entirely. This element also underwent at least two horizontal transfers between three insect orders. These results not only reinforce that parasitoid wasps are frequently involved in horizontal transfers, but also demonstrate the first case of a transposon that effectively became a viral segment.

- 3937–3946 **APC/C^{FZR-1} Controls SAS-5 Levels To Regulate Centrosome Duplication in *Caenorhabditis elegans***
Jeffrey C. Medley, Lauren E. DeMeyer, Megan M. Kabara, and Mi Hye Song
- Centrosomes duplicate once per cell cycle to ensure accurate chromosome segregation during cell division. Here we show that FZR-1, a co-activator of the anaphase promoting complex/cyclosome (APC/C), negatively regulates centrosome duplication in *Caenorhabditis elegans* embryos. We provide evidence that the APC/C^{FZR-1} regulates centrosome duplication by controlling the levels of the centrosome duplication factor SAS-5 through direct recognition of a conserved KEN-box motif.
- 3947–3954 **Molecular Basis of Overdominance at a Flower Color Locus**
Amy M. LaFountain, Wenjie Chen, Wei Sun, Shilin Chen, Harry A. Frank, Baoqing Ding, and Yao-Wu Yuan
- Single-gene overdominance is a mechanism proposed to explain heterosis, the phenomenon that hybrid offspring between two inbred lines or varieties show superior phenotypes to both parents. However, the molecular nature of this phenomenon remains unclear. We show that loss-of-function alleles of the *FLAVONE SYNTHASE* gene cause overdominance in anthocyanin-based flower color intensity in *Mimulus lewisii*. FNS competes with anthocyanin biosynthetic enzymes for substrates, yet also produces flavones, the colorless co-pigments required for anthocyanin stabilization. We suggest that this type of antagonistic pleiotropy is a general principle underlying single-gene overdominance.
- 3955–3966 **Modulation of Global Transcriptional Regulatory Networks as a Strategy for Increasing Kanamycin Resistance of the Translational Elongation Factor-G Mutants in *Escherichia coli***
Aalap Mogre, Reshma T. Veetil, and Aswin Sai Narain Seshasayee
- Antibiotic resistance is a serious emerging global threat. We had previously evolved a model bacterium *Escherichia coli* under aminoglycoside stress. We demonstrated that the resistance of the primary resistance conferring mutations in the translational factor Elongation Factor-G could be increased by second site mutations. Interestingly, these mutations were in regulatory genes that could, depending on the impact of the mutation, alter expression of large sets of genes via different mechanisms. Here, we uncover the impact of these mutations using a variety of biochemical tools and RNA-seq. This information could facilitate research combating aminoglycoside resistance.
- 3967–3969 **Noncanonical GA and GG 5' Intron Donor Splice Sites Are Common in the Copepod *Eurytemora affinis***
Hugh M. Robertson
- The vast majority of introns in eukaryotic genes begin with GU. The copepod crustacean *Eurytemora affinis* has 10-12% of 5' intron donor splice sites beginning with GA or GG. These non-canonical intron splice donors belong to a subset of large numbers of newly gained idiosyncratic introns in this copepod, even when compared to other sequenced copepod genomes. Their unrecognized presence compromised automated gene modeling in this species. They provide an example of unusual intron evolution, and also imply evolution of modified intron donor splice site recognition in this copepod.
- 3971–3982 **Repression of Middle Sporulation Genes in *Saccharomyces cerevisiae* by the Sum1-Rfm1-Hst1 Complex Is Maintained by Set1 and H3K4 Methylation**
Deepika Jaiswal, Meagan Jezek, Jeremiah Quijote, Joanna Lum, Grace Choi, Rushmie Kulkarni, DoHwan Park, and Erin M. Green
- The interplay between chromatin regulators and transcription factors is critical to controlling timely and accurate expression of genes required for differentiation. Jaiswal *et al.* investigate a role for the Set1 H3K4 methyltransferase in repression of meiotic genes in budding yeast. A model is developed in which Set1 promotes a chromatin state that specifically maintains the DNA-sequence dependent transcription factor Sum1 and the histone deacetylase Hst1 at a subset of middle sporulation genes. This study characterizes an unexplored repressive function for Set1 and shows that the Sum1 complex partially depends on histone methylation status, in addition to DNA sequence elements, to repress untimely expression.
- 3983–3998 **Heterogeneous Patterns of Genetic Diversity and Differentiation in European and Siberian Chiffchaff (*Phylloscopus collybita abietinus*/P. tristis)**
Venkat Talla, Faheema Kalsoom, Daria Shipilina, Irina Marova, and Niclas Backström
- A goal in evolutionary biology is to describe the genetic basis of adaptation and reproductive isolation. Contact zones between species provide opportunities for this quest. We investigate how the genomes of two closely related bird species (chiffchaffs) evolve, when species interbreed in a contact zone. We find that the level of genetic variation and the degree of genetic differentiation vary extensively across the genome, predominantly as a consequence of variation in recombination rate and genetic drift. We also identify genes with fixed differences in functional positions that might explain phenotypic differences between the species.

- 3999–4008 **Understanding microRNA Regulation Involved in the Metamorphosis of the Veined Rapa Whelk (*Rapana venosa*)**
Hao Song, Lu Qi, Tao Zhang, and Hai-yan Wang
- The present study provides the global view of the changes in miRNA that occur during rapa whelk metamorphosis. A total of 195 miRNAs was significantly differentially expressed and their target mRNAs were identified. These molecules are responsible for morphological and functional changes in organs. Some miRNAs involved in ingestion and digestion, cytoskeleton and cell adhesion and apoptosis during metamorphosis are of great interest and were listed and validated by real-time PCR. These results will provide a basis for understanding the molecular mechanisms involved in the regulation of gastropod metamorphosis.
- 4009–4018 **Long-Term Impact of Optimum Contribution Selection Strategies on Local Livestock Breeds with Historical Introgression Using the Example of German Angler Cattle**
Yu Wang, Dierck Segelke, Reiner Emmerling, Jörn Bennewitz, and Robin Wellmann
- Breeding programs for small local breeds undertake the mission of increasing genetic gain, maintaining genetic diversity, and maintaining genetic uniqueness. In this study, we explored the long-term impact of different optimum contribution selection approaches by stochastic simulation. The objective was to maximize genetic gain while the loss of genetic diversity, the migrant contributions and the kinship at native alleles, estimated from medium density SNP panels, were restricted.

REVIEWER INDEX

- 4019–4022 G3 Reviewer Index 2017