**Profiling the mammalian transcriptome**

Understanding the complexity of eukaryotic genomes requires experimental profiling of their transcriptomes. In this issue, four papers present different approaches to tackle this problem at different levels. Two groups adopt a global strategy, applying next-generation sequencing directly to the mammalian transcriptome. Grimmond and colleagues use the Applied Biosystems SOLiD technology to profile mRNA in mouse embryonic stem cells, monitoring the content—expressed single-nucleotide polymorphisms and different splice forms—as well as the developmental dynamics of the transcriptome. Wold and colleagues use the Illumina technology to profile mRNA in adult mouse tissues, demonstrating that this approach provides detailed information on transcript isoforms and allows revision of existing gene models. Both approaches provide direct quantitative information on transcript expression, and the sheer volume of sequencing data allows detection of rare transcripts. In a different strategy, focusing on specific gene loci, Vidal, Salehi-Ashtiani, Roth and colleagues combine normalized pooling of reverse-transcription–PCR products with Roche 454 sequencing to validate a pipeline for locus-by-locus genome-wide splice isoform discovery. Lastly, Guigo and colleagues use array-based normalization of rapid amplification of cDNA ends (RACE) products to identify new rare transcripts in human cells. These methods allow a much more complete survey of the content and complexity of the mammalian genome than has been possible thus far.

**Articles p613, p621, p629, Brief Communication p597, News and Views p585, p587**

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**A chip to image and sort worms**

Forward and reverse genetic approaches in model organisms such as Caenorhabditis elegans require large sample sizes and are greatly facilitated by rapid screening for interesting phenotypes. A major bottleneck for such approaches is the application of state-of-the-art technologies such as high-resolution imaging to the screening process. Lu and colleagues present a computer-controlled microfluidic chip for rapid automated imaging and accurate sorting of C. elegans based on reporter expression. The system can sort rare mutants from a background of wild-type worms with low error rates and could therefore be applied to genetic screening in the future.

**Article p637, News and Views p589**

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**Whispering-gallery-mode biosensors**

Label-free detection methods for biological molecules provide several benefits over methods that depend on potentially disruptive modification of the analyte. These methods, however, rarely provide single-molecule sensitivity. Now, whispering-gallery-mode biosensors—a new class of sensors based on detecting analyte binding–induced changes in the resonance of light circulating in microcavities—demonstrate single-molecule sensitivity. In a Perspective, Vollmer and Arnold describe the physical mechanisms that provide this sensitivity and discuss current and future applications of these sensors.

**Perspective p591**

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**Live-cell actin imaging**

Actin has an indisputably fundamental role in many cellular processes, but current approaches for imaging actin in live cells have several drawbacks. Sixt, Wedlich-Soldner and colleagues introduce Lifeact, a 17-amino-acid actin-binding peptide derived from yeast protein Abp140, which allows dynamic actin imaging in mammalian cells without disruption of function. Because of its small size, Lifeact can easily be synthesized either as an oligonucleotide for expression as a GFP fusion, or as a peptide for direct chemical labeling. Moreover, Abp140 is not present in higher eukaryotes, so Lifeact is therefore less likely to compete with endogenous mammalian actin-binding proteins.

**Brief Communication p605**