

Molecular Mechanisms of Lipid Metabolism and Obesity Modulation by Caspase-1/11 and nlrp3 Inflammasome in Mice

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Abstract : Introduction: Obesity and high-fat diet intake have a crucial impact on immune cells and inflammatory profile, highlighting an emerging realization that obesity is an inflammatory disease. In the present work, we aimed to characterize the role of caspase-1/11 and NLRP3 inflammasome in the establishment of mice obesity and modulation of inflammatory lipid metabolism induced by high fat diet intake. Methods and results: Wild type, caspase-1/11 and NLRP3 knockout mice were fed with standard fat diet (SFD) or high fat diet (HFD) for 90 days. The weight of animals was measured weekly to monitor the weight gain. After 90 days, the blood, peritoneal lavage cells, heart and liver were collected from mice studied here. Cytokines were measured in serum by ELISA and analyzed in spectrophotometry. Lipid antigen presentation molecule CD1d expression, reactive oxygen species (ROS) generation and lipid droplets biogenesis were analyzed in cells from mice peritoneal cavity by flow cytometry. Liver histopathology was performed for morphological evaluation of the organ. The absence of caspase-1/11, but not NLRP3, in mice fed with HFD favored the mice weight gain, increased liver size, induced development of hepatic steatosis and IL-12 secretion in mice compared to mice fed with SFD. In addition, caspase-1/11 knockout mice fed with HFD presented an increased CD1d molecule expression, as well as higher levels of lipid droplets biogenesis and ROS generation compared to wild type mice also fed with HFD. Conclusion: Our data suggest that caspase-1/11 knockout mice have greater susceptibility to obesity as well as increased activation of lipid metabolism and inflammatory markers.

Keywords : caspase 1, caspase 11, inflammasome, obesity, lipids

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