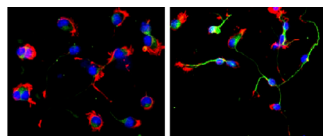


Retinoic acid keeps Lingo-1 quiet



Compared to untreated cells (left), RA treatment (right) induces the outgrowth of axons (green) from primary neurons plated on myelin.

Retinoic acid (RA) promotes axon regeneration by silencing a key inhibitory receptor, **Puttagunta et al.** report. Neuronal regrowth after injury is limited, in part, by inhibitory proteins released upon disruption of the surrounding myelin sheath. These proteins bind to the Nogo receptor complex on the neuronal plasma membrane, thereby activating the RhoA GTPase to initiate growth cone collapse. On the other hand, neuron regeneration can be boosted by the RA receptor RAR- β , although the mechanisms by which this transcription factor promotes axon growth remain unclear.

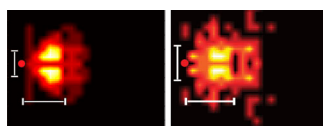
Puttagunta et al. found that RA and RAR- β specifically

counteract the inhibitory Nogo receptor pathway. RA promoted the outgrowth of neurites from wild-type neurons in the presence of inhibitory myelin proteins but had no effect on neurons lacking RAR- β . In the presence of RA, RAR- β down-regulated a key component of the Nogo receptor complex called Lingo-1 by binding to Lingo-1's promoter and repressing its transcription. RA no longer reversed myelin-dependent inhibition of axonal growth if Lingo-1 was overexpressed in cultured neurons.

The researchers also found that treating mice with RA following a spinal cord injury repressed Lingo-1 expression, whereas Lingo-1 levels remained high in mice lacking RAR- β . Senior author Simone Di Giovanni now wants to investigate whether boosting RAR- β activity at the right time after injury can improve neuron recovery and whether the RA signaling pathway promotes neurite outgrowth by other mechanisms in addition to inhibition of the Nogo receptor complex.

Puttagunta, R., et al. 2011. *J. Cell Biol.* doi:[10.1083/jcb.201102066](https://doi.org/10.1083/jcb.201102066).

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).

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.

Stephens et al. analyzed mutant yeast strains and found that yeast lacking condensin and cohesin had longer metaphase

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

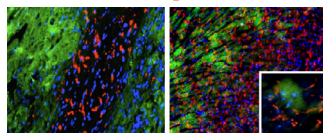
balances the microtubule-based forces pulling sister chromatids apart. Cohesin, best known as a protein that links sister chromatids together, and condensin, which helps compact DNA by organizing it into loops, are both enriched on pericentric chromatin, and both proteins have been implicated in generating tension on metaphase chromosomes.

spindles that fluctuated greatly over time, indicating that pericentric chromatin offered less resistance to spindle-pulling forces in the absence of these proteins. By mapping the organization of pericentric chromatin in wild-type and mutant cells, the researchers found that cohesin and condensin have different functions in organizing the spring. Condensin localized in line with the mitotic spindle and kept pericentric chromatin compacted along the spindle axis, whereas cohesin localized around the spindle axis and prevented the chromatin from spreading out radially.

By confining pericentric chromatin in these different directions, condensin and cohesin generate a force that resists the pull from spindle microtubules. The resulting tension signals to cells that sister chromatids are correctly attached to opposite spindle poles. Now senior author Kerry Bloom wants to investigate whether the release of this tension at the beginning of anaphase helps to propel the chromatids apart from each other.

Stephens, A.D., et al. 2011. *J. Cell Biol.* doi:[10.1083/jcb.201103138](https://doi.org/10.1083/jcb.201103138).

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).

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

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.

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.201011099](https://doi.org/10.1083/jcb.201011099).