Collaborative self-incompatibility

Most flowering plants contain male and female gametophytes but do not self-fertilize and instead exclusively mate with other individuals. One adaptation that prevents self-fertilization is self-incompatibility, the genetic recognition and rejection of self-pollen. In many plants, self-incompatibility is controlled by male- and female-specificity determinants encoded by multiallelic *S* genes. When the *S* haplotypes of the male and female gametophytes match, S-RNases (female-specific determinants) have a cytotoxic effect inside the self-pollen tube. The S-locus F-box (SLF) protein has been identified as a male-specific determinant and has been hypothesized to recognize non-self S-RNAses and mediate their degradation. Seiji Takayama and colleagues now report (*Science* 330, 796–799, 2010) that there are at least three types of SLF proteins in *Petunia*. The authors first cloned nine additional *SLF* alleles from pollen complementary DNA (cDNA), constructed transgenes and tested the effect of each of these transgenes on self-incompatibility. These *in vivo* pollination experiments identified three classes of SLF proteins, each affecting different subsets of non-self *S* haplotypes. Co-immunoprecipitation experiments showed that each type of SLF protein interacts with a specific repertoire of S-RNAses. The authors propose a 'collaborative non-self recognition' mechanism for self-incompatibility in *Petunia*, in which each SLF type recognizes a subset of non-self S-RNAses, and all SLF types are needed to recognize the entire repertoire of S-RNAses. ***PC***

Uveal melanoma metastasis suppressor

Uveal melanoma is a cancer of the eye that frequently progresses to fatal metastasis. Anne Bowcock and colleagues now report (*Science* published online, doi:10.1126/science.1194472, 4 November 2010) that class 2 uveal melanomas, which are at high risk for metastasis, frequently harbor somatic mutations in the gene encoding the BRCA1-associated protein BAP1. The authors performed exome sequencing on two class 2 uveal melanomas and discovered that both tumors harbored somatic, inactivating mutations in *BAP1*. They then sequenced *BAP1* in 29 additional class 2 uveal melanomas and found that *BAP1* was mutated in the majority of these tumors, with concomitant loss of the wildtype *BAP1* allele. Conversely, they identified only a single *BAP1* mutation among 26 class 1 uveal melanomas, indicating that *BAP1* mutations are largely specific for the more aggressive class 2 subtype. The authors also knocked down BAP1 expression in a uveal melanoma cell line using RNA interference (RNAi) and found that the treated cells developed morphological and gene expression characteristics typical of class 2 tumors. These findings strongly suggest that inactivation of BAP1 is a key step in the progression of uveal melanomas toward metastasis. *KV*

ATRX and tandem repeats

Mutation of *ATRX* causes mental retardation and α-thalassaemia with down regulation of α-globin expression (ATR-X syndrome). ATRX binds chromatin at telomeric and heterochromatic repeats, but its role in regulating gene expression is not well understood. Now, Richard Gibbons and colleagues report genome-wide maps of ATRX binding sites (*Cell* **143**, 363–378, 2010). The authors used ChIP-seq in primary human erythroid cells and mouse embryonic stem cells and showed that CpG islands and G-rich tandem repeats are the major euchromatic targets of ATRX. ATR-X syndrome is characterized by variability in α-globin expression between individuals with the same *ATRX* mutation, which manifests as varying proportions of red blood cells with hemoglobin-H inclusions and variable degrees of thalassaemia. Gibbons and colleagues identified a strong correlation between the length of a tandem repeat at the α-globin locus and the proportion of red blood cells with hemoglobin-H inclusions in 43 individuals with ATR-X syndrome. The authors also showed that the length of a tandem repeat had a *cis* effect on expression of another ATRX target, *NME4*. These findings suggest that the phenotypic variability of ATR-X syndrome may be influenced by differences in tandem repeat lengths at ATRX target genes. *EN*

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

Apical junction regulator

A defining characteristic of most epithelia is apical-basal cell polarity that partitions the 'top' and 'bottom' of cell layers. Cell-cell junctions located on the apical side of cells are important structures in the establishment of apical-basal polarity. However, the transcriptional networks that regulate the proteins that form cell-cell junctions are not well understood. Now, Kai M. Schmidt-Ott and colleagues report that the transcription factor Grainyhead-like 2 (Grhl2) is required for the expression of apical junctional components in a few types of epithelial tissues in mouse (*Development* **137**, 3835–3845, 2010). Comparison of gene expression profiles in epithelial and non-epithelial cells identified five transcription factors, including Grhl2, whose expression was perfectly correlated with E-cadherin (an apical junction component) expression. The authors generated *Grhl2* knockout mice and found that expression of E-cadherin and Claudin 4 (Cldn4), another apical junctional component, was severely reduced in *Grhl2* mutants. Subsequent chromatin immunoprecipitation experiments showed that Grhl2 binds to *cis*-regulatory regions that drive *Cdh1* (the E-cadherin gene) and *Cldn4* expression. Reporter constructs with the Grhl2 binding sites deleted and mutated showed that Grhl2 is required to activate the *Cldn4* promoter. The study suggests that Grhl2 directly regulates two key components of the apical junction complex. *PC*

Host control of HIV-1

Paul de Bakker and colleagues report a genome-wide association study for host control of HIV-1 (*Science* published online, doi:10.1126/science.1195271, 4 November 2010). They use a unique multiethnic cohort including 974 HIV-1 controllers, individuals who show a low level of plasma virus load maintained over at least one year in the absence of treatment, including individuals of European, African-American and Hispanic ancestry. They identify over 300 SNPs meeting genome-wide significance levels, all of which were located within the major histocompatibility complex (MHC). Previous studies have implicated variants in the HLA region in HIV-1 disease progression. Here, the authors used several approaches to fine map the HLA association to HIV-1 control. Using stepwise logistic regression, they identified four independent SNPs, which together account for 19% of the variance in the European sample. They used a new method for imputation of classical HLA alleles and amino acids and tested these for association. They identified three amino acids in HLA-B as being the most significantly associated. These amino acids are found in the peptide binding groove, suggesting HLA-mediated peptide presentation of viral peptides is involved in host control. These associations to SNPs, classical HLA alleles and amino acids were also replicated in the Swiss HIV Cohort. ***OB***