GENE EXPRESSION

## Anti-anti-CRISPR

*Cell* **178**, 1452–1464 (2019).

It is now known that bacterial viruses (phages) can attain genes encoding anti-CRISPR (Acr) proteins to inhibit CRISPR systems. These Acr proteins exhibit large sequence diversity, yet it is often found that *Acr* genes are adjacent to genes encoding proteins containing a helix-turn-helix (HTH) DNA-binding motif. These anti-CRISPR-associated (*Aca*) genes have been considered as markers for identifying anti-CRISPR families. In spite of the wide presence of *Aca* genes, the functions of Aca proteins have not been carefully examined. Stanley et al. used a *Pseudomonas* phage, JBD30, as a model system to study the transcript levels of an *Acr* gene (*AcrIF1*) during an infection cycle. They uncovered that Aca proteins serve as a repressor of the *Acr* promoter, and can thus attenuate anti-CRISPR transcription. In the absence of Aca activity, the strong transcription of *Acr* genes is detrimental for phage survival. These findings of inhibiting anti-CRISPR systems may add a new tuning knob for CRISPR-based genome-editing tools. *LT*

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BIOPHYSICS

## Monitoring Å-scale conformational changes

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Measuring small conformational changes within proteins, that occur at millisecond timescales, is extremely challenging. However, the problem of resolving such motions can often be reduced to resolving unique spatial orientations of a single key structural element, such as an α-helix. Lewis et al. attach a fluorophore to the protein-element of interest and track changes in its orientation using a polarization microscope. Collecting fluorescence intensities at a high rate of 50 frames per second allowed them to quantify real-time motions in a single protein. They analyzed the transitions between the three conformational states of the RCK domain of the prokaryotic $Ca^{2+}$-dependent $K^+$ channel MthK, and were able to observe states that differed by 3–8 Å. The success of the method depends on obtaining a signal-to-noise ratio that works for the desired resolution, and on choosing a structural element that is representative of the conformational changes under observation. *AS*

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NANOBIOTECHNOLOGY

## Spectroscopy goes nano

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Spectrometers are integral instruments in numerous research applications, and miniaturized versions would have widespread applications. However, making micro-scale versions of standard instruments involves miniaturization of established components, which can be technically challenging or unfeasible. Yang et al. describe an alternative approach to miniaturization of standard spectrometers that uses a single compositionally engineered nanowire as the basis of the design. To keep things small, these nanowires combine elements that separate and detect light, and they are composed such that the spectral response varies along their length. Electronic probing of photocurrents and cross-referencing to a calibrated response function enables both monochromatic and broadband spectra to be reconstructed using this nanowire. The researchers incorporated the nanowire into a mapping system, and demonstrate spectral imaging on the centimeter scale as well as in situ absorption measurements of single cells. *RS*

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SYNTHETIC BIOLOGY

## Multi-input programming of cellular response

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Engineered chemical control of cellular response is currently limited to low complexity, single-input/single-output approaches. Foight et al. describe a synthetic post-translational control system where a central receiver protein, NS3a protease in their case, is targeted by multiple clinically approved drugs. 'Reader' proteins are computationally designed to specifically recognize the drug (danoprevir or grazoprevir)-bound forms of NS3a, and to colocalize to different parts of the cell. Evaluation of the multi-input/multi-output behavior in mammalian cells shows that these reader proteins maintain specificity to the target states of NS3a in mammalian cell cultures, and provide a programmable transcriptional control when either drug is used. The system is also able to achieve proportional and graded control when using different proportions of the two drugs and corresponding reader proteins. The method, termed pleiotropic response outputs from a chemically inducible single receiver (PROCISiR), could be useful for programming in vitro and in vivo cellular control. *AS*

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