# In This Issue

Cell

## Reprogramming's Got the Beat

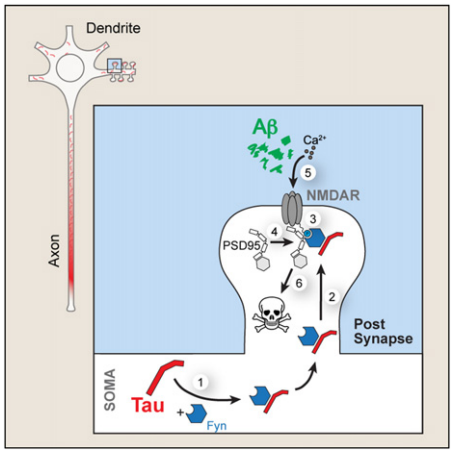
PAGE 375

Reprogramming of fibroblasts to induced pluripotent stem cells suggested that a somatic cell could be reprogrammed into alternative fates. Ieda et al. now report that a combination of three developmental transcription factors, Gata4, Mef2c, and Tbx5, rapidly and efficiently reprograms postnatal cardiac or dermal fibroblasts directly into cardiomyocyte-like cells without passing through a cardiac progenitor state. Thus, reprogramming of endogenous or explanted fibroblasts might provide a source of cardiomyocytes for regenerative approaches.

## Fyn-ally, the Missing Link between Tau and Aβ

PAGE 387

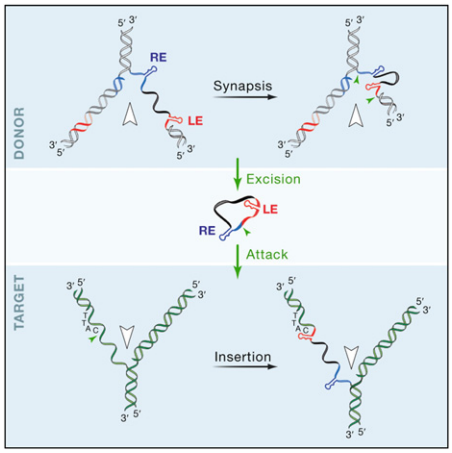
The peptide amyloid-β (Aβ) and the tau protein are both found in toxic aggregates in the brains of Alzheimer's disease (AD) patients. In this issue, Ittner et al. reveal a mechanism by which tau may collaborate with Aβ in mediating AD pathogenesis. The authors show that tau, generally thought of as an axonal protein, targets Fyn kinase to dendritic spines, where it phosphorylates NMDA receptors. This leads to increased excitotoxicity, which boosts the toxic effects of Aβ on neurons. Disruption of tau-mediated targeting of Fyn in a mouse model of AD decreases excitotoxicity via NMDA receptors and ameliorates other pathological features associated with Aβ.




## p53 Gets Linc-ed In

PAGE 409

Mammalian genomes encode numerous noncoding RNAs, including a class of large intergenic noncoding RNAs (lincRNAs) associated with p53. In this issue, Huarte et al. show that lincRNA-p21 is a direct p53 transcriptional target that also mediates p53-dependent transcriptional repression through its physical association with hnRNP-K. These results reveal a new aspect to the p53 transcriptional response and suggest that lincRNAs may serve as key regulatory hubs in transcriptional pathways.




## Lagging Strand Takes the Lead in Transposition

PAGE 398

For most transposons, excision and insertion require double-stranded templates. In one recently identified family of bacterial insertion sequences (IS*200*/IS*605*), however, the cutting and pasting is done with only a single-stranded DNA segment. Ton-Hoang et al. now show that these single strands are preferentially excised and inserted from the lagging strand of replicating DNA, coupling transposition to replication fork passage. In addition to identification of a novel transposition pathway, the unique excision and insertion properties of the IS*200*/IS*605* family may make them useful tools for probing the in vivo structures of ssDNA segments.

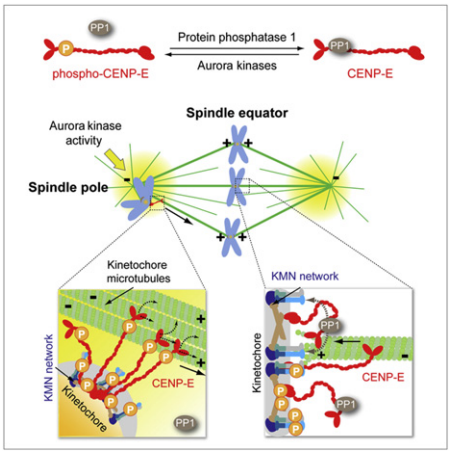
## A-PRC-iating Midzone Dynamics

PAGE 420 and PAGE 433

During cell division, microtubules are arranged in the mitotic spindle to segregate the duplicated chromosomes. In anaphase, tightly bundled antiparallel microtubules in the spindle center form the midzone structure. Using an in vitro reconstitution approach, Bieling et al. show how PRC1, an antiparallel microtubule bundler, and the processive motor kinesin-4 form the minimal module needed to dynamically organize the core structure of the vertebrate midzone. Related work from Subramanian et al. provides detailed insight into how PRC1 functions. Using structural and biophysical approaches, they find that PRC1 dimers contain both structured and unstructured domains that crosslink antiparallel microtubules, which allow the protein to track along the overlap at the midzone without substantially resisting relative filament sliding.

## Chromosomes Turn on a Phosphate

PAGE 444

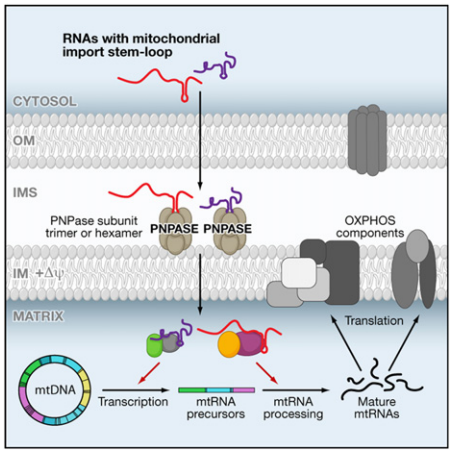



Proper orientation of chromosomes in the mitotic spindle ensures accurate segregation and guards against aneuploidy, a common feature of human cancers. In this issue, Kim at al. demonstrate that CENP-E, a kinetochore motor protein, is phosphorylated at a single site by Aurora kinases at the spindle poles to promote chromosome congression. CENP-E is subsequently dephosphorylated by PP1 at the outer kinetochore, enabling bistable orientation. These findings explain how spatially regulated phosphorylation can control chromosome movements during mitosis.

## Protecting the Family Jewels

PAGE 468

The mTORC1-signaling pathway is a critical regulator of cell growth. Aberrant mTORC1 activation is associated with stem cell depletion through poorly characterized targets. Now, Hobbs et al. demonstrate that Plzf, a transcription factor implicated in germline maintenance, opposes mTORC1 pathway activity in spermatogonial progenitor cells (SPCs). Further, they show that elevated mTORC1 activity inhibits response of SPCs to GDNF, a niche-derived growth factor required for self-renewal. This study provides important insight into mechanisms of germline maintenance and defines a model by which mTORC1 activity is detrimental to stem cell function.




## RNA Takes the Autobahn to the Mitochondria

PAGE 456

RNA import into mammalian mitochondria is poorly understood compared with protein import. Here, Wang and colleagues report the identification of a mammalian mitochondrial RNA import factor, the enzyme PNPASE. They find a 20 nucleotide stem-loop RNA structure that can mediate PNPASE-dependent mitochondrial RNA import. PNPASE-dependent imported RNAs regulate processing of long mitochondrial RNA transcripts and the translation of electron transport chain proteins for respiration. The study identifies a component of the mammalian mitochondrial RNA import pathway and a potential new approach for selectively targeting RNAs to mitochondria.

## Mini-Myc Goes Nonnuclear

PAGE 480

Myc family proteins are nuclear transcriptional regulators that control cell growth, proliferation, and apoptosis. Here, Conacci-Sorrell et al. report the characterization of Myc-nick, a truncated form of Myc generated by calpain cleavage of full-length Myc. Myc-nick lacks nuclear localization and DNA binding regions and is predominantly cytoplasmic. Myc-nick interacts with microtubules and the GCN5 acetyltransferase to promote α-tubulin acetylation, changes in cell morphology, and terminal differentiation. Proteolytic cleavage may provide a functional switch from the nuclear, proproliferation form of Myc to a cytoplasmic, prodifferentiation form.