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STEM CELLS

Maintaining genomic integrity

> “a key role for nucleostemin in the maintenance of genomic stability”

During embryogenesis, stem cells undergo frequent proliferation, but the mechanisms that cope with the resulting replication-induced DNA damage to ensure genomic stability and cell viability are poorly understood. A new study has found a key role of the stem cell marker gene nucleostemin for genome integrity in neural stem cells (NSCs).

To study the role of the essential gene nucleostemin in stem cell function, Meng *et al.* generated a mouse model in which nucleostemin was conditionally inactivated in NSCs. Embryos survived until shortly after birth but had severe defects in brain development, fewer NSCs and increased neuroepithelial staining for the DNA damage marker γH2A.X relative to wild-type embryos. Consistent with this *in vivo* data, knockdown of nucleostemin in wild-type mouse NSCs caused defects in self-renewal and induced γH2A.X foci. This spontaneous DNA damage primarily occurred in S phase cells, indicating that nucleostemin is involved in the response to DNA damage induced by DNA replication stress during NSC proliferation. Indeed, forced overexpression of nucleostemin reduced the DNA damage caused by treatment with the replication stress agent hydroxyurea.

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Further analyses showed that nucleostemin can bind to DNA double-strand breaks and is required to recruit RAD51, which is involved in the repair of replication-induced DNA damage by homologous recombination.

Overall, this indicates a key role for nucleostemin in the maintenance of genomic stability and self-renewal in NSCs, and it will be interesting to determine how widespread this mechanism in various stem cell types.

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ORIGINAL RESEARCH PAPER Meng, L. *et al.* Nucleostemin deletion reveals an essential mechanism that maintains the genomic stability of stem and progenitor cells. *Proc. Natl Acad. Sci. USA* http://dx.doi.org/10.1073/pnas.1301672110 (2013)