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Meeting Report

A new Canterbury tale: the eighth International Meeting on Yeast Apoptosis in Canterbury, UK, 2–6 May 2011

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The eighth International Meeting on Yeast Apoptosis in Canterbury, UK, 2–6 May 2011

This spring, more than a hundred scientists from around the world gathered in Canterbury, the historic city in the county of Kent in South East England, to attend the eighth International Meeting on Yeast Apoptosis (IMYA). As with every IMYA conference since its inception in 2002, the feeling of being part of a community that is almost a family was evident. In addition, this year's meeting has shown that the field of yeast programmed cell death (PCD) is growing, not only in numbers, but also in its thematic scope.

This was well exemplified by the keynote lecturer Thomas Nyström (University of Gothenburg, Sweden), who addressed the retention of damaged proteins in mother cells upon cell division, which occurs in an asymmetric manner. This process is determinant, for instance, to understand the mechanisms underlying replicative aging, defined by the number of daughters born from a single mother, and which represents a model for asymmetrically dividing stem cells. In contrast, chronological aging, defined as the lifespan of a postdiauxic, but still metabolic active yeast culture, mirrors the aging processes in postmitotic tissues of higher eukaryotes. Cristina Mazzoni (University of Rome, Italy) detailed new findings involving the Lsm4D1 decapping mutant that reportedly exhibits increased mRNA stability leading to premature chronological aging, whereas Paula Ludovico (University of Minho, Portugal) analyzed the roles of different reactive oxygen species (ROS) and proteotoxic stress as determinants of chronological lifespan (CLS). Christoph Ruckenstuhl (University of Graz, Austria) presented new data on a specific form of dietary restriction, which extends CLS in an autophagy-related manner. CLS extension is also regulated by a G0/G1 arrest modulating replication stress, as discussed by Bill Burhans (Roswell Park Cancer Institute, USA). Thereby, increased availability of dNTPs seems to be decisive to promote longevity. Maria João Sousa (University of Minho, Portugal) reported on the preventive effect of ammonium on CLS extension upon extreme caloric restriction. This effect involves various kinases and results in necrotic cell death. Both necrosis and apoptosis contribute to the cells' demise during chronological aging. Didac Carmona-Gutiérrez (University of Graz, Austria) presented evidence for a longevity-promoting anti-necrotic function of the aspartic protease Pep4p, the yeast homolog of cathepsin D. Intriguingly, this function is independent of the protein's proteolytic activity, resides in its propeptide and depends on polyamine biosynthesis. In a different approach monitoring cell death within multicellular yeast colonies (and not in liquid culture), Zdena Palková (Charles University of Prague, Czech Republic) revealed a model of vertical differentiation with two major subpopulations.

Besides aging, challenge to a variety of stresses also results in yeast PCD. Stefan Wölfl (University of Heidelberg, Germany) elucidated diverse metabolic alterations during acetic acid-induced cell death, whereas Zhaojie Zhang (University of Wyoming, USA) addressed the involvement of the mitochondrial genome in salt stress-induced apoptosis. Martin Gruhlke (Aachen University, Germany) examined the pro-death effects of the antimicrobial substance allicin, a natural compound found in damaged garlic tissue. Álvaro Cuesta-Marbán (University of Salamanca, Spain) presented a single-gene knockout collection screen to uncover genes involved in cytotoxicity of the antitumor lipid edelfosine. On a more technical level, Eugenio Meza (Chalmers University of Technology, Sweden) presented a quantitative PCR-based method, with which it is possible to detect early responses to PCD. Caroline Wilkinson (Paterson Institute for Cancer Research, UK) addressed the regulation of the fission yeast *Schizosaccharomyces pombe* MAP kinase Sty1p, which controls many stress defense mechanisms. Michael Greenwood (Royal Military College, Canada) discussed current notions in the field of anti-apoptosis and presented results from the ongoing detailed characterization of novel anti-apoptotic sequences identified as BAX-suppressors in yeast.

Also, aggregation of endogenous or heterologously expressed proteins is related to cytotoxicity and cell death in

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yeast. Joris Winderickx (Katholieke Universiteit Leuven, Belgium) reported on synphilin-1, which promotes the cytoplasmic aggregation and cytotoxicity of heterologously expressed α-synuclein, a protein associated to Parkinson's disease in humans. Ralf Braun (University of Bayreuth, Germany) addressed a further neurotoxic protein, TDP-43, which upon overexpression in yeast results in apoptotic and necrotic cell death that correlates with the degree of respiratory capacity or mitochondrial DNA stability. Mick Tuite and Wesley R Naemi (University of Kent, UK) presented data concerning the *de novo* formation and propagation of transmissible amyloid-like prion aggregates in yeast. Intriguingly, Lynn A Megeney (Ottawa Hospital Research Institute, Canada) reported that the clearance of insoluble protein aggregates requires the yeast metacaspase Yca1p exerting a non-death role.

Our understanding of the molecular network controlling cell death in yeast is gradually growing and reveals an impressive degree of functional conservation between yeast and mammals. Frank Madeo (University of Graz, Austria) added an element to this understanding by presenting the discovery of the first known Bcl2-family protein in yeast, the BAX-like BH3-only protein Ybh3p. This finding challenges the previously assumed premise that yeast might be a 'clean room' for studies involving human BAX. Birthe Fahrenkrog (University of Brussels, Belgium) showed that the activity of a further pro-apoptotic factor, the yeast homolog of Omi/HtrA2 (Nma111p) seems to depend upon the specific cell death scenario. Mark Ramsdale (University of Exeter, UK) presented data resulting from a combined proteomics and bioinformatics approach that has identified a series of proteins, whose specific degradation during acetic acid-induced cell death involves Yca1p. Yca1p is also implicated in apoptosis triggered via Yno1p, a newly identified NADPH oxidase introduced by Michael Breitenbach (University of Salzburg, Austria). Vassilios Kotiadis (University of Kent, UK) talked on the impact of cofilin, an actin-regulatory protein, on stress signaling. Stabilization of the actin cytoskeleton is known to hyperactivate the RAS signaling pathway. Interestingly, Tobias Von der Haar (University of Kent, UK) showed evidence for a dependence of translational accuracy on the RAS signaling pathway, as well as on the carbon and nitrogen sources. Katrina Cooper (University of Medicine and Dentistry of New Jersey, USA) discussed a putative evolutionarily conserved role of cyclin C in controlling mitochondrial morphology and cell death.

Mitochondria, besides having a pivotal role in cellular energy metabolism, represent crucial organelles in apoptosis regulation. Nicoletta Guaragnella and Sergio Giannattasio (Institute of Biomembrane and Bioenergetics, Italy) addressed the mitochondrial role during acetic acid-induced PCD. Manuela Côrte-Real (University of Minho, Portugal) introduced a vacuolar-mitochondrial crosstalk upon acetic acid stress, in which the aspartic protease Pep4p is released from the vacuole and induces the autophagy-independent and pro-survival degradation of mitochondria. Interestingly, autophagy-driven selective degradation of mitochondria (mitophagy) does not require mitochondrial fission, but depends on the stress response gene *WHI2*, as proposed by Andreas Reichert (University of Frankfurt, Germany). Benedikt Westermann (University of Bayreuth, Germany) further concentrated on mitochondrial dynamics by presenting novel components and pathways required for this process, including the mitochondrial protein Mdm36p and the myosin-related motor protein Myo2p. Jared Rutter (University of Utah, USA) reported on a novel Cdc48p-associated protein, Vms1p, which upon stress translocates from the cytoplasm to mitochondria, where it functions as an adapter protein for the degradation of ubiquinated mitochondrial proteins by the proteasome.

The study of fungal PCD serves the purpose of modeling the processes occurring in higher eukaryotes, but also represents a possibility to directly study and fight pathogenic fungi. Amir Sharon (Tel Aviv University, Israel) reported on the Bir homolog from the necrotrophic plant pathogen *Botrytis cinerea*; it appears to be a major regulator of anti-apoptotic response, which is critical for pathogenesis on affected plant species. Plants can counteract fungal infections by production of plant defensins. RsAFP2 from radish, for instance, induces apoptosis in the pathogenic fungus *Candida albicans*. Karin Thevissen (Katholieke Universiteit Leuven, Belgium) demonstrated that RsAFP2 interacts with the cell wall, causing morphological changes, septin mislocalization and ceramide accumulation. Nicanor Austriaco (Providence College, USA) showed that filamentation of *C. albicans* cells exerts a protective role upon PCD induction. Finally, Heinz Osiewacz (University of Frankfurt, Germany) discussed the regulation of cell death in the fungal aging model *Podospora anserina*, concentrating on the role of the mitochondrial peptidyl prolyl-cis-trans isomerase cyclophilin D.

In sum, the field of yeast PCD is diversifying and growing into different directions. Like in Geoffrey Chaucer's *Canterbury Tales*, a diverse group of – this time yeast apoptosis-devoted – pilgrims decided to travel to Canterbury in the midst of spring: 'And many little birds make melody/That sleep through all the night with open eye/(So Nature pricks them on to ramp and rage)/Then do folk long to go on pilgrimage…'. This was the yeast apoptosis own Canterbury tale, and what a pleasure it is to have left it with the feeling of having met a group of friends while having picked new input and new ideas. We all look forward to the next chapter of the IMYA meetings that will be organized by Cristina Mazzoni in Rome (Italy) from 17–20 September 2012, in the frame of the 20th Euroconference on Apoptosis organized by the European Cell Death Organization (ECDO).