Single origin for rice

Asian rice, *Oryza sativa*, is thought to have been domesticated approximately 9,000 years ago, although there are ongoing debates as to whether modern-day rice types were domesticated once or in multiple events. Now, Michael Purugganan and colleagues provide evidence that supports a single origin of Asian domesticated rice (*PNAS* published online, doi:10.1073/pnas.1104686108, 2 May 2011). The authors resequenced fragments of 630 genes totaling ~250 kb of sequence in 20 wild rice accessions and 36 accessions of domesticated rice. They identified 2,800 SNPs in *Oryza indica*, 2,070 SNPs in the tropical *Oryza japonica* subspecies and 7,274 SNPs in wild rice (*Oryza rufipogon*). The authors used this data to identify regions that have potentially undergone a selective sweep, which they excluded in their demographic analysis. Using 2,057 neutrally segregating SNPs, the authors implemented a diffusion-based approach to examine different demographic models for the origin of rice. They found more support for single-origin models as compared to multiple-origin models, although their data cannot determine whether *O. japonica* or *O. indica* was domesticated first. They estimate that rice domestication occurred approximately 8,200–13,500 years ago, which is consistent with archeological evidence that rice was first cultivated ~8,000–9,000 years ago in the Yangtze Valley in China. *PC*

Nucleotide shortage and genomic instability

Genomic instability is a feature of solid tumors and leukemias, and there are several mechanisms proposed to explain this instability. Batsheva Karem and colleagues report that recently transformed cells show lower levels of cellular nucleotides, which leads to altered DNA replication dynamics (*Cell* **145**, 435–446, 2011). The authors suggest that in the early stages of cancer, increased cell proliferation leads to a shortage of nucleotides that cannot support normal DNA replication and genome stability. In newly transformed cells, the authors observed perturbations in DNA replication dynamics consistent with replication stress, including asymmetric progression from replication forks and an increased number of active origins. Nucleotide availability is a major factor in replication dynamics, and the authors noted a 2- to 5-fold decrease in the four dNTPs in newly transformed cells. Increasing the levels of exogenous nucleosides did not lead to increased cell proliferation but did lead to an increase in replication rate, an increase in inter-origin distance and a decrease in replication-induced double-strand breaks. Increasing the nucleotide pool also decreased the rate of transformation. The authors analyzed cells over-expressing Cyclin E which further supported the hypothesis that early activation of the Rb-E2F pathway can lead to deficiencies in nucleotides, thereby leading to replication stress and DNA damage. *PC*

Selaginella genome

Selaginella moellendorffii (Selaginella) is a lycophyte and a member of the oldest extant division of vascular plants. Jo Ann Banks and colleagues report the genome sequence of Selaginella, the first non-seed vascular plant genome published (*Science Express* published online, doi:10.1126/science.1203810, 5 May 2011). The assembled Selaginella genome is 212 Mb and has an estimated 22,300 genes. In contrast to other land plants, they did not find an ancient whole-genome duplication or polyploidy event. Their comparative analyses offer clues into evolutionary transitions in land plants related to the development of vascular tissues. They built a phylogenetic tree using gene homology and hierarchial clustering based on a comparison of the proteomes of Selaginella with green algae, moss and 15 angiosperm species. Whereas the transition from single-celled green algae to multicellular land plants shows an increase in about 3,000 new genes, the transition from non-vascular to vascular plants involves about 500 new genes. Next, they defined a set of *Arabidopsis thaliana* genes with developmental function and compared homolgous genes from Physcomitrella and Selaginella. They suggest a step-wise addition in the components of developmental pathways involved in the regulation of meristem and hormone biology. They also find that Selaginella has an increased number of genes involved in secondary metabolism. *OB*

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MUC5B and pulmonary fibrosis

David Schwartz and colleagues (*N. Engl. J. Med.* **364**, 1503–1512, 2011) report that a common variant upstream of *MUC5B* is associated with a higher risk of familial interstitial pneumonia and idiopathic pulmonary fibrosis. The authors performed a genome-wide linkage scan in 82 families with familial interstitial pneumonia and identified a significant linkage peak at 11p15. Association mapping of the region in individuals with familial interstitial pneumonia or idiopathic pulmonary fibrosis identified a strong signal at a cluster of mucin genes, with the peak association at a SNP located 3-kb upstream of the *MUC5B* transcription start site. Expression studies in lung tissue from unaffected individuals showed that *MUC5B* expression was much higher in those carrying at least one copy of the disease-associated variant. *MUC5B* expression was also strongly upregulated in lung tissue from individuals with idiopathic pulmonary fibrosis compared with unaffected controls. Notably, each copy of the susceptibility allele was associated with a 3–4-fold increased risk of familial interstitial pneumonia and idiopathic pulmonary fibrosis. Based on these findings, the authors propose that elevated MUC5B expression might increase susceptibility to lung damage and infection by reducing clearance of harmful substances or by interfering with alveolar repair. *KV*

Noncanonical signaling in Marfan syndrome

Marfan syndrome is caused by mutations in fibrillin-1, an extracellular matrix component that is thought to sequester the TGFβ signaling molecule. Loss of TGFβ sequestration leads to increased TGFβ signaling, which results in stimulation of the canonical Smad signaling pathway. Other noncanonical TGFβ-stimulated pathways, such as the mitogen-activated protein kinase (MAPK) pathway, have been recently discovered. Now, Harry Dietz and colleagues determine the contributions of canonical and non-canonical signaling pathways to aortic disease phenotypes in a mouse model of Marfan syndrome (*Science* **332**, 358–361, 2011). The authors show that not only is Smad2 activated in fibrillin-1 mutant mice, but so are MAPK kinase 1 and its downstream targets ERK1 and 2. It is known that treatments with losartan, an antiotensin II type 1 receptor blocker, or with TGFβ-neutralizing antibody (TGFβNAb) mitigate Marfan phenotypes in this mouse model, and the authors show that both losartan and TGFβNAb decrease both Smad2 and ERK1/2 activation. Furthermore, treatment of Marfan mice with a MEK inhibitor decreased aortic root growth, a sign of aortic disease, without altering Smad2 activation. This work implicates this non-canonical signaling pathway in the pathogenesis of aortic disease in Marfan syndrome. *EN*