

**「Tohoku University Thematic Forum for Creativity」
Cancer – from Biology to Acceptance –**

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Geminin is essential for development of preimplantation embryos

1行あける (12Pt.)

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Abstract:12Pt. Plain

Geminin is tightly controlled to ensure that it occurs only once per cell cycle. Initiation of genomic replication depends on assembly of pre-replication complex (Pre-RC) consisting of Cdt1, Cdc6 and Mcm2-7 at replication origins. Once replication is initiated, geminin binds to Cdt1 and prevents the formation of Pre-RC onto chromatin, which leads cells to inhibit re-replication during S phase. Geminin is only expressed from S phase to late mitosis, degraded during mitosis following ubiquitination by the anaphase-promoting complex. Pre-RC is formed at G1 phase, as geminin is absent.

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Geminin must be a core regulator of genomic replication. We have generated geminin deficient-mice to elucidate the physiological role of geminin. Geminin knockout mice exhibited preimplantation lethality. The lack of geminin impaired the development to morula stage. Homozygous mutants could not progress normal cleavage after four or eight-cell stage, and the size of blastomeres were heterogeneous. Embryonic compaction was not observed. Immunofluorescent staining revealed that E3.5 embryos had multiple irregular-size nuclei in a blastomere. DNA replication was occurred even in abnormal nuclei, although M phase cells were not observed. Our results indicated that geminin is essential for the cooperative progression through S phase to M phase during the preimplantation stage of mouse development.

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