論文の内容の要旨

論文題目　DNA damage response in 1-cell stage mouse embryos
（マウス１細胞期胚の DNA 損傷応答に関する研究）

氏　名　王　媛

Cell cycle checkpoints and DNA repair coordinate with each other to safeguard a proliferating cell from DNA damage arising from endogenous and exogenous stress. Although the first cell cycle in mammalian embryos comprises four phases resembling those of a somatic cell cycle, whether and how DNA damage checkpoint works in each cell cycle phase is unclear. Besides, it remains elusive how 1-cell stage embryos with the specific chromatin structure respond to DNA damage. Therefore, this study examined the DNA damage response in the first cell cycle and its connection with embryonic sensitivity.

In chapter I, I investigated the radiosensitivity of 1-cell stage embryos and the DNA damage checkpoints in the first cell cycle. The development until the blastocyst stage was monitored in zygotes irradiated at the G1, S, G2 or M phase. Unlike the high radiosensitivity shown by G2 and M phase somatic cells, zygotes at the G2 phase seemed to be the most resistant to DNA damage, whereas zygotes irradiated during the G1, S or M phase barely developed to the blastocyst stage. Further examination of the first cell cycle revealed that DNA damage checkpoints were absent in the G1 and S phases of the first cell cycle, which presumably led to the hyper-radiosensitivity of zygotes in these phases.

In chapter II, DNA repair in the first cell cycle and the consequent chromosomal aberrations were examined. Embryos irradiated at the interphase of the first cell cycle featured micronuclei, which likely resulted from unrepaired double strand breaks induced by irradiation and acentric chromosome fragments.

Taken together, DNA damage checkpoint is activated during the G2 phase, but not in the G1, S or M phase. The defective cell cycle checkpoints contribute to insufficient DNA repair in the first interphase, which in turn causes micronucleus formation in the subsequent 2-cell stage and low blastocyte developmental rates.