The Second International Conference on Molecular Mechanisms of Fungal Cell Wall Biogenesis, Salamanca, Spain, 27 August–1 September 2003

The Second Fungal Cell Wall Meeting brought together about 115 scientists in the beautiful, historical city of Salamanca. It all had started as an initiative some years ago by Yoshifumi Jigami, who brought together the first embryonic group of fungal glycobiologists and cell wall specialists in Tsukuba, Japan. The need was felt to have more such meetings on a formal basis and thanks to the combined efforts of Markus Aebi and Widmar Tanner, the first official meeting on fungal cell walls took place in Ascona, Switzerland in 2001. This year a Spanish team led by Angel Duran and Cesar Nombela hosted the second meeting in Salamanca. Although a majority of the 115 selected participants are working with *Saccharomyces* and *Candida* cell walls, the number of attendants studying other fungi including various mycelial species has considerably increased, thereby eliminating artificial divisions created by history. Without pretending to be complete, I would like to present some highlights of this exciting and well-organized meeting. For anyone interested in more details of the topics discussed below, or other preferred topics, I refer to the website of this meeting, which presents the abstracts of 62 talks and 40 posters [1]. For a general review of the area, the reader may consult [2].

As one of the most eminent researchers in this field and presumably also the best and longest known, Enrico Cabib set the scene in his keynote lecture by analyzing the close relationship between cell wall construction and morphogenesis. For example, the septation machinery of yeast cells can be viewed as a morphogenetic program that in some mutants is carried out in full, but at the wrong location. It seems likely that discovery and detailed elaboration of more such morphogenetic programs will follow (John Pringle). Our knowledge of the molecular organization of the fungal cell wall has now advanced far enough to attempt predicting which kinds of cell wall assembly enzymes are needed to covalently couple the various cell wall components and in which order (enzymes are needed to covalently couple the various cell to attempt predicting which kinds of cell wall assembly such as formation of the linkage between chitin and possibly also in various assembly steps of the cell wall such as formation of the linkage between chitin and 1,3-β-glucan network. Another frequently asked question is why the fungal cell so often uses various isozymes to produce a particular cell wall polysaccharide. In addition to increasing the number of regulatory options, another obvious possibility is that it allows the cell to produce various isoforms of the polymer. Neil Gow and co-workers have confirmed this. They have demonstrated that individual Chs isozymes of *Candida albicans* produce fibrils of different length.

GPI proteins play an important role in constructing the cell wall and as cell wall constituents (GPI-dependent cell wall proteins or GPI-CWPs), Plasma membrane-bound GPI proteins are probably involved in processing GPI proteins destined for the cell wall, in remodeling cell wall polysaccharides (Jean-Paul Latgé, Laura Popolo), and possibly also in various assembly steps of the cell wall such as formation of the linkage between chitin and 1,3-β-glucan discussed above. Identification by mass spectrometry of GPI-CWPs and other covalently bound cell wall proteins is now feasible and will probably become the method of choice for all fully sequenced fungi in the near future (Frans Klis, Michael Weig). Importantly, Yoshifumi Jigami and Marlyn Gonzalez have successfully used green fluorescent protein-dependent cell wall fusion proteins in yeast for high-throughput screening of cell wall-related antifungal drugs. Using the mycelial fungus *Aspergillus niger* as test system, Arthur Ram presented an additional high-throughput screen based on the activation of a cell wall salvage pathway. Many GPI-CWPs are involved in adhesion. Peter Lipke presented intriguing evidence for a new adhesion mechanism involving Als5p, a *C. albicans* GPI-CWP, based on the formation of an amyloid-like...
state. As GPI proteins play such an important role in cell wall formation, biosynthesis of GPI anchors (Andreas Conzelmann, Yoshifumi Jigami, David Levin) and the transport of GPI proteins to the cell surface (Reika Watanabe) receive much attention. Interestingly, GPI proteins seem to exit the endoplasmic reticulum in specialized vesicles that do not contain other secretory proteins. Another class of cell wall proteins, the Pir cell wall proteins (Pir-CWPs), are linked to 1,3-β-glucan chains through an alkali-sensitive linkage. The nature of this linkage is unknown but might involve the repeats present in these proteins. Widmar Tanner has now shown that the linkage is indeed in the repeat and surprisingly involves a glutamine residue.

Yoshikazu Ohya presented a fascinating approach for studying yeast morphology. He has developed a computerized method to systematically describe and quantify multiple morphological changes in yeast mutants. For this he has set up the Saccharomyces Cerevisiae Morphological Database (SCMD), which can be accessed at [3]. Cell wall mutants tend to share the following characteristics. They are round with a wide neck and they show forward-directed budding and delocalized cortical actin patches. It would be interesting to try to relate the morphological changes occurring in case of cell wall stress to the transcriptional responses to cell wall stress as presented by Jean François and Javier Arroyo in their contributions. Cell wall stress and other forms of stress cause considerable changes in the composition and organization of the newly made cell wall, showing that the cell can adapt its cell wall in response to environmental conditions. For example, the chitosomes, which seem to represent an intracellular reservoir of chitin synthase, are largely depleted in the 1,3-β-glucan-deficient mutant fks1Δ, and this is accompanied by high levels of stress chitin in the wall (Hector Lucero). These and other observations raise the question how cell wall synthesis is controlled and coordinated both during growth in rich medium and under more stressful conditions (Martha Cyert, Mike Hall, Cornelia Kurischko, Maria Molina).

Although mutations in a pathogen generally lead to diminished or at best unaffected virulence, in rare cases the opposite occurs. Ken Haynes has convincing evidence that Candida glabrata deleted for ACE2, which encodes a transcription factor that activates transcription of genes expressed in the G1 phase of the cell cycle, are hyper-virulent in a murine model of candidiasis. The next question to answer is which changes in the cell wall caused by the loss of Ace2p are responsible for hyper-virulence.

Those interested in the development of fruit bodies in the Basidiomycotina should read the abstract about the identification in Coprinus cinereus of galectins and their oligosaccharide ligands and their respective locations (Markus Aebi).

Finally, it has sometimes been thought that with the sequencing of their genomes and the development of more and more ingenious genomic approaches the study of Saccharomyces cerevisiae and other fungi may rapidly reach a phase of diminishing returns, but my feeling is that we are just at the end of the beginning. A new era has begun, in which we should aim at understanding the full complexity of a living cell and at moving from a qualitative description to a more quantitative analysis. I am looking forward to the next Fungal Cell Wall Meeting, which will probably be held in The Netherlands in 2005.

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References