In This Issue

Bundle up for cytokinesis

New results from Mollinari et al. (page 1175) reveal that cytokinesis requires microtubule bundles to be formed at the spindle midzone and that the mitotic spindle-associated protein PRC1 does this bundling. PRC1 is a cyclin-dependent kinase substrate known to be localized to the central spindle midzone during mitosis, where antiparallel overlapping microtubules are the site of accumulation of many proteins required for cytokinesis. With their new results, the authors have found that the structure of the spindle midzone is maintained by PRC1 microtubule bundling activity.

Mollinari et al. found that PRC1 could form bundles of microtubules both in vitro and in vivo, where high levels of exogenously expressed PRC1 caused unusual cytoplasmic arrays of microtubules in interphase cells.

Overexpressed PRC1 bundles microtubules in interphase cells.

Bundling was required for cytokinesis; in the absence of PRC1, chromosomes separated normally along a disorganized anaphase spindle, but furrowing during cytokinesis stalled, and daughter cells failed to separate. The bundles may therefore be important for the coordinated passage of proteins at anaphase from kinetochores along microtubules to the cell cortex, where they initiate assembly of the acto-myosin ring and the onset of cytokinesis.

As other stages of the cell cycle were unaffected by the lack of PRC1 activity, bundling appears to be important only during late stages of mitosis. Mutation of the phosphorylation motif enhanced the bundling activity of PRC1, suggesting that Cdc2 inhibits the protein during early mitosis.

Prostate stem cells identified

Every organ has to have its stem cells. Now, the prostate gets in on the action. On page 1257, Tsujimura et al. identify a population of prostate cells with all the salient properties of stem cells. These cells should provide a useful system for analyzing prostate carcinogenesis.

Stem cells have three important features: they are slow cycling, have high proliferative potential, and can differentiate into progeny cell types. Tsujimura et al. found cells with these properties concentrated in the region of the mouse prostate that lies adjacent to the urethra. Now that their location is known, it will be possible to concentrate on this region of the prostate in the effort to isolate the stem cells.

The isolation of stem cells is necessary for determining what makes them unique compared with differentiated cells in the tissue. Many scientists believe that prostate tumors arise from stem cells, in part because both stem and tumor cells have high proliferative ability. If this is the case, understanding their biology will be important not only from a developmental standpoint, but also to decipher the mechanism behind prostate cancer.

 Lon plays the chaperone

Stress placed on the ER is transmitted to mitochondria, but according to new results from Hori et al. on page 1151, protective responses are also sent along. Their results are the first demonstration of a signaling pathway from the ER to mitochondria to initiate adaptive changes that support cellular respiration when protein synthesis is disturbed.

Certain cellular stresses, such as low oxygen or disturbance of Ca\(^{2+}\) levels, cause the accumulation of unfolded proteins in the ER. To limit the load on the ER, cytoplasmic protein synthesis is reduced and protein degradation rates increase. However, transcription and translation of several stress responsive genes increase. Hori’s group has identified a mitochondrial ATP-dependent protease, Lon, as one such stress-induced gene.

Lon supports mitochondrial function by facilitating assembly of essential mitochondrial proteins. ER stress caused a reduction in levels of cytochrome c oxidase (COX) subunits and the accumulation of unfolded COX proteins at the mitochondria. Overexpression of Lon in cell culture increased the amount of correctly folded COX subunits. As a result, mitochondria were less likely to lose their membrane potential during stress conditions. Hori expects that mice lacking this chaperone activity will be more sensitive to conditions that cause ER stress and plans to test this theory in Lon knock-out mice.