Bone marrow–derived germ cells

It has recently been suggested that oocyte generation in mammals is maintained postnatally by an undefined pool of germline stem cells, challenging the conventional view that mammals lose the capacity to produce oocytes shortly after birth. New work by Jonathan Tilly and colleagues (*Cell* 122, 303–315; 2005) now identifies adult bone marrow as a potential source of this germline stem cell population. On the basis of circumstantial evidence that hematopoietic stem cells and primordial germ cells might share a common embryonic origin, Tilly and colleagues reasoned that bone marrow, where adult hematopoietic stem cells reside, might also be a reservoir for adult germline stem cells. Indeed, they found that bone marrow cells isolated from adult mice expressed multiple germline markers. Closer examination of one of these markers, *Mvh*, showed marked expression changes during the estrous cycle. Transplantation of bone marrow into oocyte-depleted mice led to rapid and sustained production of oocyte-containing follicles in the ovaries of the recipient mice. Remarkably, transplantation of peripheral blood cells into chemoablated mice also led to the rapid appearance of donor-derived oocytes, suggesting that germline stem cells may transit from bone marrow to the ovaries through the blood. ***KV***

Region-specific mutagenesis

Lawriston Wilson and colleagues report results of the largest inversion screen done in mice so far (*Genome Res.* **15**, 1095–1105; 2005). The strategy relies on the visible, recessive, lethal inversion Rumpwhite (*Rw*), which spans ~50 Mb on proximal chromosome 5. The *Rw* inversion suppresses recombination in the region, thus acting as a balancer and allowing for the relatively straightforward identification and recovery of ENU-induced mutations. The authors report the generation of 1,003 pedigrees and the recovery of 43 mutants, 37 of which cause embryonic or perinatal lethality. Half of these mutations resulted in a failure of development before midgestation, characterized by craniofacial and neural tube defects, cardiovascular defects, gastrulation abnormalities, placental defects and growth retardation. A handful of mutants with defects in fertility, fitness or behavior were also identified. Both recombination mapping and complementation tests with a panel of deletions were carried out to assign rough map locations to many of the mutants. These results validate the usefulness of inversion screens in mice and suggest that positional cloning of the mutations in the *Rw* region on chromosome 5 will provide new insight into the development of the early mammalian embryo. *AP*

Deacetylases important for lifespan

Lifespan is measured in yeast by counting the number of divisions an individual cell undergoes before dying; the original cell can be followed over time because the progenitor cell is larger than the daughter cell after division. Caloric restriction extends the lifespan of many organisms, including yeast, worms, flies and mammals. In yeast, caloric restriction increases the activity of the histone deacetylase Sir2, which catalyzes the formation of heterochromatin at the repetitive rDNA locus. Loss of *SIR2* causes unstable rDNA that gives rise to circular rDNA molecules called ERCs, which are toxic at high concentration. But extension of lifespan by caloric restriction can occur in the absence of Sir2 repression of ERC formation, suggestive of the existence of another mediator of calorie restriction. Now David Sinclair and colleagues show that *HST2*, a homolog of *SIR2*, can mediate lifespan extension by caloric restriction in the absence of *SIR2* (*Science*, published online 28 July 2005; doi:10.1126/science.1113611). Notably, loss of *HST2* blocked the ability of caloric restriction to extend lifespan in the absence of *SIR2*. Like Sir2, Hst2 suppressed rDNA recombination. This work shows that histone deacetylase activity is the main mechanism of lifespan extension by caloric restriction in yeast. *EN*

Host factors in infection

Two new studies from groups at Harvard University explore the host factors involved in bacterial infection by using RNAi screens in *Drosophila melanogaster*. Jennifer Phillips and colleagues carried out a genome-wide RNAi screen in *D. melanogaster* S2 cells, a macrophage-like cell line, to identify host factors required for entry and survival of *Mycobacterium fortuitum* (*Science*, published online 14 July 2005; doi:10.1126/science.1116006). As expected, many of the dsRNAs identified block general phagocytosis, including factors involved in cytoskeleton and vesicle trafficking. A member of the CD36 family of scavenger receptors (SR), named Pes, was specifically required for mycobacterial uptake (of *Mycobacterium smegmatis* and *Listeria monocytogenes*) and infection (of *Mycobacterium fortuitum*) but dispensable for uptake of *Escherichia coli* or *Staphylococcus aureus*. HEK293 cells transfected with Pes gained the ability to be infected by *M. fortuitum*. Expression of SR-BI and SR-BII, also class B SR proteins, resulted in a greater level of infection, suggesting that class B SR proteins have a general role in mediating bacterial uptake and infection in macrophages. In a companion study, Darren Higgins and colleagues presented a similar genome-wide RNAi screen for host factors required for infection of *L. monocytogenes* in *D. melanogaster* SL2 cells, comparing these to those obtained from the *M. fortuitum* screen and confirming the role of Pes (*Science*, published online 14 July 2005; doi:10.1126/science.1116008). *OB*

Duplication of *MECP2*

Mutations in *MECP2* cause the progressive neurodegenerative disorder Rett syndrome. This X-linked syndrome affects mostly females, but mild mutations can also cause mental retardation in males. Now Hilde Van Esch and colleagues report the identification of mental retardation and neurodegeneration in males with duplications of the genomic region including *MECP2* (*Am. J. Hum. Genet.* 77, 442–453; 2005). Duplications were identified in three individuals with familial X-linked mental retardation and in an individual with sporadic mental retardation. The common region of duplication was 450 kb and included nine other genes in addition to *MECP2*. Because previous studies hinted that increased as well as decreased dosage of *MECP2* is harmful to neuronal function, and because they detected increased *MECP2* expression in individuals with duplications, the authors suggest that *MECP2* is responsible for the mental retardation phenotype. This study suggests that quantitative screening of *MECP2* copy number might be useful for screening sporadic mental retardation in males in addition to its current application for screening Rett syndrome in females. ***EN***

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