まはむど　あるしゃど

氏　　名　MAHMOOD　ARSHAD

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生命・臨床医学

学 位 論 文 題 目　Myeloid-Specific deletion of Hypoxia-inducible factor 1-alpha gene protected against Diet induced Insulin resistance
（骨髄特異的な Hypoxia-inducible factor 1-alpha 遺伝子の欠失は食餌由来ノインスリン抵抗性に対して保護作用を有する）

論 文 審 査 委 員

（主査）	教　授	齋藤　滋
（副査）	教　授	服部　裕一
（副査）	教　授	近藤　隆
（副査）	教　授	杉山　敏郎
（指導教員）	教　授	戸邉　一之

論 文 内 容 の 要 旨

Abstract

Aims/hypothesis : High-fat diet obesity causes the adipose tissue to expand at a much higher pace than the ability of vasculature to match the demand of rapid growing tissue, thus ensuing the hypoxia and induction of HIF-1α gene, which in turn causes the induction of inflammatory state through M1 macrophages and is strongly correlated with the systemic insulin resistance. Aim of this study is to investigate the effect of myeloid-specific deletion of HIF-1 alpha gene in diet-induced obesity and systemic insulin resistance in mice model. ***Methods:*** Myeloid-specific HIF-1α knockout mice (Mye-HIF-1α KO) were employed with the challenge of high-fat diet (HFD) for 18 weeks. Intra peritoneal glucose tolerance test (IP-GTT) and intra peritoneal insulin tolerance test (IP-ITT) were performed after 17 weeks of HFD. ***Results:*** WAT, liver and skeletal muscle were examined for inflammation, hypoxia, ER-stress, oxidative stress, angiogenesis and finally for insulin sensitivity through gene expression analysis, immunohistochemistry, microsphere analysis and western blotting. Results: Mye-HIF-1α KO mice revealed reduced adiposity , much rich vasculature with low hypoxic and inflammatory profile, improved glucose tolerance with markedly reduced gluconeogenic genes expression in liver and enhanced energy expenditure in skeletal muscle. ***Conclusion:*** Myeloid-specific deletion of HIF-1 alpha gene has a beneficial role against obesity-associated inflammation, thus contributing to the improvement of the whole body resistance.