# 学 位 論 文 内 容 の 要 旨

博士の専攻分野の名称　博士(生命科学)　氏　名　吉澤 晃弥

## 学 位 論 文 題 名

Tetraploidy-linked sensitisation to CENP-E inhibition in human cells
（ヒト四倍体細胞の CENP-E 阻害に対する感受性の増大）

Tetraploidy is a defining characteristic of cancer cells, and targeting the selective growth suppression of tetraploid cells presents a promising strategy for cancer therapy. However, the differences in how tetraploid cells respond to anti-proliferative treatments compared to normal diploid cells remain largely unexplored. In this study, I discovered that tetraploid cells exhibit a significantly higher sensitivity to inhibitors of the mitotic kinesin CENP-E than diploid cells. Under optimal conditions, treatment with a CENP-E inhibitor preferentially reduced the tetraploid cell population in a diploid-tetraploid co-culture. Live imaging revealed that the increased chromosome misalignment associated with tetraploidy led to substantially longer mitotic delays in tetraploid cells compared to diploid cells when subjected to moderate CENP-E inhibition. This delay in mitotic arrest resulted in cohesion fatigue and subsequent cell death specifically in tetraploids, thus causing selective growth suppression of tetraploid cells. In contrast, the microtubule-stabilising agent paclitaxel induced tetraploidy-selective suppression through the exacerbation of spindle multipolarisation. Notably, treatment with a CENP-E inhibitor demonstrated greater selectivity for tetraploid cells across a wider range of cell lines compared to paclitaxel. The findings in this study underscore the unique properties of CENP-E inhibitors in promoting tetraploidy-selective suppression and their potential application in developing therapies that specifically target tetraploid cancer cells.