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## Depletion of intracellular Homocysteine via up-regulation of Betaine-homocysteine methyltransferase is implicated in the anti-lipogenic effect of Betaine

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**P**revious studies suggested that Betaine, a methyl donor used in remethylation of homocysteine (Hcy) to methionine, may be effective against non-alcoholic fatty liver injury both in human and animals, but the mechanism of its beneficiary action remains elusive. In this study we investigated the anti-lipogenic effect of betaine in association with activation of the AMPK pathway in the liver. In rats fed methionine and choline-deficient diet (MCD) for 3 wk, accumulation of hepatic lipids was apparent while phosphorylation of AMPK, ACC, SREBP-1c and LKB1 was inhibited, which were all prevented by betaine supplementation in drinking water (1%). The reduction of S-adenosylmethionine (SAM) and the elevation of Hcy levels in the MCD-fed rats were also blocked by betaine feeding. Hcy treatment decreased pAMPK, pACC, pSREBP-1c and pLKB1 both in H4IIE and HepG2 cells. However, betaine treatment inhibited the Hcy-induced reduction of pAMPK, pSREBP-1c, pACC and pLKB1 in H4IIE cells, but not in HepG2 cells. In HepG2 cell, the metformin-induced phosphorylation of AMPK, ACC and SREBP-1c was suppressed by Hcy. Treatment with hydroxylamine, a cystathionine β-synthase inhibitor, resulted in a reduction of pAMPK, pACC and pSREBP-1c, accompanied by elevation of intracellular Hcy. The Hcy-induced elevation of intracellular Hcy and inhibition of protein expression of betaine-homocysteine methyltransferase (BHMT), an enzyme deficient in HepG2 cells, were blocked by betaine in H4IIE cells. Taken together, the results indicate that the beneficial effect of betaine against hepatic lipid accumulation may be attributed to the depletion of Hcy via up-regulation of BHMT in hepatocytes.

## Biography

Young Chul Kim is currently a Professor of Toxicology at Seoul National University, College of Pharmacy since 1986. He has authored more than 100 papers in reputed journals. He is a recipient of several prestigious international and national awards including the Theme Most Innovative Original Paper Award at GA (2014) and the Korean Teachers' Award (2015).

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