NANYANG TECHNOLOGICAL UNIVERSITY

School of Biological Sciences

SBS Seminar Announcement

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Abstract

Biotin-dependent carboxylases are widely distributed in nature and have central roles in the metabolism of fatty acids, amino acids, carbohydrates, cholesterol and other compounds. Five such enzymes exist in humans: acetyl-CoA carboxylase 1 (ACC1), ACC2, propionyl-CoA carboxylase (PCC), 3-methylcrotonyl-CoA carboxylase (MCC), and pyruvate carboxylase (PC). Deficient mutations in PCC, MCC and PC are linked to serious metabolic diseases, and ACCs are attractive targets for drug discovery against diabetes, cancer and other diseases.

Based on sequence analysis, we have recently identified a novel member of this family in a collection of bacteria, and its holoenzyme is a 720 kD homohexamer. The holoenzymes of PCC and MCC are 750 kD $\alpha_6\beta_6$ dodecamers. Our studies have revealed striking structural diversity in the architectures of these holoenzymes, despite the fact that their subunits share significant amino acid sequence identity. These structures have also provided molecular insights into the catalysis by these enzymes.

In addition, we have recently discovered that the PC from *Listeria monocytogenes* is regulated by the bacterial second messenger cyclic-di-AMP, which is important for bacterial growth, stress response, antibiotic resistance and virulence. Our structural, biochemical and functional studies demonstrate that cyclic-di-AMP is an allosteric inhibitor of this enzyme, and that this regulation is crucial for maintaining metabolic balance and for intracellular growth/infection by this pathogen.

Tuesday, 2 December 2014 11.00am to 12.00pm SBS Classroom 2 (SBS-01n-22)

Host: A/Prof Gao Yonggui

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