In This Issue

Retinoic acid keeps Lingo-1 quiet

Retinoic acid (RA) promotes axon regeneration by silencing a key inhibitory receptor, Lingo-1. RA treatment induces the outgrowth of axons from primary neurons plated on myelin. Compared to untreated cells (left), RA treatment (right) induces the outgrowth of axons (green) from primary neurons plated on myelin.

Cohesin and condensin spring into action

Heat maps of pericentric chromatin position show that, compared to wild-type cells (left), the pericentric chromatin of condensin mutants (right) stretches out toward the spindle pole (red dot). Stephens et al. describe how cohesin and condensin organize pericentric chromatin into a spring that resists the pull of mitotic spindle microtubules. During metaphase, the chromatin surrounding each chromatid’s centromere is thought to act as a spring that balances the microtubule-based forces pulling sister chromatids apart. Cohesin, best known as a protein that links sister chromatids together, and condensin, which helps compact DNA by organizing it into loops, are both enriched on pericentric chromatin, and both proteins have been implicated in generating tension on metaphase chromosomes.

miRNAs prevent a change of heart

Cells derived from Sgcb-null progenitors (green) don’t express the cardiomyocyte marker Cx43 (red), unless miR669 expression is artificially restored (right). Crippa et al. identify a family of microRNAs that stop cardiac progenitors from abnormally differentiating into skeletal muscle, a function that may be disrupted in some types of human muscular dystrophies. Some pericytes—the cells that wrap around the outside of blood vessels—have the ability to differentiate into cardiac or skeletal muscle, depending on the tissue in which they are located. Crippa et al. isolated these progenitors from the hearts of mice lacking β-sarcoglycan (Sgcb), a protein that maintains the integrity of both skeletal and cardiac muscle cells. Surprisingly, Sgcb-null cardiac progenitors differentiated into skeletal muscle myofibers in vitro, and the master regulator of skeletal myogenesis, MyoD, was abnormally expressed in the hearts of Sgcb-knockout animals.

The researchers found that the miRNA miR669a was strongly down-regulated in Sgcb-null cardiac progenitors because the leaky membranes of these cells let in calcium ions that activate calpain proteases, resulting in the degradation of a transcription factor required for miR669a production. In addition, a closely related miRNA, miR669q, was encoded within the Sgcb gene itself and was therefore completely absent from Sgcb-null progenitors. Both miRNAs were found to inhibit skeletal myogenesis by targeting MyoD directly.

Sgcb-null cardiac progenitors were unable to regenerate damaged heart tissue unless miR669 expression was restored to prevent their aberrant differentiation into skeletal myofibers. Conversely, cardiac progenitors lacking Sgcb and miR669 efficiently repaired damaged skeletal muscle. The authors now want to investigate whether mutations in human Sgcb, which cause limb-girdle muscular dystrophy type 2E, also perturb miRNA expression and cardiac progenitor differentiation.

Crippa, S., et al. 2011. J. Cell Biol. doi:10.1083/jcb.201103138.

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