# B6 Albino Mice Show Enhanced Diet Induced Nonalcoholic steatohepatitis Susceptibility

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Nonalcoholic fatty liver disease (NAFLD) is an alarmingly rising metabolic disorder. Nonalcoholic steatohepatitis (NASH) is the progressive liver damage with inflammation, leading to fibrosis and carcinogenesis. Interestingly, enhanced susceptible for NASH was observed in B6 albino mice (albino) with high cholesterol diet (HCD), compared to wild type B6 black mice (black), a phenotype not reported before. This study was led to understand the underline mechanism of elevated NASH susceptibility of albino mice. B6 albino mice carry a point mutation in *tyrosinase* gene and this is the only genetic difference compared to B6 black mice. Albino and black mice were fed with HCD for 10 weeks. Normal diet fed mice used as controls. Body weights, blood indices and liver damage related serum parameters were monitored. Liver samples were histologically analyzed. Mice carrying only the G291T mutation were developed using CRISPR/Cas9 technology and employed to confirm that the observed phenotype is resulted from that specific mutation. Liver injury was observed in albino mice from post day 1 HCD feeding, with elevated serum liver injury markers. 2 weeks of HCD induced NASH in albino mice, but no symptom was observed in black mice even after 10 weeks of diet. Histological analysis of albino mice livers revealed significant inflammatory cells and lipid infiltration, and severe fibrosis. Distorted serum lipoprotein profile was observed in albino mice, resulted from altered cholesterol absorption in small intestines. Similar to B6 albino, CRISPR generated mice exhibited the same liver damage phenotype, confirming the contribution of G291T mutation. This work uncovered a novel genetical factor for NASH development and expanded the understanding on NASH pathophysiology.

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