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Kinase mediated regulation of lipid metabolism and the crosstalk with drug tolerance mechanisms in *Candida albicans*

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The occurrence of pathogenic fungal infections has been rising all over the world. Although the research is developing the field of mycology, there is still a need for the identification of reliable determinants of virulence and obtain successful therapy in human. *Candida albicans* synthesizes the major lipids component such as sterol and its membranes contain typically eukaryotic lipid species like phospholipids, phosphoglycerides, etc., which play important role in cellular processes such as membrane homeostasis, signaling, morphogenesis, cell wall integrity, etc. The incidences of *Candida albicans* cells acquiring multidrug resistant (MDR) are common, which in turn hamper their successful chemotherapy. In membrane of *C. albicans* changes in ergosterol composition by disruption of ERG genes results in improper surface localization of drug efflux pumps like Cdr1p. There are also instances where common regulation of MDR and lipid metabolism genes has been observed. MDR in *C. albicans* is closely linked to the status of membrane lipids like ergosterol. However mechanisms, which regulate these lipid changes at compositional level, are largely unknown. A recent study showed that several kinase defective mutants of *C. albicans* were susceptible to azoles which target ergosterol biosynthesis suggesting that these kinases somehow, either directly or indirectly, affect ergosterol biosynthesis pathway. In the present study we screened for the kinases whose knockouts might show an abrupt or depleted ergosterol levels. Based on thin layer chromatography and gas chromatography-mass spectrometry screens; we found some kinases, which showed defects in ergosterol biosynthesis. Interestingly, we found high ergosterol content in several kinase mutants, yet these were susceptible to azoles. Next we screened these select kinase mutants with drugs affecting different MDR pathways namely the cell wall and mitochondria. We further checked for the mycelia formation in these mutants. We have found some interesting correlation among these different pathways and based on our previous studies we hypothesize that ergosterol remains the key component of major MDR mechanism and that several kinases are involved in regulating the level of this fungal lipid. Though, the complete understanding of the ergosterol regulation via kinase circuitry requires further validation by correlation of molecular and lipidomic study, our study points towards a new functional role to these kinases in *C. albicans.*

Biography

Kaushal Kumar Mahto has completed his Master's degree in Biotechnology from Lalit Narayan Mithila University, India in 2010 after that he got registered as PhD student in 2012 in life science stream. Presently, he is working in collaboration with expertise's in the field of fungal genetics and biochemistry of pathogenic yeast *Candida albicans* at school of life sciences, JNU India. Recently he was awarded, as Senior Research Fellow (SRF) of Indian Council of Medical Research, India. However, he is working in the field of Mycology, so he is trying to understand that how lipids directly and indirectly regulate and involve in terms of multi drug resistance (MDR) mechanism and virulence of pathogenic fungus Candia albicans via set of kinases mutants. He had already obtained some significant interesting results by lipidomics approaches and many basic techniques, during his research work and some of the finding and study has been published in very reputed peer reviewed journal such as *Plos One* and OMICS. He is member of the Society of Biological Chemists (India) and American Society of Microbiology, etc.

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