The Rise of Epigenetics in Microbial Eukaryotes

Junhyun Jeon¹ and Yong-Hwan Lee¹,²

¹Department of Agricultural Biotechnology, College of Agriculture and Life science, Seoul National University, Seoul 151-921, Korea
²Center for Fungal Genetic Resources and Center for Fungal Pathogenesis, Seoul National University, Seoul 151-921, Korea

Corresponding author: Yong-Hwan Lee, Department of Agricultural Biotechnology, College of Agriculture and Life science, Seoul National University, Seoul 151-921, Korea, Tel.: ; E-mail: yonglee@snu.ac.kr

Abstract

The 12th European Conference on Fungal Genetics (ECFG) was held in Seville, Spain on March 23-27, 2014. The meeting covered topics as diverse as fungal genetics, genomics, molecular cell biology, evolution, pathogenesis, and biotechnology. Despite such diversity, as the meeting progressed, it became evident that epigenetics are now an important part of genomic studies on fungal biology and evolution. In the meeting, regulation of genome integrity, secondary metabolism gene cluster and light responses by histone modifications and also small RNA-mediated antifungal drug resistance were reported. In this report, we highlight those epigenetics-related talks presented in the 12th ECFG that give new insights into the biology and evolution of microbial eukaryotes.

Keywords: Fungi; Genetics; Fungal biology; Epigenetics; Epigenomics; Non-coding RNA introduction

Standing on the Shoulders of Giants

The 12th European Conference on Fungal Genetics was held in the warm and sunny city, Seville, Spain, from the 23rd to the 27th of March this year. More than 700 attendees joined the meeting from all around the globe. There were three plenary sessions, nine concurrent sessions and two poster sessions covering topics ranging from genetics and genomics to molecular cell biology, evolution, pathogenesis, and biotechnology. The three morning sessions were devoted to plenary sessions that consist of fifteen lectures. Each plenary session was dedicated to Drs. Charles Yanofsky, John Clutterbuck, and Claudio Scizazzocchio, respectively, who have made lasting impact on the molecular genetics of fungi. Some plenary session speakers reminisced about their lives and legacies, reminding young scientists like us of the fact that we all are standing on the shoulders of the ‘giants’. Recently, high throughput sequencing technologies have enabled complete genome sequencing of diverse fungal species and the analysis of genome evolution and epigenetic attributes. This advancement has helped scientists address both old and new questions about fungal biology and evolution from genomic and epigenomic perspectives. In particular, recent epigenetic studies generated novel insights into the molecular basis of fungal lifestyles. The scope of the meeting was far beyond what can be covered in a short report, so I will highlight some of the exciting presentations about fungal epigenetics and epigenomics.

Histone Modifications and Fungal Biology

Neurospora crassa has been a model for studying DNA methylation and other epigenetic factors such as histone modifications in filamentous fungi. The first plenary speaker, Eric Selker (University of Oregon, USA) has made major contributions to understanding fungal DNA methylation and histone methylation associated with DNA methylation (H3K9me3, a heterochromatic mark). Selker first described how he identified and characterized genes encoding proteins that directly or indirectly influence DNA methylation in N. crassa by combining genetic and biochemical approaches in his earlier studies [1-3]. He then summarized his recent works showing that distinct DNA methylation and histone deacetylation complexes are required for heterochromatin formation and gene silencing [4]. He also discussed the presence and the role of H3K27me3 in N. crassa [5]. Considering that H3K27me3 is absent in the chromatin of Saccharomyces cerevisiae and many filamentous fungi, its evolution and function in fungal species will be of great interest.

Zachary Lewis (University of Gerogia, USA) gave a concurrent session talk about γH2A and heterochromatin in N. crassa. γH2A is a phosphorylated form of H2A and recruits chromatin-binding proteins that stabilize stalled replication forks or promote DNA repair [6]. Through a ChIP-seq experiment, he showed that γH2A is enriched in heterochromatin domains in a DIM-5 (a histone methyltransferase for H3K9me3) dependent manner (unpublished). However, γH2A is required neither for H3K9 methylation nor DNA methylation. Given that γH2A is a biomarker for double strand break induced by DNA damage, his data suggest that proper heterochromatin formation is important for DNA repair and replication.

In fungi, it was known that secondary metabolite (SM) gene cluster are silenced by the formation of facultative heterochromatin [7]. In another concurrent session, Joseph Strauss (BOKU University, Austria) reported a genetic and biochemical investigation of two histone demethylases that are involved in the regulation of SM clusters in Aspergillus nidulans: KdmA and KdmB (unpublished). KdmA acts as a repressor of SM clusters by binding to H3K9me3 and demethylating H3K36me3, whereas KdmB acts as an activator by binding to H3K4me3 and demethylating H3K9me3. Deletion of the genes followed by transcriptome and ChIP analysis showed that the enzymes really regulate transcription of genes at the tested SM clusters.

Jessica Soyer (National Institute for Agricultural Research (INRA), France) showed in her concurrent session talk that epigenetic control of gene expression could be extended to the regulation of genes encoding putative secreted proteins (possibly effectors) [8]. In many
Northern and Western blot analyses showed that the expression of...of fungal virulence is not clear, since knockdown
mediated repression on fungal virulence is not clear, since knockdown
expression allows the pathogen to escape detection by cognate R gene,
effector genes located in AT-isochores is under regulation at the
diversity for adaptation. Epimutation in fungal pathogens certainly
induced in the promoter regions to which FphA is recruited for
transcriptional activation. This suggests that H3K9ac is important for
light-induced changes in gene expression of A. nidulans.

Unlike other talks that focused on histone methylation, Reinhard
Fisher (Karlsruhe Institute of Technology, Germany) presented
evidence that histone acetylation is involved in light regulation in A.
nidulans (unpublished). He showed that in the mutant of FphA, the
red-light sensor phytochrome, H3K9 acetylation (H3K9ac) is not
induced in the promoter regions to which FphA is recruited for
transcriptional activation. This suggests that H3K9ac is important for
expression of epimutation in fungal pathogens surely deserves further investigation in the future, since it has significant clinical and agricultural ramifications.

In contrast to siRNAs, long non-coding RNAs (lncRNA) in fungi
are just beginning to be appreciated. Yi Liu (Southwestern Medical
Center, USA) presented a good example of such lncRNA in N. crassa
in his concurrent session talk. He elegantly showed that light-inducible
expression of the antisense transcript, qrf, from the frq locus, one of
the circadian genes, is required for the resetting of clock property by
silencing at the circadian loci. It would be interesting to see in the
coming years how prevalent lncRNAs and natural antisense transcripts
are and their implications in fungal biology.

Conclusions

The 12th European Conference on Fungal Genetics was a great
success in inspiring people with thought-provoking talks given by
great speakers and also in paving the path to future investigations by
touching on a broad range of topics. There were many more exciting
talks including ones about endosome trafficking, fungal effectors and
evolution of fungal sexual reproduction that we unfortunately do not
have enough space to discuss here. Approaching the end of the
meeting, it was obvious that epigenetic factors such as histone modifications and non-coding RNAs have become an important part
of many genomic studies, especially in filamentous fungi. Considering
that the number of sequenced fungal genomes represents the widest
sampling of genomes from any eukaryotic kingdom, the coming years
would be exciting and mind-blowing with a better understanding of life and its evolution.

Acknowledgements

This work was supported by Basic Science Research Program
through the National Research Foundation of Korea (NRF) funded by
the Ministry of Education, Science and Technology (2013-056580).

References

1. Kouzminova E, Selker EU (2001) dim-2 encodes a DNA
methyltransferase responsible for all known cytosine methylation in Neurospora. EMBO J 20: 4309-4323.
2. Tamara H, Selker EU (2001) A histone H3 methyltransferase controls DNA methylation in Neurospora crassa. Nature 414: 277-283.
3. Selker EU, Tountas NA, Cross SH, Margolin BS, Murphy JG, et al. (2003) The methylated component of the Neurospora crassa genome. Nature 422: 893-897.
4. Honda S, Lewis ZA, Shimada K, Fischle W, Sack R, et al. (2012) Heterochromatin protein 1 forms distinct complexes to direct histone deacetylation and DNA methylation. Nature Structural & Molecular Biology 19: 471-U424.
5. Jamieson K, Rountree MR, Lewis ZA, Stajich JE, Selker EU (2013) Regional control of histone H3 lysine 27 methylation in Neurospora. Proceedings of the National Academy of Sciences of the United States of America 110: 6027-6032.
6. Kuo LJ, Yang LX (2008) Gamma-H2AX - a novel biomarker for DNA double-strand breaks. In Vivo 22: 305-309.
7. Gacek A, Strauss J (2012) The chromatin code of fungal secondary metabolite gene clusters. Appl Microbiol Biotechnol 95: 1389-1404.
8. Soyer JL, El Ghalid M, Glaser N, Ollivier B, Linglin J, et al. (2014) Epigenetic control of effector gene expression in the plant pathogenic fungus Leptosphaeria maculans. PLoS Genet 10: e1004227.
9. Grandaubert J, Balesdent MH, Rouxel T (2013) [Transposable elements reshaping genomes and favouring the evolutionary and adaptive potential of fungal phytopathogens]. Biol Aujourdhui 207: 277-280.
10. Qutob D, Chapman BP, Gijsen M (2013) Transgenerational gene silencing causes gain of virulence in a plant pathogen. Nat Commun 4: 1349.
11. Kramer C, Loros JJ, Dunlap JC, Crosthwaite SK (2003) Role for antisense RNA in regulating circadian clock function in Neurospora crassa. Nature 421: 948-952.