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## DIFFERENTIAL IMMUNOMETABOLIC PHENOTYPE IN TH1 AND TH2 DOMINANT MOUSE STRAINS IN RESPONSE TO HIGH-FAT FEEDING

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**Introduction:** Evidence is accumulating that immune reactivity plays an important role in metabolic diseases.

**Aims:** Therefore, we have investigated the strain-dependent differences of adipose tissue and liver immunophenotype in high-fat diet induced obesity, liver steatosis and fibrosis, and glucose metabolism in the two, C57Bl/6 and BALB/c, prototypic Th1 and Th2 mouse strains.

**Material and Methods:** Male C57Bl/6 and BALB/c, 8-week old mice received HFD (60% kcal fat) or standard chow diet (10% kcal fat) for 24 weeks. We performed histological and immunophenotypic analyses as well as gene expression of profibrogenic and lipid metabolism-related molecules in liver and adipose tissue.

**Results:** After 24 weeks of dieting BALB/c mice had higher weight gain on standard diet, while C57Bl/6 mice exhibited higher weight gain on HFD. The amount of visceral fat and fasting blood glucose levels were higher in C57Bl/6 mice on both diets. In contrast to BALB/c mice, HFD in C57Bl/6 mice led to a significant increase of the amount of VAT and number of VAT associated CD3<sup>+</sup>CXCR3<sup>+</sup> Th1 cells, dendritic cells (DCs) and F4/80<sup>+</sup> macrophages. In livers, higher number of CD3<sup>+</sup> and CD8<sup>+</sup> T lymphocytes, myeloid DCs, proinflammatory macrophages (F4/80<sup>+</sup>CD11b<sup>+</sup>CD11<sup>+</sup> and F4/80<sup>+</sup>IL-1β<sup>+</sup>) and CD11b<sup>+</sup>Ly6C<sup>+</sup> monocytes and higher levels of IL-6, TNF-α and IFN-γ were detected in HFD-fed C57Bl/6 mice than in BALB/c mice. C57Bl/6 mice which had scarce liver steatosis, while BALB/c mice showed prominent high-fat diet induced liver steatosis, associated with increased expression of genes related to lipid metabolism and higher serum levels of cholesterol and triglycerides with lower glycogen deposition in the liver. In contrast, BALB/c mice developed scarce liver collagen deposition while C57Bl/6 mice had prominent liver fibrosis. The expression of genes related to fibrosis such as procollagen, IL-13 and TGF-β and the levels of profibrogenic cytokines IL-13 and TGF-β in sera and liver homogenates were significantly higher in C57Bl/6 mice with the most prominent increase in liver IL-33 levels.

**Conclusions:** Th1 type response appears to favour inflammation and fibrosis in the liver while mice with dominant Th2 response are prone to steatosis.