Cell Death and Differentiation (2014) 21, 1178–1179

www.nature.com/cdd

Meeting Report

The death of plant cells: from proteases to field applications

S Stael[1,2,3,4], MK Nowack[1,2], F Breusegem[1,2], M Valls[5,6] and NS Coll*[,6]

Cell Death and Differentiation (2014) **21,** 1178–1179; doi:10.1038/cdd.2013.190; published online 10 January 2014

The Death of Plant Cells, CosmoCaixa, Barcelona, Spain, 2–4 October 2013

The meeting 'The Death of Plant Cells: From Proteases to Field Applications' was jointly organized in October 2013 in Barcelona by B·Debate, the Centre for Research in Agricultural Genomics (CRAG) and the Flanders Institute for Biotechnology (VIB), www.bdebate.org/en/forum/death-plant-cells-proteases-field-applications. It gathered 60 international experts working on plant and animal proteases and programmed cell death (PCD), and was instrumental in drafting future directions concerning plant PCD research, including the largely unexploited potential of PCD for agricultural applications.

The challenges of plant PCD

More than a decade ago, researchers assumed that the basic molecular control of PCD might be largely conserved between animals and plants. With the advent of complete genome sequences, however, it became clear that central apoptotic regulators, like Bcl-2 family members or caspases, were not encoded in plant genomes. Hence, many attempts to translate knowledge from the more advanced animal PCD field proved unsuccessful and even detrimental to the development of independent PCD hypotheses in the plant field. This conviction was voiced by representatives of the animal and plant community during the debates. Guy Salvesen (Sanford–Burnham Medical Research Institute, USA) lamented the misleading term 'metacaspases' (which have an entirely different substrate specificity than caspases) in plants and urged to use the specific proteolysis probe used instead of maintaining caspase-like terms. Richard Vierstra (University of Wisconsin-Madison, USA) added to this that 'discovering *Bax* was probably the worst thing that happened to plants' and that the animal PCD paradigm in plants is history.

According to Guy Salvesen, plant PCD mostly appears as a terminal differentiation event, rather than the activation of a process, as it is the case for animal apoptosis. Renier van der Hoorn (Max Planck Institute, Germany) mentioned that there are not many studies showing inhibition or activation of plant PCD, as one would expect for a programmed process. A notable exception would be the pathogen-induced hypersensitive response (HR) cell death, which is distinctly regulated and executed compared to developmental PCD in plants. Susana Rivas (French National Institute for Agricultural Research, France) raised the question that besides the 'how & what', the 'why' has not sufficiently been addressed yet in plant PCD. For example, why HR cell death does not influence bacterial growth in most cases as initially hypothesized?

Peter Bozkhov (Uppsala Biocenter, Sweden) pointed out that the significance of plant PCD has not been widely recognized in biological research in contrast to animal PCD, clearly linked to cancer research. One of the key challenges of plant PCD research is to bring the importance of cell death in plant development and biotic and abiotic stress resistance to the attention of the scientific community, since it is essential to crop yield and food security and thus to the society at large. Unfortunately, a systematic overview of cellular and molecular events during the different types of PCD is lacking in plants. As Morten Petersen (University of Copenhagen, Denmark) stressed, this would be instrumental in providing a framework for future research in this field.

The future of plant PCD research

Having identified some of the issues challenging present plant PCD research, the discussions were focused on future research strategies. As Morten Petersen elaborated, genetic markers or use of systemic loss-/gain-of-function backgrounds have significant limitations. Plants are plastic and acclimate to lasting challenges, leading to the observation of pleiotropic or secondary effects that are difficult to discern

[1]Department of Plant Systems Biology, VIB, Gent, Belgium; [2]Department of Plant Biotechnology and Bioinformatics, Ghent University, Gent, Belgium; [3]Department of Medical Protein Research, VIB, Gent, Belgium; [4]Department of Biochemistry, Ghent University, Gent, Belgium; [5]Department of Genetics, Universitat de Barcelona, Av. Diagonal 643, Barcelona, Catalonia, Spain and [6]Centre for Research in Agricultural Genomics (CSIC-IRTA-UAB-UB), Edifici CRAG, Bellaterra, Catalonia, Spain
*Corresponding author: NS Coll, Molecular Genetics, Centre for Research in Agricultural Genomics (CSIC-IRTA-UAB-UB), Edifici CRAG, Campus UAB, Bellaterra (Cerdanyola del Valles), Catalonia 08193, Spain. Tel: +34 935636600; Fax: +34 935636601; E-mail: nuria.sanchez-coll@cragenomica.es

from primary effects. Therefore, discovery and implementation of inducible model systems might prove to be valuable to the plant PCD community.

Concerning model systems, Pierre Golstein (Centre d'Immunologie de Marseille-Luminy, France) put things in perspective: among the approximately 10 million different eukaryotic species present on earth, only 13 are recognized as model organisms. Apoptosis is a rare event found mainly in mammals, a minority of the biological diversity on the planet. PCD should be explored in representatives of different eukaryotic groups, also because the current models were initially not selected to study PCD, and hence might drag inherent disadvantages. New plant PCD models could be specifically selected based on the decision to look at more and different PCD mechanisms, but concerns were raised on whether this research would be financed when not involving crops. Some model systems have proven extremely useful to start defining certain types of plant PCD: poppy pollen for self-incompatibility, Zinnia for xylem differentiation and Arabidopsis for HR and lateral root cap cell death. It would thus be extremely important to determine which species are best to study each PCD type found in plants.

Promising technological advances include various proteomic approaches, such as N-terminomics/degradomics to discover protease substrates, peptide chips covering entire proteomes and advanced protease activity probes. In the nearby future, chemical activity probes are expected to become more specific by designing novel probe derivatives (peptidomimetics, unnatural amino acids, etc). Genetically encoded activity probes, mostly based on green fluorescent protein technology, have proven to be of more limited usage, but remain useful together with chemical probes for a comprehensive analysis of protease function during PCD.

Crop improvement and PCD

As an agricultural biotech representative, Fabien Poree (Bayer CropScience, Germany) claimed for re-establishing the interaction between companies and academic institutes, which has been more fluent in the past, although communication is often non-trivial due to intellectual property issues. However, he stated the intrinsic interest of companies in plant PCD research, in views of its potential applications in crop improvement and pest control (i.e. HR regulators as drug targets). Isabel Diaz (Centre for Plant Biotechnology and Genomics, Spain) presented promising new strategies where certain protease inhibitors can be used for pest control and to precisely regulate germination and senescence. The continuity of this PCD meeting and the creation of a network of plant PCD researchers may be a way to strengthen public-private interactions.

Building a plant PCD community

The meeting attendees unanimously agreed that the time is ripe to join efforts and better structure the plant PCD community, to increase visibility and communication within the field and facilitate the exchange of ideas and the establishment of collaborations. Part of the discussion was dedicated to the question of whether plant proteases and PCD research should make an effort to join in a single community, or whether the researchers in these two closely cooperating fields should organize themselves independently. The two meetings that have taken place so far (Hemavan, Sweden 2011 and Barcelona, Spain, 2013) have been organized jointly, trying to integrate research on both fields.

As Richard Vierstra explained, the community might take an example of proteolysis research that separated over the years into rather independent proteaseome, ubiquitin and autophagy subfields. He suggested keeping the newly established plant proteases and PCD communities together with the possibility to divide later. Sophien Kamoun (Sainsbury Laboratory, UK) stressed that the creation of a community should imply bringing people together rather than separating them from others. He proposed that the community should be limited to plant researchers to avoid mimicking the mammal PCD field and to raise the profile of an independent plant PCD community. Nonetheless, guest speakers from the animal PCD community should always be invited, to broaden views and extend our intellectual and technological reach. Renier van der Hoorn volunteered to organize a follow-up meeting on plant proteases and PCD in 2015. Another initiative launched in the meeting has been the creation of a mailing list as communication platform (mail to moritz.nowack@vib.be to join).

Conflict of Interest

The authors declare no conflict of interest.

Acknowledgements. The authors would like to thank B-Debate International Center for Scientific Debate Barcelona, a Biocat initiative with support from 'la Caixa' Foundation for providing the means to organize the meeting and in particular, Ms. Laia Arnal. The Research Foundation-Flanders (G.0038.09N) and Agrisera (Vännäs, Sweden) kindly provided additional funds to support the meeting.