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## The roles of checkpoint related protein phosphatases and regulators in regulating morphogenesis and virulence in *Candida albicans*

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Phosphorylation and dephosphorylation of the checkpoint kinase CaRad53 is crucial for fungal cells in response to genotoxic stresses. The catalytic subunit CaPph3 of protein phosphatase 4 (PP4) forms a complex with the regulatory subunit CaPsy2, which dephosphorylates activated CaRad53 during adaptation to and recovery from MMS-mediated DNA damage. We show here that the N-terminal Y33A mutation of CaPsy2 blocks the interaction between CaPph3 and CaRad53, the deactivation of CaRad53 and the morphologic switch in recovery from genotoxic stress. In *Saccharomyces cerevisiae*, the ScPph3-ScPsy2-ScPsy4 complex functions to dephosphorylate  $\gamma$ H2A. Here, we also show that CaPsy4 is a functional homolog of ScPsy4, but not involved in the deactivation of CaRad53 or CaHta, the ortholog of H2A. However, deletion of CaPSY4 causes *C. albicans* cells a sensitivity to genotoxic reagents and a defect in DNA damage-induced filamentation. In *S. cerevisiae*, ScTip41 and ScTap42 are two regulators of CaPph3. In *C. albicans*, we show that deletion of CaTIP41 causes cells to be sensitive

to DNA damaging agents, MMS and cisplatin. In addition, cells lacking CaTIP41 show a delay in the recovery from MMS-induced filamentation to yeast form, decreased total PP2A activity and a defect in deactivation of CaRad53 during recovery from DNA damage. We also show that CaTip41 interacts with CaPph3, CaPsy2 or CaTap42. And deletion of CaTIP41 promotes the interaction between CaTap42 and CaPph3. Finally, *C. albicans* cells lacking CaPPH3, CaPSY2, CaPSY4 or CaTIP41 and CaTAP42, and the cells carrying the Y33A mutation of CaPSY2, show increased virulence to mice. Therefore, CaPph3 and its regulators play negative roles in regulating the DNA damage-induced filamentation and the virulence in *C. albicans*.

### Speaker Biography

Jinrong Feng has completed his PhD from Tianjin University, China. Currently, he is an Associate Professor at School of Medicine, Nantong University. He has mainly focused on checkpoint related protein phosphatases in *Candida albicans*. He has published over 10 papers in reputed journals.

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