報告番号	香大医博甲 第736号

様式１０２

学位論文の内容の要旨

Summary of the Substance of Dissertation

専攻 Major Field	医学	部門 Department	
学籍番号 Student No.	16D717	氏名 Name	董涛
論文題目 Thesis Subject	**Selective peroxisome proliferator-activated receptor-α modulator K-877 regulates the expression of ATP-binding cassette transporter A1 in pancreatic beta cells**		

（論文要旨）

Background

ATP-binding cassette transporter A1 (ABCA1) protein is a pivotal regulator of cholesterol and phospholipid efflux from cells to high-density lipoprotein (HDL) particles. Pancreatic ABCA1 functions in beta cell cholesterol homeostasis and affects insulin secretion. In this study we investigated the effect of pemafibrate, a novel selective PPARα modulator (SPPARMα), on pancreatic ABCA1 expression in vitro and in vivo.

Methods and Results

In vitro experiments, pancreatic ABCA1 expression was examined by real-time polymerase chain reaction and Western blot analysis in INS-1 cells. Cellular cholesterol content was measured in INS-1 cells. Pancreatic ABCA1 promoter activity was measured in INS-1 cells. Glucose dependent insulin secretion was analyzed in both INS-1 cells and mouse isolated islets. We revealed that pemafibrate increased both protein and mRNA of ABCA1 expression in INS-1 cells. Pemafibrate reduced cellular cholesterol content in INS-1 cells. ABCA1 promoter activity was increased by pemafibrate treatment as a dose dependent manner. Glucose dependent insulin secretion was ameliorated by pemafibrate -treatment in both INS-1 cells and mouse isolated islets. In vivo experiments, mice were divided into four groups and treated for 8 weeks, the normal food plus placebo group, the high fat diet (HFD) plus placebo group, the normal food plus pemafibrate (0.3 mg/kg/day) group, and the HFD plus pemafibrate (0.3 mg/kg/day) group. Mouse body weight, blood glucose and oral glucose tolerance test were recorded. ABCA1 expression was examined by real-time polymerase chain reaction and Western blot analysis in mouse pancreas. Although the HFD treatment reduced the expression of ABCA1, both the protein and mRNA of ABCA1 expression were ameliorated in mouse treated with HFD and pemafibrate. Pemafibrate-treatment reduced body weight and improved glucose intolerance induced by HFD in mouse.

Conclusion

Pemafibrate increased pancreatic ABCA1 and reduced cholesterol content in pancreatic beta-cells in vivo and in vitro. These findings raise the possibility that K877 may affected insulin secretion by controlling ABCA1 expression in pancreatic beta cells, which may also be one of therapeutic value in the treatment of diabetes mellitus.

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(備考) 論文要旨は，日本語で１，５００字以内にまとめてください。
(Recital) Sum up the within １５００ letters.