

## Abstract

In multicellular organisms, programmed cell death (PCD) is an essential mechanism during development, morphogenesis and during the interaction with the environment. The regulation of PCD is highly regulated and conserved throughout the evolution. Animal apoptosis is the best described PCD type which is characterized by the condensation of cytoplasm, specific DNA fragmentation and the formation of apoptotic bodies which are finally engulfed by neighboring cells. Due to the structural specificities of plant cells, plant PCD exhibits rather autophagic character.

In mammals, DSBs-induced PCD is mainly governed by ATM kinase. This response also involves downstream ATM effectors like p53 and E2F factors. P53 stabilization leads to the cell cycle arrest in G1/S whereas E2F can promote apoptosis by activating PCD-related genes including caspases. PCD could be induced also by E2F ectopic expression. In spite of a conservation of PCD signaling among Eukaryotes, number of animal PCD regulators was not identified in plants (caspases, p53), thus in plants the PCD response induced by DSBs is still poorly understood. On the contrary, E2F transcriptional factor is conserved between animals and plants but its role during plant PCD was not evaluated till now.

The main goal of my thesis was to characterize the PCD in response to DNA damage induced by DBSs in two models: unicellular non differentiated system of tobacco BY-2 cell suspension and Arabidopsis roots, a well defined multicellular structure. BY-2 cell treatment with a DSB inducer bleomycin led to rapid cell cycle arrest in G2/M, transcriptional activation of ROS- and PCD-related genes, disintegration of vacuole and subsequent autophagic PCD. We have demonstrated that the pro-death E2F function observed in animals is lost in plants. In addition E2F deregulation led to PCD inhibition or to increased genomic instability through a bypass of the G2/M checkpoint depending on dose of BLM. In Arabidopsis, DBSs induced not only PCD but also endoreduplication specific for surviving tissues. According to our results, we propose a model of DSB response which strongly depends on genotoxic concentration. We suggest a distinct role of vacuolar processing enzymes (VPEs) and the factor SOG1 which are plant specific. Whereas PCD seems to be a direct effect of DSB sensed through ATM signaling, endoreduplication is only indirect developmental consequence of cell death in Arabidopsis meristem. Taking our results together we demonstrate plant specificities of DNA damage induced PCD probably coming from the different living strategies between animals and plants.