Stroke association

Risk of stroke is known to have a heritable component, but efforts to identify specific genetic susceptibility factors have had limited success. Arfan Ikram and colleagues (*N. Engl. J. Med.* 360, 1718–1728; 2009) now report identification of common variants on chromosome 12p13 that confer increased risk of ischemic stroke. The authors conducted a genome-wide association study of 1,544 incident stroke cases of European ancestry drawn from four large prospective cohorts and identified two SNPs on 12p13 associated with stroke risk at $P < 5 \times 10^{-8}$. When they restricted the analysis to ischemic stroke cases, they found that the evidence for association was strengthened, whereas the association with nonischemic stroke was not significant. The association of one of the SNPs with ischemic stroke was further replicated in African American cases drawn from the ARIC cohort and in an independent Dutch case-control sample. The lead SNP is located immediately upstream of the *NINJ2* gene, which encodes a cell adhesion molecule that is upregulated in response to nerve injury in rodent models. On the basis of these findings, the authors speculate that variation in *NINJ2* expression might influence the brain's response to ischemic insults. ***KV***

Ping-pong piRNA pathways

Piwi-interacting RNAs (piRNAs) associate with Piwi family proteins to silence transposons in germ cells. piRNAs are encoded in heteromatic clusters, and in *Drosophila* they associate with three Piwi proteins, Piwi, Aub and AGO3, forming an amplification loop called the ping-pong cycle to increase the production of piRNAs antisense to transposons. Now, two groups have determined that there is an AGO3-independent piRNA pathway functioning in *Drosophila* somatic gonadal cells (*Cell* **137**, 509–521; 2009 and *Cell* **137**, 522–535; 2009). Phil Zamore and colleagues report persistence of a specific class of piRNAs in ovaries of flies with loss-of-function mutations in *ago3*; these Ago3-independent piRNAs target transposons expressed in somatic cells of the ovary. Greg Hannon and colleagues report the identification of distinct piRNA populations in somatic ovarian cells; these piRNAs associate exclusively with the Piwi protein complex. Together, these reports illuminate the existence of a somatic piRNA pathway that operates distinctly from the germline ping-pong cycle and that selectively silences mobile elements that are expressed in the somatic cells of the ovary. *EN*

All around Africa

Sarah Tishkoff and colleagues report a large-scale study of African genetic variation including 121 African populations, 4 African American populations and 60 non-African populations (*Science* published online 30 April 2009; doi: 10.1126/science.1172257). They examine patterns of genetic variation at 1,327 nuclear microsatellite and indel markers within several thousand individuals. Overall, they find that African populations show the greatest levels of within-population diversity, and that levels of genetic diversity decline with distance from Africa. Within Africa, they resolved 14 main ancestral population clusters, and showed that genetic variation correlated to linguistic and subsistence classifications, in addition to geography. They highlight some new and unexpected relationships, including suggested shared common ancestry for hunter–gatherer populations at geographically diverse locations across Africa. They also suggest that modern human migration originated in southern Africa near the border between Namibia and South Africa. The authors note that although this is the largest survey to date of African genetic variation, there remain some further 2,000 ethnolinguistic populations that were not included. Given the extent of genetic diversity among these African populations, they recommend that genetic association and sequencing studies include ethnically and geographically diverse populations within Africa to better capture this variation. *OB*

Written by Orli Bahcall, Pamela Colosimo, Lily Khidr, Emily Niemitz & Kyle Vogan

Synaptic profiling

Synapses are highly diverse structures that transmit specific signals to specific targets. Disturbances in brain function often involve faulty information processing at synapses, and synaptic defects in humans have been linked to several neurological disorders, including autism, mental retardation and Alzheimer disease. Although the molecules that carry out the functional transmission of synaptic signals are well known, the proteins responsible for generating synaptic specificity have been difficult to identify. Nathaniel Heintz and colleagues (*PLoS Biol.* **7**, e1000083; 2009) describe a new approach for establishing the proteomic profile of individual synapse types by combining cell-specific genetic targeting, molecular tagging and biochemical purification. The authors generated mice that express an affinity-tagged postsynaptic protein (Venus-GluRδ2) at a single synapse type, the parallel fiber/Purkinje cell (PF/PC) synapse. In a biochemical feat, the authors co-immunopurified 65 candidate postsynaptic proteins with Venus-GluRδ2, 25 of which had not been previously associated with synaptic localization. The authors validate the majority of these proteins as PF/PC synapse components and demonstrate a new role for the kinase MRCKγ in the morphogenesis of PF/PC synapses. Given the available tools to target gene expression in a wide range of neurons, future work with this approach may reveal the 'molecular code' responsible for synaptic diversity. *PC*

Understanding loss

Oxytricha trifallax, a ciliated protozoan, contains two types of nuclei in the same cytoplasm: diploid micronuclei, which are transcriptionally silent during vegetative growth but transmit the germline genome through sexual conjugation, and gene-rich macronuclei, which govern somatic gene expression but degrade after sex. The molecular machinery responsible for this specific, reproducible genome reorganization cycle involving DNA excision and recombination in ciliates remains unknown. Now, Laura F. Landweber and colleagues find that germline-limited transposable elements in the diploid micronucleus are critical for somatic DNA deletion and rearrangement during macronuclear development (*Science* published online 16 April 2009; doi: 10.1126/science.1170023). Microinjection of dsRNA targeted to the encoded transposases at three different stages during conjugation altered the efficiency of developmental DNA rearrangements, leading to accumulation of long, nonprocessed DNA molecules. This suggests that a high level of transposase activity may be necessary to facilitate DNA rearrangements, and that germline-limited transposable elements, present in large quantities and previously considered as parasitic invaders that reduce host fitness or have little phenotypic effect, have an indispensible role. ***LK***