IN BRIEF

MICROSCOPY

Chromatin dynamics get mapped

Shaban, H. A. et al. *Genome Biol.* **21**, 95 (2020).

Studying genome organization and dynamics is crucial for understanding the regulation of gene expression. Although genome movement has been explored, a method for studying bulk chromatin dynamics at high resolution was not available. Shaban et al. have developed high-resolution diffusion mapping (Hi-D) to quantitatively map the dynamics of chromatin and abundant nuclear proteins. In Hi-D, labeled DNA or nuclear proteins are imaged over time, and then dense optical flow reconstruction is used to quantify the local motion at sub-pixel accuracy. Next, a Bayesian interference approach is employed to classify local types of diffusion, and biophysical properties such as diffusion constants are used to create two-dimensional maps of dynamics. With Hi-D the researchers were able to map the dynamics of chromatin under multiple conditions as well as the dynamics of RNA polymerase II. A key observation of the study is that chromatin dynamics are dictated by DNA–DNA contacts and protein binding rather than chromatin density and compaction. *RS*

https://doi.org/10.1038/s41592-020-0870-4

SIGNAL TRANSDUCTION

Identifying phosphorylation-site-specific kinases

Watson, N. A. et al. *Nat. Commun.* **11**, 1684 (2020).

Kinase phosphorylation site dependencies have been studied to identify targets for a kinase of interest; however, identification of kinases that phosphorylate a particular site is not routine. To address this problem, Watson et al. have developed KiPIK (kinase inhibitor profiling to identify kinases). The researchers collected data for a large number of kinase inhibitors on in vitro inhibitory activity against a panel of about 500 recombinant human kinases. This information can be interpreted as inhibition fingerprint for kinases. Next, the researchers obtained cell extracts exhibiting phosphorylation activity of interest and screened against the inhibitors in the panel. Quantification of substrate phosphorylation in the presence of each inhibitor provides the inhibition fingerprint, which can then be matched with the previously determined fingerprints for recombinant kinases. The authors have validated this method on many known phosphorylation sites, as well as made predictions for unknown kinases. *AS*

https://doi.org/10.1038/s41592-020-0872-2

DATABASES

Harmonizing cancer variant knowledgebases

Wagner, A. H. et al. *Nat. Genet.* **52**, 448–457 (2020).

Sequencing genomes from cancer samples reveals somatic mutational changes. While potentially informative, observed variants need to be carefully interpreted to assess biological and clinical significance. Knowledgebases collecting information about genomic variants, diseases and drugs from published literature are important resources. However, disparities between knowledgebases are not uncommon and can cause inconsistency. The Variant Interpretation for Cancer Consortium harmonized variant interpretations across six widely used somatic cancer variant knowledgebases. Different data types were mapped to established standards and ontologies describing genes, variants, diseases, drugs and evidence levels, generating a single meta-knowledgebase composed of 12,856 interpretations. Testing results using data from the GENIE cohort showed improved interpretation performance and efficiency after harmonization. The group developed a web interface for searching and exploring the meta-knowledgebase. *LT**

https://doi.org/10.1038/s41592-020-0871-3

DEVELOPMENT

A digital embryo

Sladitschek, H. L. et al. *Cell* **181**, 922–935 (2020).

Single-cell RNA sequencing (scRNA-seq) has become a valuable tool for revealing transcriptomic patterns during embryonic development. Yet it is still not an easy task to map single-cell expression profiles onto spatial organization in a developing embryo. Sladitschek et al. examine the optically transparent embryo of *Phallusia mammillata*, a marine tunicate that recapitulates the embryonic cell diversity of a vertebrate. The researchers describe a scRNA-seq computational framework for identifying cell types and inferring the lineage history of each cell within the embryo. In addition, they use multiview light-sheet microscopy to image the whole embryo and capture the morphology and physical position of each cell, as well as its developmental evolution in the embryo. The integration of scRNA-seq and imaging data yields a digital embryo with spatiotemporally resolved transcriptomic and morphological profiles at single-cell resolution. *LT*

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