

ISSUE HIGHLIGHTS

Genetics, Vol. 191, JUNE 2012, Copyright © 2012

APL-1, the Alzheimer's amyloid precursor protein in *Caenorhabditis elegans*, modulates multiple metabolic pathways throughout development, pp. 493–507

Collin Y. Ewald, Daniel A. Raps, and Chris Li

A hallmark of Alzheimer's disease is the deposition of senile plaques, whose major component is the beta-amyloid peptide, which is a cleavage product of the amyloid precursor protein (APP). The function of APP and its cleavage products is still unclear. This article reports that the *Caenorhabditis elegans* APP-related protein APL-1 has multiple functions during development, including modulating the insulin pathway.

Population genetics models of local ancestry, pp. 607–619

Simon Gravel

Genomes are mosaics of chromosomal tracts that originate from a finite number of ancestors. These mosaics, which are shaped by historical migration patterns, are key to understanding genomic diversity in complex populations. This article presents gene flow models for inferring migration history using such patterns. When applied to HapMap African-American (ASW) data, a two-epoch migration model agrees with the data better than the commonly used single-migration model.

Synaptic polarity depends on phosphatidylinositol signaling regulated by myo-inositol monophosphatase in *Caenorhabditis elegans*, pp. 509–521

Tsubasa Kimata, Yoshinori Tanizawa, Yoko Can, Shingo Ikeda, Atsushi Kuhara, and Ikue Mori

Lithium relieves bipolar disorder by inhibiting the evolutionarily conserved enzyme myo-inositol monophosphatase (IMPase), which is essential for polarized localization of synaptic molecules. These authors show that mutations in two enzymes that degrade membrane phosphatidylinositol 4,5-bisphosphate (PIP₂) suppress the synaptic defects of IMPase mutants and confer resistance to lithium treatment. These results provide the first *in vivo* evidence that lithium impairs neuronal PIP₂ synthesis through inhibition of IMPase.

Analysis of *Cryptococcus neoformans* sexual development reveals rewiring of the pheromone-response network by a change in transcription factor identity, pp. 435–449

Emilia K. Kruzel, Steven S. Giles, and Christina M. Hull

Gene regulatory networks evolve, sometimes radically. This article describes the pheromone response network of the human pathogen *Cryptococcus neoformans*. The authors map transcriptional regulatory changes that occur during sexual development leading to the discovery of a key *cis*-regulatory element and its binding protein. The resulting regulatory architecture could not have been predicted based on comparative sequence analyses.

A non-Mendelian MAPK-generated hereditary unit controlled by a second MAPK pathway in *Podospora anserina*, pp. 419–433

Hervé Lalucque, Fabienne Malagnac, Sylvain Brun, Sébastien Kicka, and Philippe Silar

There are many ways to produce a prion, and this article describes yet another one. The *Podospora anserina* PaMpk1 MAP kinase signaling pathway can generate “C”, a hereditary unit resembling prions. These authors show that another MAP kinase pathway, PaMpk2, controls the generation of “C” by activating PaMpk1, revealing unexpectedly complex regulation of a prion-like trait.

Allopolyploidization lays the foundation for evolution of distinct populations: Evidence from analysis of synthetic *Arabidopsis* allohexaploids, pp. 535–547

Starr C. Matsushita, Anand P. Tyagi, Gerard M. Thornton, J. Chris Pires, and Andreas Madlung

Allopolyploidy—carrying complete chromosome sets of at least two different species—has been seen as a mechanism for instant speciation. This article shows that different somatic cells of the same neoallopolyploid individual can exhibit different karyotypes, and that somatic mosaics can persist in subsequent generations. The authors characterize and quantify aneuploidy over seven generations in several sibling lines of a synthetic allopolyploid. Their results suggest that this phenomenon has the potential to lead not only to instant speciation but also to instant radiation.

The nearly neutral and selection theories of molecular evolution under the Fisher geometrical framework: Substitution rate, population size, and complexity, pp. 523–534

Pablo Razeto-Barry, Javier Díaz, and Rodrigo A. Vásquez

This article puts forth that nearly neutral evolution cannot explain the high rate of fixations driven by positive selection found in DNA sequences. The authors use Fisher's geometrical model (FGM) to simulate evolution from biologically interpretable distributions of mutations. They find that nearly neutral and selection scenarios predict molecular patterns different from previous models. In a selective scenario in the FGM, evolutionary rate depends not on population size, but rather on the complexity of organisms and mutation size.

Investigating natural variation in *Drosophila* courtship song by the evolve and resequence approach, pp. 633–642

Thomas L. Turner and Paige M. Miller

A powerful compliment to genome-wide association studies—which are often underpowered—is to divergently select populations for the trait of interest and resequence their genomes. These investigators show that this method is a powerful way to differentiate selected variants from other genomic variants.

This Month's Perspectives

The centenary of Janssens's chiasmotype theory, pp. 309–317

Romain Koszul, Matthew Meselson, Karine Van Doninck, Jean Vandenhoute, and Denise Zickler

and

La théorie de la chiasmotypie. Nouvelle interprétation des cinésés de maturation, pp. 319–346

Frans A. Janssens

(Translated by Romain Koszul and Denise Zickler)

Showing that the random assortment of characters observed by Mendel has its basis in the behavior of chromosomes in meiosis requires an understanding of the meiotic behavior of chromosomes. A crucial step was Janssens's interpretation in 1909 of chiasma structure as the breakage and joining of homologous non-sister chromatids. Janssens's article found a broad, appreciative audience, but his ideas were resisted by many geneticists and cytologists for several decades. Koszul *et al.* revisit Janssens's findings and the controversies that surrounded them. The journal also publishes here a new translation—the first in English—of the original Janssens's article.

This Month in the American Journal of Human Genetics

RAD21 mutations cause a human cohesinopathy, Am. J. Hum. Genet. 90(6)

Matthew A. Deardorff, Jonathan J. Wilde, Melanie Albrecht, Emma Dickinson, Stephanie Tennstedt, Diana Braunholz, Maren Mönnich, Yuqian Yan, Weizhen Xu, Maria Concepcion Gil-Rodríguez, Dinah Clark, Hakon Hakonarson, Sara Halbach, Laura Daniela Michelis, Abhinav Rampuria, Eva Rossier, Stephanie Spranger, Lionel Van Maldergem, Sally Ann Lynch, Gabriele Gillessen-Kaesbach, Hermann-Josef Ludecke, Robert G. Ramsay, Michael J. McKay, Ian D. Krantz, Huiling Xu, Julia A. Horsfield, and Frank J. Kaiser

The eukaryotic cohesin complex is required for genome replication, DNA double-strand break repair, and transcriptional control. Not surprisingly, then, mutations that affect the function of this complex cause a range of human disorders, including Cornelia de Lange and Roberts syndromes. Now, Deardorff *et al.* identify a previously uncharacterized cohesinopathy, and show that it is caused by mutations in *RAD21*, which encodes a key structural component of the cohesin complex. The authors' functional studies demonstrate that these mutations affect all facets of cohesin function, thus leading to a wide spectrum of phenotypes. These findings suggest that we still have much to learn about how cohesin function influences human development.