BMPs and adult neurogenesis

The signals that regulate the growth of new neurons in the mature adult brain are not well known. Now, Fred Gage and colleagues report that neural stem cells (NSCs) in the adult hippocampus are regulated by BMP signaling through the BMPR-IA receptor (*Cell Stem Cell* 7, 78–89, 2010). Because BMP signals influence self-renewal of stem cells in various niches, the authors hypothesized that the BMP pathway may regulate adult NSCs. Treatment of hippocampal adult NSCs with BMP2 led to a decrease in cell proliferation and an increase in the percentage of quiescent cells. To test if BMPs regulated NSC proliferation *in vivo*, the authors blocked BMP signaling by delivering Noggin to the lateral ventricle of the adult mouse brain. After a week of infusion with Noggin, hippocampal neurogenesis was increased in the mouse brain. Conditional deletion of *Bmpr1a* and *Smad4* in NSCs showed that BMP signaling is required for maintenance of adult neurogenesis *in vivo*. The authors speculate that environmental neurogenic stimuli, such as learning and voluntary exercise, may converge on the BMP signaling pathway. Interestingly, it has previously been reported that running increases *Noggin* expression and decreases *Bmp4* expression in the hippocampus, suggesting that BMP signaling may mediate the neurogenic effects of exercise in mice. ***PC***

Web-based GWAS

Nicholas Eriksson and colleagues at 23andMe, a direct-to-consumer genetic testing company, report results of a web-based, participant-driven genome-wide association study for 22 common traits (*PLoS Genet.* **6**, e1000993, 2010). To collect data for this study, the authors invited research participants, who had consented to the use of their data for research, to contribute phenotypic data on themselves through a series of web-based surveys. The surveys collected data on commonly studied traits such as eye and hair pigmentation and freckling, as well as on less commonly studied traits such as laterality preferences, simple physical characteristics and behavioral preferences. To minimize study heterogeneity and to maximize power, the authors restricted their analyses to individuals of Northern European ancestry and to traits for which data were available from a sufficient number of respondents. The authors replicated several published associations with eye color, hair color and freckling, and discovered new genome-wide significant associations with two less commonly studied traits: the ability to smell the urinary metabolites of asparagus and the tendency to sneeze when moving from relative darkness into bright light. This study shows the potential for this type of web-based study design to yield insights into the genetics of common traits. *KV*

HOTAIR scaffold

Long intergenic noncoding RNAs (lincRNAs) have recently emerged as an important class of regulatory RNAs that recruit histone modification complexes such as PRC2 to target sites in chromatin to influence gene expression. Howard Chang and colleagues (*Science* published online, doi:10.1126/science.1192002, 8 July 2010) now report that the HOTAIR lincRNA, produced from the *HOXC* cluster, acts as a modular scaffold that contains binding sites for both PRC2, which harbors histone H3 lysine 27 methylase activity, and a second histone modification complex that includes the histone H3 lysine 4 demethylase LSD1. Using deletion constructs, the authors showed that PRC2 binds to the 5′ region of HOTAIR, whereas the LSD1 complex binds to the 3′ region of HOTAIR. They further showed that knockdown of HOTAIR results in coordinated loss of PRC2 and LSD1 binding at many genomic sites, which is accompanied by loss of H3 lysine 27 trimethylation, gain of H3 lysine 4 dimethylation and increased transcription. These findings are consistent with a general model in which lincRNAs act as modular scaffolds that facilitate the coordinated recruitment of distinct histone modification complexes to target loci, where they can act synergistically to influence chromatin states. *KV*

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

microRNAs and metastasis

microRNAs (miRNAs) are often globally reduced in human cancers, but the clinical relevance of miRNAs in cancer is unclear. Now, Stefano Piccolo and colleagues report a role for miRNAs in regulation of metastasis (*Cell* **141**, 1195–1207, 2010). The authors determined that the miR103-107 family of miRNAs target transcripts encoding Dicer, the endonuclease that processes precursor miRNAs. Overexpression of miR103-107 decreased Dicer levels and globally decreased levels of mature miRNAs. In human tumors, high expression of miR103-107 is associated with reduced levels of Dicer and a higher probability of metastatic disease. *In vitro* assays in nonmetastatic tumor cell lines showed that overexpression of miR103-107 or downregulation of Dicer increased migratory cellular behavior without compromising cell viability. This effect was rescued by coexpression of a miR-insensitive Dicer transgene. Conversely, silencing of miR103-107 or overexpression of Dicer in highly metastatic cell lines reduced migratory activity. *In vivo* metastasis assays confirmed that overexpression of miR103-107 or depletion of Dicer increased metastatic activity, which can be rescued by Dicer overexpression. At the cellular level, expression of miR103-107 caused changes characteristic of an epithelial-to-mesenchymal transition. The authors further attributed this function of miR103-107 to downstream regulation of the miR200 family, which has previously been shown to suppress this transition. *EN*

Divergence in gene regulation

Differences in chromatin structure between species may underlie differences in gene regulation and divergent expression patterns. Oliver Rando and colleagues report an analysis of chromatin structure and gene expression in 12 *Hemiascomycota* yeast species spanning over 250 million years of evolution (*PLoS Biol.* 8, e1000414. doi:10.1371/journal.pbio.1000414). Although several well-known features of chromatin packaging near coding regions—such as the 5′ and 3′ nucleosome-free regions, a well-positioned +1 nucleosome and less well-positioned nucleosomes across the exons—are conserved across *Hemiascomycota*, other features are more variable. For example, nucleosome spacing within coding regions was variable, as was the distance between the nucleosome-free region and the start codon. In some instances, differences in expression of functional gene sets between species were accompanied by corresponding changes in chromatin structure and also by variation in intrinsic anti-nucleosomal poly(dA-dT) sequences. Nevertheless, differences in chromatin structure and anti-nucleosomal sequences were not sufficient to explain differences in gene expression between species. This analysis suggests that the complex interactions between many variables determine nucleosome positions, and argues against the hypothesis that DNA sequence has full predictive power over nucleosome positions. These data provide a resource for future experiments addressing chromatin structure, regulation of gene expression and evolution. ***PC***