**Dynamic interactomes with AP-SWATH**

Affinity purification–mass spectrometry (AP-MS) is a widely used method for mapping protein-protein interactions under close-to-physiological conditions. Though powerful, this method has not been broadly applied to characterize dynamic changes in protein interactomes because obtaining accurate absolute quantitative measurements is limited with traditional data-dependent acquisition-based MS. Two papers in this issue show that dynamic interactome changes can be robustly and sensitively monitored using AP coupled with a data-independent acquisition-based MS approach called SWATH (sequential window acquisition of all theoretical spectra). Gingras, Tate and colleagues map changes in the CDK4 kinase interactome upon mutation or drug inhibition, and Aebersold and colleagues monitor the dynamics of the 14-3-3ζ scaffold protein interactome following IFG1 stimulation. Each group also provides a robust analysis pipeline for processing AP-SWATH data and scoring protein interactions.

**Articles p1239, p1246**

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**Profiling chromatin with ATAC-seq**

DNA is regulated by the proteins that bind it. Several methods such as DNase footprinting and micrococcal nuclease digestion followed by deep sequencing have been used to profile the binding sites of transcription factors and nucleosomes, respectively. Now a method based on the transposition of sequencing adaptors into open chromatin, followed by high-throughput sequencing of the resulting fragments, profiles chromatin accessibility and yields information on the positions of DNA-binding proteins and nucleosomes simultaneously. ATAC-seq (assay for transposase-accessible chromatin using sequencing) is simpler than nuclease-based protocols and requires less input material. Its rapid workflow allows the profiling of chromatin within a day: a timescale that could facilitate applications for epigenome profiling in a clinical setting.

**Article p1225**

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**Modeling for biological discovery**

As researchers accumulate data on experimental organisms, the hope is that *in silico* models will increasingly contribute to biological understanding and will help direct and prioritize future experiments. Covert and colleagues now give an example of how this may be done. They made a systematic and quantitative comparison of the growth-rate predictions of a whole-cell model of *Mycoplasma genitalium* with all experimentally measurable growth rates of single-gene mutants in this bacterium. By identifying and following up discrepancies in experimental measurements and model predictions, they made novel testable predictions about *Mycoplasma* enzyme kinetics that they then verified in experiments and used to further refine the model. In the future, whole-cell models may also contribute to discovery in more complex organisms.

**Brief Communication p1192**

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**Cell-specific thermometers**

Endotherms maintain their body at a metabolically appropriate temperature by producing heat through different mechanisms, including active metabolic processes that take place in specific organelles such as mitochondria. Evaluating this process, called thermogenesis, in living mammalian cells hasn’t been easy. Fluorescent thermosensors offer good spatiotemporal resolution and can directly sense variations in temperature, but most of the available sensors are synthetic, and it is cumbersome to get them into cells. Once inside cells, they are difficult to target to specific areas. To overcome this, Mori and colleagues describe a genetically encoded fluorescent thermosensor based on a fusion between GFP and a thermosensing protein from *Salmonella enterica*. The sensor can be selectively expressed in living cells and targeted to specific subcellular organelles.

**Article p1232**

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**High-throughput stem cell profiling**

Human pluripotent stem cell (hPSC) lines can show substantial variation in their response to exogenous factors, due to either inherent differences or uncontrolled variation in the culture environment. Zandstra and colleagues describe a high-throughput platform in a 96-well format that optimizes several parameters—including colony size, culture medium and substrate—and provides a controlled environment for the study of stem cell responses. Using this platform, the researchers identify a simple Oct4-Sox2 code to predict lineage bias of hPSC lines and optimize the dose of several signaling factors for cell fate induction under defined conditions. This platform should prove useful for profiling newly generated hPSC lines and for studying the signaling events that drive stem cell differentiation.

**Article p1222**