

# International Conference & Exhibition on Cell Science & Stem Cell Research

29 Nov - 1 Dec 2011 Philadelphia Airport Marriott, USA

## Regulation of the mobility and assembly of the 26s proteasome by *int6* in fission yeast

Zhe Sha

Harvard Medical School, USA

*Mammalian int6* gene has been implicated in breast cancer formation; but its molecular functions remain unclear. We previously characterized *yin6*, the fission yeast homolog of *int6*, and demonstrated that it binds and regulates proper localization and/or assembly of 26S proteasomes. These data support the hypothesis that Yin6 regulates proteasome, abnormalities in which can disrupt homeostasis of regulatory proteins leading to tumor formation. The goal of this study is to investigate the mechanisms.

From a genetic screen, we established that overexpression of two proteins, Rpn7 and Arc3, rescued proteasome defects in *yin6*-null cells. Rpn7 is a proteasome subunit that contains a PCI domain, also found in Int6/Yin6. We identified a conserved Leu/Met residue in the PCI domain. Bioinformatics predicted that the hydrophobicity of this residue is critical for arrangement of  $\alpha$ -helical repeats within the PCI domain. Consistently, replacing it with Asp in Rpn7 and Yin6 inactivated these proteins and blocked their binding to other proteins.

Arc3 is a subunit of the Arp2/3 complex, whose major role is to nucleate F-actin and regulate intracellular trafficking. We found that proteasome mobility, and nuclear import in particular, were reduced when Arc3 was inactivated, leading to proteasome defects in the nucleus. To further explore proteasome nuclear transport, I investigated how Yin6 interacted with importins. Our genetics and mass-spectrometry data suggested that Yin6 selectively interacted with Sal3 to regulate proteasome nuclear import. In conclusion, our studies provided mechanistic insight into the role of Yin6 in ensuring proper proteasome assembly and mobility to influence many cellular processes.

### Biography

Zhe Sha got his Ph.D degree from Baylor College of Medicine under the supervision of Professor Eric C. Chang. The work presented here was completed during his Ph.D research, during which he published 3 papers in reputed journals.