Unpacking condensins' function in embryonic stem cells

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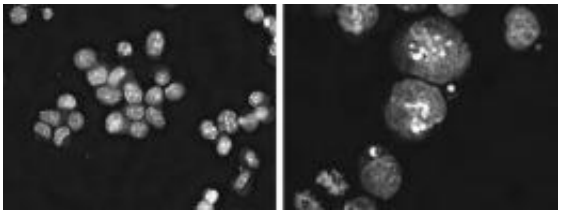

The nuclei of embryonic stem cells lacking Smc2 (right) are large and misshapen. Credit: Fazzio, T.G., and B. Panning. 2010. J. Cell Biol. doi:10.1083/jcb.200908026.

Regulatory proteins common to all eukaryotic cells can have additional, unique functions in embryonic stem (ES) cells, according to a study in the February 22 issue of the *Journal of Cell Biology*. If cancer progenitor cells—which function similarly to stem cells—are shown to rely on these regulatory proteins in the same way, it may be possible to target them therapeutically without harming healthy neighboring cells.

The new study, by Thomas Fazzio and Barbara Panning (University of California, San Francisco) finds that two chromatin regulatory proteins essential for ES cell survival, Smc2 and Smc4, together form the heart of the condensin complexes that promote chromosome condensation in mitosis and meiosis. Because somatic cells lacking condensins continue to proliferate with relatively minor mitotic defects, Fazzio and Panning wondered why ES cells died in the absence of Smc2 or Smc4.

ES cells lacking the condensin subunits accrued massive amounts of DNA damage that resulted in cell death. It isn't clear why ES cells are so sensitive to the loss of condensins, but it may be connected to two other phenotypes seen in ES, but not somatic, cells. After Smc2 or Smc4 was blocked, mitotic ES cells arrested in metaphase and interphase ES cell nuclei were enlarged and misshapen.

This suggests that condensins promote mitotic progression and maintain interphase chromatin compaction in ES cells—functions that they don't have in somatic cells. In fact, many other chromatin regulatory proteins involved in ES cell survival can be depleted in differentiated cells without affecting viability, indicating that the chromatin of ES cells—and possibly cancer progenitor cells—is fundamentally different from somatic cell chromatin.

More information: Fazzio, T.G., and B. Panning. 2010. J. Cell Biol. doi:10.1083/jcb.200908026

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