METHODS IN BRIEF

GENOMICS

Are super-enhancers really super?

Super-enhancers are a recently described class of transcriptional regulators that are thought to be more than the sum of their parts and exert higher-order control. Hay *et al.* focused on a super-enhancer in the α-globin locus with features that fit the current definition: multiple enhancers in close proximity, binding of the Mediator complex and acetylation of histone H3 at lysine 27. They characterized transcription factor binding at the five enhancer-like elements found in this 24-kb region as well as the impact of single and double enhancer knockouts. All enhancer elements acted in an additive manner, and no single element was critical for globin expression or chromatin structure. The authors stress that new classes of transcriptional regulators should be subject to functional analysis because, at least for the α-globin locus in mouse erythroid cells, there is no evidence of a super-enhancer.

Hay, D. *et al. Nat. Genet.* **48**, 895–903 (2016).

MOLECULAR BIOLOGY

Imaging chromosome organization

Chromosome conformation capture methods such as Hi-C have been crucial for studying the structural organization of chromosomal DNA. However, these ensemble measurements may average out structural details, as they occur on the single-chromosome scale. To bypass this potential limitation, Wang *et al.* developed an imaging-based approach for mapping the spatial organization of chromosomes. Specifically, they mapped structures known from Hi-C data as topologically associated domains (TADs) using a combination of a modified version of the Oligopaint labeling strategy and a multiplexed *in situ* hybridization approach previously developed in the laboratory of Xiaowei Zhuang at Harvard University. Using this approach, they labeled known TADs on several human chromosomes, as well as active and inactive X chromosomes. Their results correlated well with many results obtained with Hi-C, including the observation of active and inactive regions within individual TADs, and allowed for complementary discoveries.

Wang, S. *et al. Science* **353**, 598–602 (2016).

CELL BIOLOGY

Model colons

Tissue models are needed to study human cancer progression. To generate a realistic model of the colon, Chen *et al.* decellularized healthy human colon tissue with detergent and seeded the remaining extracellular matrix scaffold with primary colonic epithelial cells, endothelial cells and myofibroblasts. The native matrix provided a physiological *ex vivo* model containing intact wild-type mucosa and muscularis mucosa layers as well as vasculature. Seeding with cells carrying mutations in *APC* and *KRAS* caused noninvasive tumors to form, and led to submucosal invasion in a background of reduced TGF-β signaling. The system allowed the authors to carry out a transposon-based mutagenesis screen for functional driver mutations leading to colorectal cancer.

Chen, H.J. *et al. Nat. Biotechnol.* **34**, 845–851 (2016).

IMAGING

Expanding expansion microscopy

Expansion microscopy (ExM) is a super-resolution imaging technique in which scientists anchor labels to targets of interest within a sample and then increase the size of that sample using a swellable gel. This swelling allows subdiffraction-limited structures to be imaged with conventional microscopes. One drawback of ExM is that native proteins are digested by proteases prior to expansion and therefore cannot be probed directly. Papers from two groups describe improvements to ExM that bypass this limitation. Tillberg *et al.* developed protein retention ExM (proExM), in which proteins, rather than labels, are cross-linked to the gel for expansion. Ku *et al.* developed magnified analysis of the proteome (MAP), a method that prevents protein cross-linking and denatures proteins prior to expansion, preserving protein content. Both methods now allow users to label with conventionally labeled antibodies and endogenous fluorescent proteins, broadening the utility of ExM.

Ku, T. *et al. Nat. Biotechnol.* http://dx.doi.org/10.1038/nbt.3641 (2016).

Tillberg, P.W. *et al. Nat. Biotechnol.* http://dx.doi.org/10.1038/nbt.3625 (2016).