Role of MKP-2 in Hepatic Inflammatory Response to Fasting in Mice

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Introduction
➢ The effect of nutritional status on the expression of MAPK phosphatases-2 (MKP-2) and the effect of MKP-2 deletion on liver metabolism and inflammation in response to fasting.
➢ Treatment groups: MKP-2 KO and MKP-2 WT mice fed ad libitum or fasted for 48 h prior to sacrifice. Mice were fasted for 48 h and refed either a chow of high fat diet (HFD).
➢ MKP-2 expression in the liver and the effect on downstream targets – p38 MAPK, JNK and ERK.

Conceptual Framework
➢ Understanding the molecular underpinnings of the complications that ensue in obesity continues to be of paramount clinical importance.
➢ The function of MKP-2 in metabolic regulation to fasting is largely unknown.
➢ There is lack of information on the timeline during the development of obesity, insulin resistance and type 2 diabetes, indicating an important gap in our understanding of metabolic disorders.

Key Findings
➢ Fasting stress induced MKP-2 expression in the liver (A).
➢ In the fasted state, MKP-2 KO mice exhibited significant decrease in liver weight compared with MKP-2 WT mice (B).
➢ In the fasted state, MKP-2 KO mice exhibited significantly enhanced spleen weight compared with MKP-2 WT mice (C).
➢ No difference in fasting blood glucose concentration between the two genotypes (D).
➢ Figure E, shows p38 MAPK phosphorylation in the livers of MKP-2 KO and MKP-2 WT mice.

Conclusions
➢ Data indicate that upregulation of MKP-2 is a physiological relevant response and might be beneficial in hepatic lipid utilization during fasting in the liver by antagonizing the MAPK signaling module.
➢ These findings support the benefits of fasting in improving the potency of tyrosine kinase inhibitors in the treatment of metabolic disorders and cancer.

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