

2nd World Congress on Diabetes & Metabolism

6-8 December 2011 Philadelphia Airport Marriott, USA

TITLE

Targeting inflammation and ER stress for diabetes management

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Diabetes is the fifth deadliest disease in the United States, accounting for 17,000 deaths per year. Disruption of the interface between inflammatory and stress pathways, specifically ER stress, is central to the pathogenesis of obesity, hepatic insulin resistance and type 2 diabetes (T2D). Accumulation of unfolded and misfolded proteins in ER activates the unfolded protein response (UPR), leading to increased expression of molecular chaperone Grp78/BiP and ATF4/CREB-2, an activating transcription factor. In addition, GADD153/CHOP, a growth arrest- and highly stress-inducible gene sensitizes cells to ER stress through enhancing production of reactive oxygen species that can promote inflammation. Ayurvedic medicine, *Momordica charantia* (bitter melon, BM) is traditionally used in the management of diabetes and its complications. The aim of this study was to examine the effects of BM on hepatic ER stress and systemic inflammation in mice fed high-fat diet (HFD). Our studies indicate that HFD significantly elevated Grp78, ATF4 and GADD153 protein levels, while BM normalized levels of hepatic ER stress proteins in mice fed HFD with BM. Furthermore, BM attenuated systemic inflammation by reducing secretion of plasma proinflammatory cytokines, INF γ , IL-17, TNF α , exotaxin-2, lymphotactin and IL-1b in mice fed HFD with BM. Interestingly, BM upregulated specific Th2 cytokines IL-5, IL-10 and IL-13, which have been demonstrated to protect obesity-associated inflammation. These data indicate a role for dietary therapies in reducing HFD-associated hepatic ER stress and inflammation. [Grants: NCMHD (P20MD000173-06), NCCAM (R21AT003719), RCMI, NCRR (5G12RR003061-23), NIH].

Biography

Dr. Pratibha V. Nerurkar obtained her Ph.D from Bombay University, India and completed her postdoctoral studies at National Cancer Institute/ National Institutes of Health (NCI/NIH). She leads the Laboratory of Metabolic Disorders and Alternative Medicine at College of tropical Agriculture, University of Hawaii. She has published more than 30 manuscripts in peer-reviewed journals.