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Antioxidant CoQ10 restores fertility by rescuing bisphenol A-induced oxidative DNA damage in the *Caenorhabditis elegans* germline, pp. 381–395

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Studies have shown an association between female infertility and exposure to endocrine-disrupting chemicals (EDCs), yet strategies for neutralizing such effects are lacking. Bisphenol A (BPA) is a prevalent EDC that affects the germline leading to chromosomal aberrations and aneuploidy in worms, mice and chimps. Here, Hornos Carneiro *et al.* show that BPA increases oxidative DNA damage in the *Caenorhabditis elegans* germline, which CoQ10 supplementation then counteracts by rescuing the germline-specific altered expression of oxidative stress response genes and impaired DNA double-strand break repair progression. Therefore, CoQ10 may constitute a low-risk and low-cost strategy to attenuate BPA's impact on fertility.

Epistatic transcription factor networks differentially modulate *Arabidopsis* growth and defense, pp. 529–541

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How a plant regulates the relationship between plant growth and plant defense is critical for understanding plant fitness or yield. Yet, little about the required complex underlying interactions are understood. Li *et al.* used a large collection of single and pairwise transcription factor (TF) mutants in *Arabidopsis* to investigate how they connect regulation of the defensive aliphatic glucosinolates and growth. There are a large number of significant main and epistatic effects on plant growth that are conditional on the environment. Their findings indicate that complex TF networks independently regulate growth and defense to coordinate responses across complex environments.

Tissue-specific DNA replication defects in *Drosophila melanogaster* caused by a Meier-Gorlin syndrome mutation in Orc4, pp. 355–367

Stephen L. McDaniel, Allison J. Hollatz, Anna M. Branstad, Marissa M. Gaskill, Catherine A. Fox, and Melissa M. Harrison

Meier-Gorlin syndrome (MGS) is a recessive disorder caused by mutations in genes associated with DNA replication. Despite the fact these proteins are essential for replication in every cell, patients with MGS have tissue-specific defects. To understand how these mutations lead to disease, McDaniel *et al.* used genome engineering to create an *orc4* MGS mutation in *Drosophila*. Like MGS patients, these flies are viable. However, tissue-specific replication defects in the ovary contribute to female sterility. Together, the authors provide evidence that the Orc4 MGS mutation leads to DNA replication defects that may particularly affect tissues that require rapid or efficient DNA replication.

Selective inbreeding: genetic crosses drive apparent adaptive mutation in the Cairns-Foster system of *Escherichia coli*, pp. 333–354

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In the Cairns-Foster adaptive mutation system, *lac* mutant cells are plated on lactose medium where 50 revertant colonies accumulate over 5 days above a non-growing lawn. A new model attributes this behavior to selective over-replication of the F'*lac* plasmid, which carries the mutant *lac* allele and the *dinB* gene for an error-prone polymerase. Following transfer, recombination initiates rolling-circle plasmid over-replication. DinB over-production causes mutagenesis. Transfer of the revertant *lac* allele away from deleterious associated mutations gives the appearance that mutations were directed to adaptive targets. This model is supported by analysis of 59 revertant whole genome sequences

Genetic paths to evolutionary rescue and the distribution of fitness effects along them, pp. 493–510

Matthew M. Osmond, Sarah P. Otto, and Guillaume Martin

Novel environments can cause strong selection and rapid adaptation. The genetic basis of such rapid adaptation tends to be composed of few loci of large effect. Current theory qualitatively agrees but largely neglects the demographic decline — and potential extinction — these novel environments can precipitate. Here, Osmond, Otto, and Martin show how a race between adaptation and extinction is expected to promote a genetic basis of adaptation that is composed of even fewer loci of even larger effect, especially with rare mutations in moderately novel environments. As mutation rates and environmental novelty increase, the authors quantify how the number of contributing loci is predicted to increase – each buying the population more time to adapt.

Leveraging family history in case-control analyses of rare variation, pp. 295–303

Claudia R. Solis-Lemus, S. Taylor Fischer, Andrei Todor, Cuining Liu, Elizabeth J. Leslie, David J. Cutler, Debashis Ghosh, and Michael P. Epstein

Standard methods for case-control association studies of rare and common variation often treat disease outcome as a dichotomous phenotype. However, recent studies have demonstrated that cases with a family history of disease can be enriched for risk variation relative to sporadic cases. Assuming family-history information is available, Solis-Lemus *et al.* replace the standard dichotomous outcome variable in case-control studies with a more informative outcome variable that distinguishes cases and controls with and without family history. The authors show that leveraging family-history information can greatly improve power in rare-variant association tests compared to standard dichotomous modeling of disease phenotypes that disregard such information.

Binding and regulation of transcription by yeast Ste12 variants to drive mating and invasion phenotypes, pp. 397–407

Wei Zhou, Michael W. Dorrity, Kerry L. Bubb, Christine Queitsch, and Stanley Fields

Here, Zhou *et al.* took advantage of *Saccharomyces cerevisiae* and its well-characterized mating and invasion pathways to explain how transcription factor variants alter motif recognition and gene expression, and ultimately, organismal phenotypes. Specifically, they profiled transcriptome and *in vivo* bound genomic sites by using the "calling card" method (Wang *et al.* 2007) for six Ste12 variants. They found examples of specific changes in binding sites and expression that likely contribute to the observed phenotypes.