In This Issue

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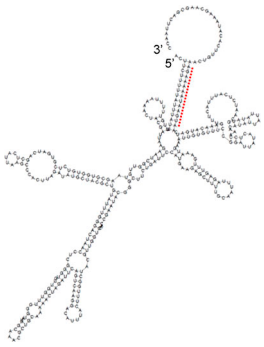
sisRNAs engage with their hosts



The secondary structure of *sisR-1* is predicted to expose 29 nucleotides at its 3′ end.

Pek et al. describe how a stable, intron-derived RNA regulates the expression of its host gene during *Drosophila* embryogenesis.

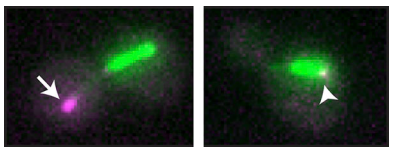
Once they are spliced out of nascent mRNAs, noncoding intron sequences are usually degraded rapidly. At least in *Xenopus* eggs and human cell lines, however, some intronic RNAs persist for long periods, although the function of these stable intronic sequence (sis) RNAs remains unknown. Pek et al. used deep sequencing to look for sisRNAs in newly fertilized *Drosophila* embryos, whose initial development depends on a pool of stable RNA generated several hours earlier during oogenesis.

The researchers identified over 30 candidate sisRNAs, including one, dubbed *sisR-1*, that was derived from the fourth intron of a gene called *rga*. After being spliced out of the *rga* pre-mRNA, *sisR-1* was processed into longer and shorter versions that localized to the nucleus and cytoplasm, respectively. Structural predictions suggested that the 3′ region of nuclear *sisR-1* is exposed and available to base pair with an antisense transcript, named *ASTR*, that is also produced from the *rga* locus.

Pek et al. discovered that *ASTR* promoted transcription of the *rga* gene in early embryos, causing *sisR-1* to gradually accumulate until, later in development, it was able to suppress *ASTR* and shut down *rga* expression. Knocking down *sisR-1* delayed the downregulation of *ASTR* and *rga*, but otherwise embryogenesis proceeded normally. Senior author Jun Wei Pek now wants to investigate how *sisR-1* is stabilized, and whether its knockdown affects fly development in sensitized genetic backgrounds.

Pek, J.W., et al. 2015. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201507065

Num1 relieves dynein's inhibitions



In a control cell (left), dynein (magenta) localizes to the plus ends (arrow) of astral microtubules (green). Overexpressing a Num1 fragment (right) prompts the motor's relocalization to microtubule minus ends (arrowhead).

Lammers and Markus describe how dynein is activated at the budding yeast cell cortex so that it can pull on astral microtubules and position the mitotic spindle.

During mitosis, dynein motors are anchored at the yeast cell cortex by the receptor protein Num1. Dynein is transferred to Num1 from the plus ends of dynamic astral microtubules. Pac1 (a homologue of human LIS1) links dynein to the plus-end tracking protein Bik1 and prevents the motor from prematurely walking away toward the microtubule minus end. Once anchored to Num1, though, dynein's minus end–directed motility is activated and the mitotic spindle is pulled into the bud. Whether Num1 directly activates dynein is unknown, however.

Lammers and Markus found that overexpressing the dynein-binding domain of Num1 prompted the motor protein's premature disappearance from astral microtubule plus ends. Live imaging of cells expressing this Num1 domain showed dynein moving toward microtubule minus ends attached to the yeast spindle pole body, a phenomenon never seen in wild-type cells. The Num1 fragment reduced dynein's colocalization with Pac1, suggesting that receptor binding might activate dynein by disrupting the motor's association with its inhibitor. Accordingly, overexpressing Pac1, or a dynein mutant with increased affinity for Pac1, restored the motor protein's localization to microtubule plus ends in cells expressing the Num1 fragment.

Senior author Steven Markus now wants to test his model of cortical dynein activation by reconstituting the process in vitro.

Lammers, L.G., and S.M. Markus. 2015. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201506119

Trypanosomes show their commitment

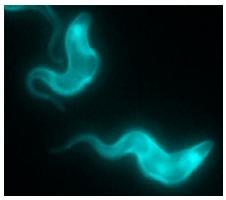


IMAGE COURTESY OF DR. FEDERICO ROJAS, UNIVERSITY OF EDINBURGH

Cultured *T. brucei* cells in the pleomorphic bloodstream form.

Domingo Sananes et al. investigate how the parasite *Trypanosoma brucei* transitions between different developmental stages.

Many protozoan parasites undergo complex life cycles that require their adaptation to drastically different environments. *T. brucei*, for example, must switch from a growth-arrested "stumpy" form in mammalian blood to a proliferative "procyclic" form in the tsetse fly gut. In vitro, this differentiation step can be induced by cis-aconitate (CA). Domingo Sananes et al. found that the parasite only responded above a threshold of 1 mM CA but that, after exposure to this signal for 2–3 hours, the cells were committed to differentiation, even if CA was subsequently depleted from the surrounding medium.

The stumpy-to-procyclic transition is therefore an irreversible bistable switch, a mechanism commonly used to govern biological events such as differentiation or mitotic entry. In vivo, the switch would aid parasite survival by making their differentiation quick and decisive.

Domingo Sananes et al. discovered that protein synthesis was required for *T. brucei* to "remember" the CA signal and retain their commitment to differentiation. Accordingly, the parasite's proteome showed numerous changes after three hours of CA exposure. Differentiation was also accompanied by many changes in protein phosphorylation. The researchers focused on a protein kinase, NRK, that is highly expressed in stumpy cells and found that knocking down this kinase inhibited the parasite's transition to the procyclic form.

Author Keith Matthews now wants to investigate how NRK promotes Trypanosome differentiation, and to determine how it is linked to upstream signaling events that initiate the response to CA.

Domingo Sananes, M.R., et al. 2015. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201506114

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