Algal Research 12 (2015) 126–133

Contents lists available at ScienceDirect

Algal Research

journal homepage: www.elsevier.com/locate/algal

Apoptosis-like cell death in unicellular photosynthetic organisms — A review

Krishna Chaitanya Kasuba, Sirisha L. Vavilala, Jacinta S. D'Souza *

UM-DAE Centre for Excellence in Basic Sciences, Kalina Campus, Santacruz (E), Mumbai 400 098, India

ARTICLE INFO

Article history:
Received 7 February 2015
Received in revised form 3 July 2015
Accepted 28 July 2015
Available online xxxx

Keywords:
Algae
Apoptosis
Programmed cell death
Metacaspases
APAF-1
PARP-1

ABSTRACT

The study of cell death in higher plants and animals has revealed the existence of an active ('programmed') suicidal process and similarities in this machinery between these two kingdoms suggest an evolutionarily ancient origin. Genetic, molecular and biochemical approaches have begun to reveal candidate regulators in plants that show both similarities and novel properties compared with their animal counterparts. In recent years, it has also been convincingly shown that several unicellular organisms from bacteria to ciliates possess the ability to undergo programmed death. In particular, the unicellular algal cells *Chlamydomonas reinhardtii*, *Micrasterias denticulata*, *Chlorella saccharophila* and *Dunaliella tertiolecta* as well as several protozoans, die in an apoptotic-like manner in response to exposure to various stress agonists. And, these organisms share several apoptotic hallmarks with metazoans. To date, three related issues that remain elusive in these unicellular organisms are, the signalling pathway and the key molecular players involved in this process as well as the precise physiological role (or requirement) of this cellular mechanism. Currently, there seem no convincing arguments about the evolutionary significance of such a death pathway of unicellular organisms. The past decade has seen a rise in the number of reports on PCD-like process in unicellular photosynthetic organisms. This review provides a historical perspective of the occurrence of algal PCD and lists out the molecular players while comparing them with metazoans and multicellular plants.

Contents

1. Introduction to apoptosis as a term and discovery

Every cell has a time to live and a time to die; death could be accidental due to injury or otherwise. Cell death was observed as a part of the

* Corresponding author.
E-mail address: jacinta@cbs.ac.in (J.S. D'Souza).

http://dx.doi.org/10.1016/j.algal.2015.07.016
2211-9264/

physiological process of multicellular organisms such as plants and animals since the mid of the 19th century [1]. However, a form of non-accidental yet, controlled cell deletion/removal observed in the year 1964 was termed programmed cell death [2,3]. Originally discovered in 1972 by Kerr and co-workers [4], if cells are no more needed, they die by activating an intracellular death programme, aptly named as programmed cell death. The term 'apoptosis' comes from plant kingdoms for the old Greek apoptosis that originally means the 'falling off or loss of petals/leaves'. It is emphasized that, by definition, apoptosis is a well-established and possibly the most frequent form of programmed cell death; but, other non-apoptotic types of cell death (especially in plants) also might be of biological significance [5]. With time, it was shown to play a major role in development and homeostasis, in response to environmental cues and in the manifestation of many diseases of all multicellular organisms [6]. Of late, the term 'apoptosis' has undergone debate and discussion; and therefore, as a matter of semantics, one may note that the term Programmed cell death (PCD) is used as an umbrella term for all types of deaths observed in organisms and cells. The Nomenclature Committee on Cell Death (NCCD) has recently revised the terminology to define various forms of PCD and the reader is directed to its proper usage [7,8].

2. Apoptosis in metazoans: morphological features of the process

Programmed cell death in metazoans is characterized by several morphological and biochemical changes, typically referred to as hallmarks; these being, shrinkage of the cytoplasm, nuclear condensation, membrane blebbing, externalization of phoshatidylserine, mitochondrial membrane potential breakdown with the release of Cytochrome c, formation of apoptotic bodies with their engulfment by phagocytes, release of (at least in mammalian cells) ATP and UTP, and induction of cysteine proteases and endonucleases [9]. In its active form, it requires intact subcellular structures and synthesis of phylogenetically conserved proteins. Variations of this classical form of apoptosis have also been observed in animal cells and these are:

- *Para-apoptosis* is a type of non-necrotic cell death characterized by condensed chromatin, cytoplasmic vacuolization due to swollen mitochondria and endoplasmic reticulum [10].
- *Paraptosis* is a modified version of para-apoptosis, in which cells are TUNEL-negative, caspase-9-dependent, has morphological resemblance to necrosis and features similar to classical apoptosis [11].
- *Lipo-apoptosis/lipoptosis* in which the balance in lipid metabolism is lost leading to a disturbance in homeostasis with accumulation of fatty acids followed by apoptosis [12].
- *Neosis* in which DNA damage-induced multinucleate giant cells are thought to die via mitotic catastrophe [13].
- *Necroptosis* is a programmed necrosis-like death, induced by the compound, necrostatin-1 (Nec-1) and is associated with characteristics of autophagy. In this form of death, the classical Fas/TNFR family of death-domain receptor pathway that sequentially turns on multiple caspase scan induce cell death even when caspase signalling—and therefore apoptosis—is inhibited [14].
- *Autophagy*, means 'eating of self' is more of a survival mechanism and at the regulatory level thought to be considered a non-apoptotic type of cell death [15].

3. Apoptosis in multicellular plants: accumulating evidence

3.1. Comparison of the process between animals and plants

It is now well-established that parts of the apoptotic process are conserved across worms, insects, vertebrates [9] and plants [16–19]. PCD in plants encompasses a diverse set of mechanisms from initiation of the trigger to cell death itself [20–23]. Although the differences in the details of the mechanism between plants and animals are now clear, many cellular and molecular features still remain the same. The common morphological and biochemical features are loss of plasma membrane integrity, cytoplasmic shrinkage, chromatin condensation, nuclear DNA fragmentation, loss of mitochondrial membrane potential, Cytochrome c release and participation of caspase-like proteases. Besides, nuclear fragmentation to form the classical DNA ladder involves more than one endonuclease [24]. But, externalization of phosphotidylserine and formation of apoptotic bodies have not been reported in multicellular plants. Also, plants do use PCD as a mechanism to remove the unwanted or damaged cells; or to ward off pathogens; but, the cells do not engulf their dead neighbours. Moreover, it is now known that apoptotic-like PCD can be easily distinguished from other forms of plant cell death. The latter involves protoplast condensation that results in a morphologically distinct cell corpse [19].

3.2. PCD in multicellular plants

Similar to animal apoptosis, plants also use the process of PCD as one of the many mechanisms that are required for their defence and normal development. Starting from germ cell formation to reproduction and senescence, plant cells undergo some form of PCD in their life time. Examples of these include, *Differentiation* of specialized cell types such as tracheary elements, *Xylogenesis*, a process of the formation of mature xylem and phloem vessels [25], and *Germ cell formation* where tissues with ephemeral functions are deleted by the process of PCD [26]. Another process called *Anther dehiscence* releases the mature pollen to the environment. This process is also a result of PCD of cells that occupy specific sites in the anther wall [27], *Reproduction* during somatic embryogenesis of Norway spruce, the nuclei displayed DNA strand breaks with 3'OH ends and apoptotic bodies [28]. And, sex determination in maize encompasses the 'selective killing' of the female reproductive primordia for the normal development of the stamens in the tassel and the involvement of a *tasselseed2* gene in this cell death process has been identified [29], *Organ or shoot morphogenesis*: such as the formation of functionally unisexual flowers from bisexual floral primordia [22, 30–32], *Pathogenesis*: When attacked/infected, plants recognize certain pathogens and activate the resistance response; thereby restricting the growth of the former at the site of infection. This restriction is precisely because of the induction of the hypersensitive response at the site of infection; and, is likely to be important for limiting a pathogen's nutrient supply, since the dying tissue rapidly becomes dehydrated. In addition, the HR also occurs in response to various abiotic stresses [22,23]. *Senescence*: Overlaps between the processes of senescence and PCD are still under debate. Many believe that the two are fully synchronous. But, both the processes involve time and proceed towards death [33]. *Abiotic stress*: Plants respond apoptotically to abiotic stress such as, desiccation, nutrient deprivation, oxidative stress, osmotic stress, and toxins [34–36]. In comparison, several occurrences of cell death-like processes have now been reported in unicellular organisms, an account of which follows in the subsequent paragraph.

4. Programmed cell death in unicellular organisms: a historical perspective

4.1. PCD in non-photosynthetic unicellular organisms

The first study on the presence of PCD in a unicellular organism was reported during the *in vitro* differentiation of the proliferating epimastigote stage into the G0/G1 arrested trypomastigote stage of the parasite *Trypanosoma cruzi* [37]. Subsequent reports have shown ConA-induced apoptotic death in *Trypanosoma brucei rhodesiense* [38–40], heat shock-induced apoptosis in *Leishmania amazonenis* [41], a variety of stress conditions (serum deprivation, heat shock and nitric oxide exposure) in *Leishmania major* [42], NO-mediated PCD in *Leishmania* [43], H_2O_2-induced PCD in *Leishmania donovani* promastigotes