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Protein isoprenylation in yeast targets COOH-terminal sequences not adhering to the CaaX consensus, pp. 1301–1316

Brittany M. Berger, June H. Kim, Emily R. Hildebrandt, Ian C. Davis, Michael C. Morgan, James L. Hougland, and Walter K. Schmidt

In vitro and *in silico* studies of the CaaX-type prenyl transferases suggest a wider array of prenylatable sequences than those determined *in vivo*. Berger and Kim *et al*. investigate whether this disconnect is due to use of *in vivo* reporters that undergo multi-step post-translational modification rather than prenylation-only reporters. In this study, they report the identification of Cxxx sequences permitting Ydj1p isoprenylation that are distinct from those previously identified using a multi-step reporter. Their results reveal that the yeast CaaX-type prenyltransferases can recognize a range of Cxxx sequence combinations that extend beyond those typically defined as CaaX.

Carotenoid presence is associated with the *Or* gene in domesticated carrot, pp. 1497–1508

Shelby L. Ellison, Claire H. Luby, Keo E. Corak, Kevin M. Coe, Douglas Senalik, Massimo Iorizzo, Irwin L. Goldman, Philipp W. Simon, and Julie C. Dawson

Ellison *et al.* provide the first evidence that the genomic region bearing the *Or* gene is involved in the presence of carotenoids in carrot. Using a global collection of diverse carrot accessions, they identify 12 genomic regions containing selection signatures. One region overlaps with the *Or* region, advancing *Or* as a candidate for carotenoid presence in carrot. The *Or* domestication allele appears to have been selected after the initial domestication of yellow carrots in the East, and its rapid fixation in almost all orange and non-orange carrots in the West may explain why it has not been found with less genetically diverse mapping populations.

Origin, composition, and structure of the supernumerary B chromosome of *Drosophila melanogaster*, pp. 1197–1212

Stacey L. Hanlon, Danny E. Miller, Salam Eche, and R. Scott Hawley

In addition to a defined number of essential chromosomes, extra chromosomes called "B chromosomes" are present in roughly 15% of eukaryotic species. In this study, Hanlon *et al*. analyzed the recently discovered *Drosophila melanogaster* B chromosomes to determine their origin, composition, and structure. Understanding how the B chromosomes formed and what sequence information they carry will bolster further study into the mechanism of how new chromosomes may arise, as well as what components may be required to maintain a non-essential chromosome through many generations.

Gap junctions and NCA cation channels are critical for developmentally timed sleep and arousal in *Caenorhabditis elegans*, pp. 1369–1381

Huiyan Huang, Dustin J. Hayden, Chen-Tseh Zhu, Heather L. Bennett, Vivek Venkatachalam, Lukas L. Skuja, and Anne C. Hart

The molecular mechanisms of sleep are not fully understood. Huang *et al*. demonstrate that loss of *Caenorhabditis elegans* UNC-7 or UNC-9 innexins dramatically reduces sleep during L4/A lethargus and that those innexins are partially required in pre-motor interneurons and motor neurons during sleep. Genetic epistasis analysis during lethargus sleep places *unc-7* and *unc-9* downstream of *egl-4*, a conserved cGMP-dependent kinase. Loss of the NCA cation channel increases arousal thresholds while elevated channel activity decreases sleep. This study emphasizes the conservation and importance of neuronal activity modulation during sleep and demonstrates that gap junction function is critical for normal sleep.

PRP4KA, a putative spliceosomal protein kinase, is important for alternative splicing and development in *Arabidopsis thaliana*, pp. 1267–1285

Tatsuo Kanno, Peter Venhuizen, Tuan-Nan Wen, Wen-Dar Lin, Phebe Chiou, Maria Kalyna, Antonius J. M. Matzke, and Marjori Matzke

Prp4 kinase (Prp4k) is the first spliceosome-associated kinase shown to regulate splicing in fungi and metazoans, but nothing is yet known about its functions in plants. Here, Kanno and Venhuizen *et al*. report the recovery of the first mutations in a plant PRP4K through a forward genetic screen. They describe the abnormal phenotype of the *prp4ka* mutants and determine changes in pre-mRNA splicing patterns and protein phosphorylation, finding that PRP4KA may modulate alternative splicing by phosphorylating splicing regulatory proteins.

Incompatibilities in mismatch repair genes *MLH1-PMS1* contribute to a wide range of mutation rates in human isolates of baker's yeast, pp. 1253–1266

Vandana Raghavan, Duyen T. Bui, Najla Al-Sweel, Anne Friedrich, Joseph Schacherer, Charles F. Aquadro, and Eric Alani

Baker's yeast bearing incompatible *MLH1* and *PMS1* mismatch repair alleles are mutators that can adapt more rapidly to stress—but do so at the cost of long-term fitness. Raghavan *et al*. characterized two clinical yeast isolates containing the incompatible *MLH1-PMS1* genotype in a heterozygous, non-mutator state. Their meiotic spore progeny displayed mutation rates varying by 340-fold, with *MLH1-PMS1* incompatibility being the major driver of mutation rate. These data are consistent with variance in mutation rate contributing to adaptation to stress conditions, with high mutation rates leading to long-term fitness costs that are buffered by mating or eliminated through natural selection.

Ras-dependent cell fate decisions are reinforced by the RAP-1 small GTPase in *Caenorhabditis elegans*, pp. 1339–1354

Neal R. Rasmussen, Daniel J. Dickinson, and David J. Reiner

Investigation into the signaling relationship between closely related small GTPases Ras and Rap1 has a complicated past. Rasmussen, Dickinson, and Reiner use *Caenorhabditis elegans* to investigate the role of RAP-1 in LET-60/Ras-dependent developmental events. RAP-1 is sufficient to induce LET-60-dependent cell transformations. Like RAP-1, its putative upstream activating GEF PXF-1 is also necessary for maximum induction of 1° vulval fate. Expression from the *pxf-1* promoter is reprogrammed during the vulval inductive process, as observed with other signaling genes in this system. The authors hypothesize that RAP-1 plays a minor Ras-like role in support of LET-60 in inductive signaling events.

Genetic dissection of hybrid male sterility across stages of spermatogenesis, pp. 1453–1465

Denise J. Schwahn, Richard J. Wang, Michael A. White, and Bret A. Payseur

Hybrids between new species are often sterile. To understand the causes of this reproductive barrier, Schwahn *et al*. examined testis histology in a large number of hybrids between two nascent species of house mice. They found a range of abnormalities, with many pointing to defects in the first meiotic division. Genetic mapping localized seven quantitative trait loci (QTL) controlling five histologic traits. Using their unique dataset, they assign these QTL to specific processes during spermatogenesis and provide a rare portrait of hybrid male sterility from a developmental perspective.

This Month's Perspectives

Mogens Westergaard's contributions to understanding sex chromosomes

Deborah Charlesworth

Sixty years ago, Mogens Westergaard published a review analyzing genetic studies from a range of flowering plants. Westergaard provided strong genetic evidence that two separate factors are involved in sex determination—with close linkage between the two giving the appearance of a single gene system. This offered a solution to the long-standing puzzle of how sex-determination could involve a single genetic locus even though two mutations are clearly required to evolve two sexes from an ancestral hermaphroditic state.

Evolutionary virology at 40

Jemma L. Geoghegan and Edward C. Holmes

Geoghegan and Holmes describe the history of evolutionary ideas in the study of viruses, showing that two different approaches to studying virus evolution—the comparative and the experimental—were both established in seminal papers published in the late 1970s and have run in parallel, often antagonistically, since then. The authors show how these two approaches may be resolved within an evolutionary genetic framework with the transformative data produced by next-generation sequencing and metagenomics.