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**Meeting Report**

# Yeast between life and death: a summary of the Ninth International Meeting on Yeast Apoptosis in Rome, Italy, 17–20 September 2012

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Ninth International Meeting on Yeast Apoptosis in Rome, Italy, 17–20 September 2012

Remembering the ancient latin saying *omnes viae Romam ducunt*, the yeast cell death community came to the eternal city to attend the 9th International Meeting on Yeast Apoptosis (IMYA), from 17–20 September 2012. More than one hundred investigators from around the world presented and discussed their researches on programmed cell death (PCD) and its role in stress responses, aging and development employing yeast as model organism. On the first day, the meeting took place at the historical Angelicum Congress Center, sharing its opening session with the last session of the 20th Euroconference on Apoptosis (ECDO).

## Aging

The opening EMBO Lecture by Guido Kroemer (France) introduced the concept of autophagy as a cytoprotective defense mechanism. He showed that autophagy-inducing pharmacological agents, such as resveratrol and spermidine, increase longevity in an autophagy-dependent fashion. He also described the related modification of the acetylproteome, which underscores the importance of an autophagy-regulatory network of antagonistic deacetylases and acetylases that can be pharmacologically manipulated. Valter Longo (USA) underlined the impact of certain mutations in Ras-cAMP-PKA and TOR-Sch9p signaling on aging and the central role of the kinase Rim15p in longevity mutants as well as in calorie-restricted cells. Frank Madeo (Austria) presented results on the polyamine spermidine, which acts as a novel autophagy inducer and a longevity elixir in yeast, flies and worms. The administration of spermidine may help to combat age-associated pathologies.

## Cell Death and Immunity

Kodi Ravichandran (USA) showed that airway epithelial cells are efficient phagocytes of dying cells and that the clearance process plays a significant role in limiting airway inflammation. Laurence Zitvogel (France) presented evidence that anthracyclines generate a *de novo* immunogenic T-cell response against tumor antigens through an ATP-dependent pathway involving GMP and $CD11b^{+}Ly6C^{high}$ antigen-presenting cells conveying immunity.

## Homeostasis and Lifespan I

Paula Ludovico (Portugal) showed that $\alpha$-synuclein-induced toxicity is dependent on mitophagy regulated by ROS and through a mechanism mediated by Sir2p, which functions as a transcriptional regulator of both autophagy and mitophagy. Ian Dawes (Australia) presented evidence about the relations between cell redox homeostasis and aging, underlying the complexity of the relations among ROS types and ROS levels in affecting cellular responses to different environmental conditions. He also identified genes involved in setting the glutathione redox state in the cytoplasm.

## Cell Cycle and Lifespan

William Burhans (USA) underlined the complex interplay between oxidative stress and DNA replication stress related to glucose metabolism and signaling in stationary-phase yeast cells. Katrina Cooper (USA) revealed that following ROS stress cyclin C is exported from the nucleus to the cytoplasm, where it mediates

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mitochondrial fission by associating with the Dnm1p/Drp1 complex. This function and the requirement for cyclin C in normal apoptosis execution is conserved from yeast to humans.

### Homeostasis and Lifespan II

Zdena Palkova (Czech Republic) presented evidence that yeast colonies differentiate into two major cell subpopulations occupying the upper (U) and lower (L) colony regions. U-cells, which have active autophagy and consume nutrients released by L-cells, gain stress resistance and longevity features compared to L-cells, and can represent a valuable model to investigate tumorigenesis. Pieter Spincemaille (Belgium) described the antiapoptotic effects of certain compounds able to rescue copper and cisplatin-induced apoptosis-like cell death either in yeast or in human cell lines. Marc Meneghini (Canada) described a developmentally programmed nuclear destruction occurring during yeast gametogenesis. As diverse cell death-related processes converge during gametogenesis in yeast, he highlighted gametogenesis as a possible process for the evolution of PCD mechanisms.

### Mitochondrial Function in Stress Response

Nicoletta Guaragnella (Italy) illustrated the role of mitochondrial components, such as cytochrome *c*, in cell death and adaptation following acetic acid stress in *S. cerevisiae*. Heinz Osiewacz (Germany) showed that different components of the mitochondrial protein control system (i.e., iAAA protease, ClpP protease) are part of a hierarchical network allowing organisms to adapt to changing environmental conditions in the aging model *Podospora anserina.*

### Stress and Cellular Death

Campbell W Gourlay (UK) demonstrated that the loss of electron transport chain function leads to a strong accumulation of hyper-active Ras at mitochondrial compartment. Consequently two ER-localized enzymes, Yno1p and Ero1p, trigger ROS production promoting oxidative stress. Fedor Severin (Russia) raised the possibility that replicative aging acts as a mechanism of differentiation after various stresses, suggesting that cell stress resistance is also age-dependent. Vanessa Palermo (Italy) showed that decapping mutants exhibited low levels of Sir2p, with a reduction of silencing and elevated transcription of rDNA intergenic spacer regions.

### Signal Transduction

Manuela Corte-Real (Portugal) demonstrated that *isc1*$\Delta$ and *lag1*$\Delta$ mutants exhibited a higher resistance to acetic acid in association with lower levels of some phytoceramide species as well as higher levels of long-chain base phosphates that have been suggested to exert antiapoptotic functions, providing the first *in vivo* indication of ceramide involvement in mitochondrial outer membrane permeabilization in yeast. Zhengchang Liu (USA) reported on mitochondrial biogenesis regulation in yeast showing that the mitochondrial functional states affect *HAP4* expression at both transcriptional and post-translational levels.

### Mitochondrial Function in Cell Death

Michael Breitenbach (Austria) discussed the role of Afo1p protein in yeast. Deletion of the *AFO1* gene induces loss of the mitochondrial genome and an extension of replicative lifespan. The *afo1*$\Delta$ mutant also produced ethanol and biomass on glucose similarly to the wild type. Jared Rutter's talk (USA) was focused on the identification and study of mitochondrial proteins with new functions, including mitochondrial pyruvate transporter, fatty acid oxidation and mitochondrial supercomplex assembly.

### Protein Aggregation and Toxicity

Sofie Van Rossom (Belgium) showed that the expression of *DFNA5*, a gene associated with autosomal dominant form of hearing impairment and related to different types of cancers, induced PCD when expressed in the yeast *S. cerevisiae*. Mutant *DFNA5* toxicity is higher during the exponential phase but it is abrogated in cells lacking the ATP/ADP carrier Aac1p or Aac3p. Lynn Megeney (Canada) presented evidence supporting a role for mammalian and yeast metacaspase activities in normal cell function, independent of cell death regulation. He identified a Yca1p subdomain regulating autocatalytic process of this protease.

### Humanized Yeast Models

J Marie Hardwick (USA) described a new powerful tool to reliably detect gene-dependent yeast cell death and to identify a surprising number of pro- and anti-death yeast genes. Amir Sharon (Israel) talked on heterologous expression of human Bcl-2 proteins and of *Botrytis cinerea* Bir1p in *S. cerevisiae*. Results obtained with a yeast two-hybrid screening and CoIP revealed putative Bcl-2- and Bir-mediating proteins. Ralf J Braun (Germany) showed the effects of heterologous expression of human proteins, such as ubiquitin B, resulting in loss of survival, induction of oxidative stress, apoptosis and necrosis in yeast. Christophe Cullin (France) reported that intracellular toxicity triggered by A$\beta$ peptides was not due to endocytosis dysfunction but rather implicates other cellular targets, supporting yeast as a model to study neuronal cell death in Alzheimer's disease.

### Yeast Death Networks

Dina Petranovic (Sweden) presented a yeast cell death database, which could enable the storage of all the information such as data, protocols, models, network, etc. She developed the yeast apoptosis network useful for data integration and constructed the first Boolean model of yeast apoptosis. Gaspar Banfalvi (Hungary) described new technologies for the study of interphase chromosome in mammalian cells, taking into consideration the differences in chromatin condensation patterns between mammalian cells and fungi.

The 9th IMYA gathered a great interest around yeast cell death and aging research from an expanding audience, the highest up to now, witnessing the emerging complexity of the intracellular signaling network controlling cell aging and death in response to environmental stress in this unicellular model organism. The yeast cell death community thus made an appointment for the next IMYA meeting, which will be organized in the Spring of 2014 in Göteborg (Sweden) by

Dina Petranovic, with a glance to systems biology and 'omics' research for which yeast cells seem to have a genius for!

## Conflict of Interest

The authors declare no conflict of interest.

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