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Humoral and cellular immune responses in mice against modified Hepatitis B plasmid DNA vaccine

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Background: Hepatitis B virus (HBV) infection is one of the most widespread viral infections of humans. The recombinant hepatitis B surface antigen (HBsAg), the most commonly used vaccine against HBV, has been used for many years but with limiting efficacy.

Objective: This study aimed to evaluate the immunogenicity and type of immune responses of a quality controlled modified gWizHBs plasmid encoding the HbsAg following intramuscular injection of the plasmid in mice.

Methods: The characterized plasmid DNA was used in immunization of Balb/c mice by intramuscular route. Three groups of mice were injected with three different concentrations of the modified plasmid. The humoral immune response was monitored by ELISA while the cellular immune response was investigated through analysis of the spleen cytokine profile [TNF α , IFN γ , and IL2] as well as the CD69 expression level in CD4 and CD8 positive cells.

Results: In general the percent of activated CD4 cells showing intracellular cytokines was higher than the CD8 positive population of cells. These findings indicate that the vaccine induced both a humoral and cellular immunity. The serum antibody showed first an IgM response at the 2nd and 3rd weeks followed by IgG response that appeared at week 3 and lasted for 6 weeks. This serum antibody level varied with the concentration of plasmid DNA injected and the highest level was obtained when the animals were immunized using 10 μ g of gWizHBs. The cytokine profile also showed high levels of TNF α , IFN γ , and IL2 and CD69 expression in the group of animal immunized using a dose of 10 μ g.

Conclusion: Intramuscular injection of the modified DNA-based vaccine encoding HBsAg of 10 μ g dose in mice induced both high humoral and cellular immune responses.

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Proteomics studies of the impact of high fat diet on proteome of mouse liver and dual mode of pharmacological action of Mangiferin

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Chronic over-nutrition is a major contributor to the rapidly growing incidence of obesity and its related metabolic disorders such as non-alcoholic fatty liver disease (NAFLD). The molecular mechanisms of metabolic dysregulation leading to these pathological conditions remain unclear, thus no effective therapy is currently available. We have identified a natural compound, mangiferin (MGF) (a predominant component of the plants of *Anemarrhena asphodeloides* and *Mangifera indica*), that can protect against high fat diet (HFD) induced obesity, hyperglycemia, insulin resistance and hyperlipidemia in mice. To understand MGF molecular mechanisms of action, we developed stable isotope labeling of mammalian (SILAM) technology and performed unbiased quantitative proteomic analysis of protein profiles in liver of mice fed with chow diet (CD) and HFD with or without MGF treatment, utilizing ¹⁵N metabolically labeled liver proteins as internal standards. We detected and quantitatively compared 965 proteins between CD and HFD groups and 865 proteins between HFD and HFD + MGF. We found that HFD significantly altered 192 proteins and MGF significantly differentially regulated 87 proteins. Among all significantly altered proteins 50% are involved in metabolic processes, which are further classified into 8 - 9 metabolic processes. The majority of HFD modulated proteins participate in lipid metabolism. HFD induced proteins involved in fatty acid uptake and subsequent oxidation and suppressed lipid biosynthesis-related proteins. Impressively, MGF was able to differentially regulate proteins that are altered by HFD. MGF up-regulates proteins pivotal for mitochondrial bioenergetics which are networked to PPAR α and PGC-1 α , and down-regulates proteins that control de novo lipogenesis and networked to SREBP and PPAR γ . This novel mode of dual pharmacodynamic actions enables MGF to enhance energy expenditure and inhibit lipogenesis, and thereby correct HFD induced liver steatosis and prevent adiposity. This provides a molecular basis supporting development of MGF or its derivatives into therapeutics to treat metabolic disorders.

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