PLOS | ONE

RESEARCH ARTICLE

Differential Immunometabolic Phenotype in Th1 and Th2 Dominant Mouse Strains in Response to High-Fat Feeding

Nemanja Jovicic[1,2☯], Ilija Jeftic[1,3☯], Ivan Jovanovic[1], Gordana Radosavljevic[1], Nebojsa Arsenijevic[1], Miodrag L. Lukic[1]*, Nada Pejnovic[1,3]*

1 Center for Molecular Medicine, Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia,
2 Institute of Histology, Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia,
3 Institute of Pathophysiology, Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia

☯ These authors contributed equally to this work.
* miodrag.lukic@medf.kg.ac.rs (ML); nadap@ikomline.net (NP)

Citation: Jovicic N, Jeftic I, Jovanovic I, Radosavljevic G, Arsenijevic N, Lukic ML, et al. (2015) Differential Immunometabolic Phenotype in Th1 and Th2 Dominant Mouse Strains in Response to High-Fat Feeding. PLoS ONE 10(7): e0134089. doi:10.1371/journal.pone.0134089

Editor: Pratibha V. Nerurkar, College of Tropical Agriculture and Human Resources, University of Hawaii, UNITED STATES

Received: December 7, 2014

Accepted: July 6, 2015

Published: July 28, 2015

Data Availability Statement: All relevant data are within the paper and its Supporting Information files.

Funding: This work was supported by grants from the Serbian Ministry of Science and Technological Development (175071 and 175069) (Belgrade, Serbia), Joint research project (SCOPES, IZ73Z0_152407) and Internal projects of Faculty of Medical Sciences (JP 02-14, JP 03-14) (Kragujevac, Serbia). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Abstract

Immune reactivity plays an important role in obesity-associated metabolic disorders. We investigated immunometabolic phenotype of C57Bl/6 and BALB/c mice, prototypical Th1 and Th2-type strains, fed chow or high-fat diet (HFD) for 24 weeks. In comparison to C57Bl/6 mice, chow-fed BALB/c mice had higher body weight and weight gain, lower glycemia, more pronounced liver steatosis, but less inflammation and collagen deposition in liver. In response to HFD C57Bl/6 mice exhibited higher weight gain, higher glycemia, HbA1c and liver glycogen content, increased amount of visceral adipose tissue (VAT) and number of VAT associated $CD3^+CXCR3^+$ T cells, $CD11c^+$ dendritic cells (DCs) and $F4/80^+$ macrophages than BALB/c mice. More numerous $CD3^+$ and $CD8^+$ T lymphocytes, myeloid DCs, proinflammatory macrophages ($F4/80^+CD11b^+CD11^+$ and $F4/80^+IL\text{-}1\beta^+$) and $CD11b^+Ly6C^{high}$ monocytes and higher levels of proinflammatory IL-6, TNF-α and IFN-γ were present in liver in HFD-fed C57Bl/6 mice compared with diet-matched BALB/c mice. As opposed to C57Bl/6 mice, HFD induced marked liver steatosis and upregulated the hepatic LXRα and PPARγ genes in BALB/c mice. C57Bl/6 mice fed HFD developed liver fibrosis and increased hepatic procollagen and TGF-β mRNA expression, and IL-33, IL-13 and TGF-β levels in liver homogenates, while BALB/c mice fed HFD had scarce collagen deposition in liver. The obtained results suggest inherent immunometabolic differences in C57Bl/6 and BALB/c mice. Moreover, HFD Th1-type mice on high fat diet regimen are more susceptible to adiposity, liver inflammation and fibrosis, while Th2-type mice to liver steatosis, which is associated with differential immune cell composition in metabolic tissues. Strain-dependent differences in immunometabolic phenotype may be relevant for studies of obesity-associated metabolic diseases in humans.