2019 Spring
Life Sciences & IBB Seminar

"Systematic dissection of complex signaling pathways governing the brain infection of Cryptococcus neoformans"

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- **Date: 4:30PM/Apr. 5(Fri.)/2019**
- **Place: Auditorium(1F), Postech Biotech Center**
- **Inquiry: Prof. Sin-Hyeog Im (279-2356)**
- **Abstract:**

Cryptococcus neoformans is a causative agent of global fungal meningoencephalitis, which results in more than 180,000 deaths annually. Nevertheless, its treatment option is highly limited mainly due to a lack of complete understanding how the pathogen interacts with the host during infection and disease progression. Although a number of signalling components and pathways involved in the pathogenicity of C. neoformans have been characterized past years, it remains elusive how complex signalling pathways are coordinated and regulated during the whole infection process. To comprehensively understand complex pathobiological signaling networks in the basidiomycete fungal pathogen, we have constructed high-quality libraries of signature-tagged gene-deletion strains through homologous recombination methods for putative transcription factor, kinase, and phosphatase genes and examined their in vitro and in vivo phenotypic traits under 32 distinct growth conditions. This high-functional-coverage phenome analysis uncovered myriad novel signaling components, which play critical roles in growth, differentiation, stress responses, antifungal drug resistance, and virulence. Large-scale virulence and infectivity assays in insect and mouse host models identified a number of pathogenicity-related transcription factors, kinases, and phosphatases that are involved in the following biological functions: growth and the cell cycle, nutrient metabolism, the stress response and adaptation, cell signalling, cell polarity and morphology, vacuole trafficking, tRNA modification, and other previously unknown functions. Furthermore, we performed signature tagged mutagenesis (STM)-based lung and brain infectivity assays and NanoString-based in vivo transcription profiling of 183 kinases and 178 transcription factors during the whole infection process of C. neoformans. This comparative STM and in vivo transcription profiling analysis of the infected lungs and brains revealed that C. neoformans employs not only core signalling pathways that are required for both initial and late stage of infections, but also utilizes infection stage specific signalling pathways. In conclusion, our phenome-based functional analyses of the C. neoformans transcription factor, kinase, and phosphatase mutant libraries provide key insights into regulatory networks of basidiomycetous fungi as well as the ubiquitous human fungal pathogen.

***This seminar will be given in English.**

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