Maternal MEMI promotes female meiosis II in response to fertilization in Caenorhabditis elegans, pp. 1461–1477

In most animals, female meiosis completes only after fertilization. In Caenorhabditis elegans, fertilization is required to initiate female meiosis II, but it is unclear how the oocyte “senses” sperm entry. Ataeian et al. identify an oocyte-specific factor that is required for the female meiosis II program. Using a sensitive genetic screen, they also identify a sperm-specific phosphatase that could be part of the elusive signal that triggers meiosis II.

Integrated post-GWAS analysis sheds new light on the disease mechanisms of schizophrenia, pp. 1587–1600
Jih-Hong Lin, Ying Cai, Quanwei Zhang, Wen Zhang, Rubén Nogales-Cadenas, and Zhengdong D. Zhang.

Although genome-wide association studies (GWAS) have successfully identified many schizophrenia-associated common variants, it is difficult to use GWAS signals alone to pinpoint the underlying true risk genes. Lin et al. developed a general computational framework for post-GWAS analysis and identified 132 putative schizophrenia risk genes associated with GWAS loci. Involved in distinct biological processes, these genes show distinctive temporal expression patterns and play specific biological roles during brain development.

Stochasticity in the genotype-phenotype map: implications for the robustness and persistence of bet-hedging, pp. 1523–1539
Daniel Nichol, Mark Robertson-Teas, Peter Jeavons, and Alexander R.A. Anderson.

Stochastic variation in phenotypes, or bet-hedging, can serve as a survival mechanism in unpredictable environments. In isogenic bacterial populations, dormant ‘persistor’ cells emerge stochastically, buffering the population from extinction during antibiotic therapy. Nichol et al. introduce a mathematical model to demonstrate that the evolutionary fate of this phenomenon is dependent on the structure of the molecular networks that drive it. Critically, they find the genotype-phenotype map is key in predicting how bet-hedging is lost through natural selection, and in designing therapeutic strategies to overcome bet-hedging-driven drug resistance.

Genetics of skeletal evolution in unusually large mice from Gough Island, pp. 1559–1572

Organisms on islands often undergo rapid morphological evolution, but the genetic basis of this conspicuous pattern of evolutionary change remains poorly understood. Gough Island provides a striking example, harboring the largest wild house mice on record. The authors used this unique population to dissect the genetics of skeletal evolution associated with island colonization. They identified loci responsible for global expansion of the skeleton and shape changes in the skull and limbs, positioning Gough Island mice as a model system for understanding rapid evolution in the wild.

Evolution of the genotype-to-phenotype map and the cost of pleiotropy in mammals, pp. 1601–1612
Arthur Porto, Ryan Schmelzer, John L. VandeBerg, Gabriel Marroig, and James M. Cheverud.

The genetic architecture of traits holds important microevolutionary consequences. Yet, studies comparing genetic architecture across species are rare, and discussions of the evolution of genetic systems hinge on theoretical arguments rather than empirical evidence. Using laboratory populations of opossums and mice, Porto et al. look at the evolution of the genetic architecture of craniofacial traits. These species diverge in the genetic architecture of cranial traits, suggesting that genotype-to-phenotype maps can change even when species share most of their genes. This highlights the context dependency of gene effects and is relevant to current discussions concerning the cost of pleiotropy.

Detecting sources of transcriptional heterogeneity in large-scale RNA-Seq data sets, pp. 1391–1396
Brian C. Searle, Rachel M. Gittelman, Ohad Manor, and Joshua M. Akey.

Gene expression levels are dynamic molecular phenotypes that respond to biological, environmental, and technical perturbations. Searle et al. develop a novel method for discovering transcriptional signatures and apply it to the Genotype-Tissue Expression (GTEX) dataset. The method identified many factors contributing to expression heterogeneity, including collection center and ischemia time, and can statistically stratify these factors by effect strength. Strikingly, transcriptional expression in blood alone could help predict heart disease and stroke in some patients.

Sequence of the sugar pine Megagenome, pp. 1613–1626

The sugar pine has the largest genome assembled to date, with nearly 50% more DNA than the current record holder. It is also the first representative of the Pinus subgenus Strobus (white pines) to be sequenced. Stevens et al. describe the first draft of the reference genome. The data reveal the genomic origins of the major dominant gene for resistance to the devastating pathogen white pine blister rust, including a promising candidate gene.

Reconstructing demography and social behavior during the neolithic expansion from genomic diversity across Island Southeast Asia, pp. 1495–1506
François Vallée, Aurélien Luciani, and Murray B. Cox.

The farming revolution drove human groups from mainland Asia into the islands of Southeast Asia. Key features of this migration remain poorly understood. An ‘agent based’ model was built to simulate human interactions across this region from the Neolithic period to the present. The genomes of 2,299 Island Southeast Asians showed that greater migration was more influential than higher birth rates, that offspring preferentially resulted from Asian women and Papuan men, and that individuals with Asian ancestry were likely distributed across parts of western Island Southeast Asia before the farming expansion.

This Month in the American Journal of Human Genetics

Mutations in three genes encoding proteins involved in hair shaft formation cause uncombable hair syndrome, Am. J. Hum. Genet. 99(6)

Although relatively benign, uncombable hair syndrome (UHS), is an interesting phenotype in which the hair shaft is defective resulting in hair that is resistant to being combed down. In this issue, Basmanav et al. report mutations in PADI3, TGM3 and TCH that are associated with UHS in eleven children. PADI3 and TGM3 post-translationally modify TCH, and aberrant modification alters the structural organization of the hair shaft. Additionally, PADI3 knockout mice also demonstrate hair defects recapitulating the findings from humans. Children affected with UHS typically outgrow the phenotype so future work to uncover the mechanism by which hair morphology normalizes will be required to fully understand this syndrome.