The Effect and Mechanism of Trimethylamine-N-oxide, a Metabolite of Intestinal Flora, on Coronary Heart Disease in Type 2 Diabetic Patients

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Study protocol

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Abstract

Background

Trimethylamine N-Oxide (TMAO) has been shown to be an independent risk factor for cardiovascular disease. Our aim is to study the effects of TMAO on type 2 diabetes mellitus-coronary heart disease and to explore its mechanism.

Methods

A total of 50 healthy controls, 50 T2DM patients and 50 T2DM combined with CHD patients were enrolled. Serum samples were collected to detect glucose, myocardial enzyme spectrum and TMAO level. The 16S rRNA gene sequencing analyzed the diversity of intestinal flora. Taking the ZDF rat as the experimental object, the model of T2DM combined with CHD was established in rats. Blood samples were taken to detect glucose, myocardial enzyme spectrum and TMAO level. The inflammatory protein and mRNA expression of TLR4, NLRP3, Caspase-1 and IL-1 β were detected by Western blot and RT-qPCR. In vitro culture of H9c2(2-1) for experiments. The CCK-8 method was used to detect the survival rate of cells after glucose and TMAO treatment. After the cells were treated with selected glucose and TMAO, the cells were treated with selected glucose, TMAO and BAY11-7082, Western blot detected the presence of pyroptosis and the pathway of TLR4/NF- κ B/NLRP3. RT-qPCR was used to determine the mRNA level of inflammatory factor.

Discussion

Changes in the composition of intestinal flora in patients with type 2 diabetes can lead to elevated serum TMAO levels. Animal and cell experiments have confirmed that elevated TMAO level may lead to inflammatory myocardial injury in rats and is related to the mechanism of TLR4/NF- κ B/NLRP3.

Full Text

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Figures

Figure 1

The serum levels of TMAO

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The serum levels of TMAO

Figure 2

Weight and blood glucose in rats.

Figure 2

Weight and blood glucose in rats.

Figure 2

Weight and blood glucose in rats.

A

B

Figure 3

Weight and blood glucose in rats.

A

B

Figure 3

Weight and blood glucose in rats.

A

B

Figure 3

Weight and blood glucose in rats.

Figure 4

Glucose and myocardial enzymes in rats.

Figure 4

Glucose and myocardial enzymes in rats.

Figure 4

Glucose and myocardial enzymes in rats.

Figure 5

HE staining of rat heart (×400).

Figure 5

HE staining of rat heart (×400).

Figure 5

HE staining of rat heart (×400).

Figure 6

Serum TMAO levels in rats.

Figure 6

Serum TMAO levels in rats.

Figure 6

Serum TMAO levels in rats.

Figure 7

Protein expression levels in control group, T2DM group, T2DM combined with CHD group and T2DM combined with CHD plus DMB group.

Figure 7

Protein expression levels in control group, T2DM group, T2DM combined with CHD group and T2DM combined with CHD plus DMB group.

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Protein expression levels in control group, T2DM group, T2DM combined with CHD group and T2DM combined with CHD plus DMB group.

Figure 8

The level of TLR4, NLRP3, Caspase-1 and IL-1 β mRNA expression.

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Figure 9

Survival rate of H9c2(2-1) treated with different concentrations of glucose or TMAO.

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Survival rate of H9c2(2-1) treated with different concentrations of glucose or TMAO.

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Figure 10

Effects of glucose, TMAO, glucose and TMAO on pyroptosis and pathway activating protein expression in H9c2(2-1).

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Effects of glucose, TMAO, glucose and TMAO on pyroptosis and pathway activating protein expression in H9c2(2-1).

Figure 11

Effects of BAY11-7082 on pyroptosis and pathway activating protein expression in H9c2(2-1).

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Figure 12

The expression of TLR4, NLRP3 , Caspase-1 and IL-1β mRNA under different treatments in H9c2(2-1).

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Figure 13

The expression of TLR4, NLRP3, Caspase-1 and IL-1 β mRNA under different treatments in H9c2(2-1).

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Figure 13

The expression of TLR4, NLRP3, Caspase-1 and IL-1 β mRNA under different treatments in H9c2(2-1).

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