1. **No.**

   FP01912001

2. **Title**

   Molecular Mechanism and Pathological Relevance of Diploidization of Polyploid Cancer Cells

3. **Period**

   2018-2020

4. **Summary**

   Polyploidy and subsequent re-diploidization through drastic chromosome loss is a hallmark of cancer cells. In this study, I aimed to elucidate the mechanism that governs this re-diploidization process. Though long-term live imaging, I found that a small proportion of polyploid cells survive through multipolar mitoses and form viable diploid-like progenies. I also found that the supernumerary centrosomes that form through polyploidization get clustered before the entry into the next mitosis in polyploid cells. This supernumerary centrosome clustering allowed each single centrosome to capture chromosomes from multiple nuclei (in multi-nucleated polyploid cells), causing the mixing of aneuploid chromosomes during the subsequent chromosome segregation process. To test the causality among this supernumerary centrosome clustering, chromosome segregation patterns in multipolar mitoses, and the fate of chromosome-losing polyploid cells, I sought for molecules involved in the centrosome clustering. Through a target RNAi screen, we identified several microtubule- and centrosome-associated factors required for the establishment/maintenance of the supernumerary centrosome clustering in cancer cells. The achievement above would enable the intervention in chromosome segregation in polyploid cells and testing its effect on the fate of the chromosome-losing polyploid cells.