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Author(s)	松浦, 暉
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Abstract of Doctoral Dissertation

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Title of Doctoral Dissertation

An optochemical approach to elucidate the consequences of transient mitotic errors
during zebrafish early development
(ゼブラフィッシュ初期発生における光応答性試薬を用いた
一過的な有糸分裂異常の影響の解明)

Because early animal embryos must generate a sufficient number of cells within a programmed developmental time course, the relative demands for mitotic speed and accuracy are likely to change across developmental stages. However, the extent of mitotic errors that can be safely endured at different stages of development is unclear due to technical limitations. Here, using a recently developed photoswitchable CENP-E inhibitor, I introduced transient mitotic errors at various developmental windows and addressed their organismal effects in zebrafish embryos. Upon CENP-E inhibition in the pre-gastrula period, embryos suffered developmental defects. Conversely, embryos tolerated several hours of consecutive CENP-E inhibition in the gastrula period, frequently achieving full development. Live imaging revealed that chromosome misalignment was partially, but not completely, resolved during the prolonged mitotic progression in gastrula embryos, whereas no such resolution occurred in pre-gastrula embryos due to no delay in mitosis. Perturbation of the spindle assembly checkpoint (SAC) abolished the tolerance and the mitotic delay in the gastrula period. Therefore, the gastrula-period-specific incomplete SAC alleviates the effects of mitotic errors to a manageable level. Our results demonstrated that optochemical approaches advanced the understanding of chromosome dynamics in specific developmental windows.