Faculty of Science & Natural Resources Seminar
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Glycolysis and Pathogenicity: Unsolved problems

Dr Min-Kyu Kwak
Senior Researcher, Seoul National University, South Korea
Director, IRWEE Corp, South Korea
Visiting Professor, Universiti Malaysia Sabah

Abstract:

Background: High methylglyoxal content disrupts cell physiology, but mammals have scavengers to prevent glycolytic and mitochondrial dysfunctions. In yeast, methylglyoxal accumulation triggers methylglyoxal-oxidizing alcohol dehydrogenase (Adh1) activity. While methylglyoxal reductases and glyoxalases have been well studied in prokaryotes and eukaryotes, experimental evidence for methylglyoxal dehydrogenase (Mgd) and other catalytic activities of this enzyme affecting glycolysis and the tricarboxylic acid cycle is lacking.

Methods: A glycine-rich cytoplasmic Mgd protein, designated as Mgd1/Grp2, was isolated from glutathione-depleted *Candida albicans*. The effects of Mgd1/Grp2 activities on metabolic pathophysiology were investigated using knockout and overexpression mutants. We measured glutathione-(in)dependent metabolite contents and metabolic effects, including viability, oxygen consumption, *ADH1* transcripts, and glutathione reductase and α-ketoglutarate dehydrogenase activities in the mutants. Based on the findings, methylglyoxal-oxidizing proteins were monitored to determine effects of *MGD1/GRP2* disruption on methylglyoxal-scavenging traits during glutathione deprivation.

Results: Methylglyoxal-oxidizing NAD(H)-linked Mgd1/Grp2 was found solely in glutathione auxotrophs, and it catalyzed the reduction of both methylglyoxal and pyruvate. *MGD1/GRP2* disruptants showed growth defects, cell-cycle arrest, and methylglyoxal and pyruvate accumulation with mitochondrial impairment, regardless of *ADH1* compensation. Other methylglyoxal-oxidizing enzymes were identified as key glycolytic enzymes with enhanced activity and transcription in *MGD1/GRP2* disruptants, irrespective of glutathione content.

Conclusions: Failure of methylglyoxal and pyruvate dissimilation by Mgd1/Grp2 deficiency leads to poor glutathione-dependent redox regulation despite compensation by Adh1.

General significance: This is the first report that multifunctional Mgd activities contribute to scavenging methylglyoxal and pyruvate to maintain metabolic homeostasis and the redox pool via glycolytic enzymes and Adh1 expression.

Dr Min-Kyu Kwak received his PhD from Seoul National University, South Korea in 2009. He has published several research papers in high impact journals. He is actively involved in several research projects and holds 11 international and Korean patents derived from his work.

Programme

2.00 pm: Arrival of participants
2.30 pm: Talk begins
3.15 pm: Q & A
3.30 pm: End of seminar

Further enquiries:

Call: Chong Khim Phin
088-320000 ext 5655
Email: chongkp@ums.ed.my

All Are Welcome