論文の内容の要旨

論文題目 Studies on roles of the ATM-dependent DNA damage response pathway on control of development in plants

（ATM 依存的 DNA 損傷応答経路が植物の発生に果たす役割の解明）

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During leaf development, a decrease in cell number often triggers an increase in cell size. This phenomenon, called compensation, suggests that some system coordinates cell proliferation and cell expansion but how this is mediated at the molecular level is still unclear. The *fugu2* mutants in Arabidopsis thaliana exhibit typical compensation phenotypes. I have reported that the *FUGU2* gene encodes FASCIATA1 (FAS1), the p150 subunit of chromatin assembly factor-1 (CAF-1). To uncover how *fas1* mutation induces compensation, I performed microarray analyses and found that many genes involved in the DNA damage response are up-regulated in *fas1*.

In the chapter one, my genetic analysis showed that activation of the DNA damage response and accompanying decrease of cell number in *fas1* depend on ATAXIA TELANGIECTASIA MUTATED (ATM) but not on ATM AND RAD3

RELATED (ATR). Kinematic analysis suggested that the delay in the cell cycle leads to a decrease in cell number in *fas1* and that loss of ATM partially restores this phenotype. Consistently, both cell size phenotypes and high ploidy phenotypes of *fas1* are also suppressed by *atm*, supporting that ATM-dependent DNA damage response contributes to these phenotypes. Altogether, these data suggested that ATM-dependent DNA damage response acts as an upstream trigger in *fas1* to delay the cell cycle and promote an entry into the endocycle, resulting in compensated cell expansion.

In the chapter two, to characterize ATM-dependent DNA damage response in plants, I isolated a novel downstream factor of ATM named DNA DAMAGE INDUCIBLE1 (DDI1). My genetic analyses revealed that the *ddi1* mutation suppresses a decrease in cell number without suppressing compensated cell expansion in *fas1* leaves. Observation of the root meristem in *fas1 ddi1* suggested that the *ddi1* mutation suppresses cell number phenotype in *fas1* through suppressing cell death. Expression analyses indicated that the expression of *DDI1* is induced in *fas1* and under genotoxic stress in an ATM-dependent manner. Furthermore, comet assay and marker assay suggested that the *ddi1* mutants have defects in repairing the DNA double strand breaks via homologous recombination. These data suggests that DDI1 functions in the ATM-dependent DNA repair pathway and is involved in the control of cell death.

Altogether, my findings revealed an important connection between the DNA damage response and plant organ-size control. The DNA damage response pathway causes both the cell cycle arrest and cell death, leading to a decrease in cell number in organs. These results help us understand how plants modify their organ size when they are faced to genotoxic stress.