News Release

Title

Transcriptome and metabolome analyses in exogenous FABP4- and FABP5-treated adipocyte-derived stem cells

Key Points

- Both FABP4 and FABP5 were significantly induced after adipocyte differentiation of ADSC and were secreted from the differentiated adipocytes.

- Analysis of microarray data, including gene ontology enrichment analysis and cascade analysis of the protein-protein interaction network using a transcription factor binding site search, demonstrated that treatment of ADSC with FABP4 or FABP5 affected several kinds of genes related to inflammatory and metabolic responses and the process of cell differentiation. Notably, myogenic factors, including myocyte enhancer factors, myogenic differentiation 1 and myogenin, were modulated by treatment of ADSC with FABP4, indicating that exogenous FABP4 treatment is partially associated with myogenesis in ADSC.

- Metabolome analysis showed that treatment of ADSC with FABP4 and with FABP5 similarly, but differently in extent, promoted hydrolysis and/or uptake of lipids, consequentially together with enhancement of β oxidation, inhibition of downstream of the glycolysis pathway, accumulation of amino acids, reduction of nucleic acid components and increase in the ratio of reduced and oxidized nicotinamide adenine dinucleotide phosphates ($NADPH/NADP^+$), an indicator of reducing power, and the ratio of adenosine triphosphate and adenosine monophosphate (ATP/AMP), an indicator of the energy state, in ADSC.

- Secreted FABP4 and FABP5 from adipocytes as adipokines differentially affect transcriptional and metabolic regulation in ADSC near adipocytes.

- The adiposity condition in the host of regenerative medicine may affect characteristics of ADSC by exposure of the balance of FABP4 and FABP5.

Summary

Adipocyte-derived stem cells (ADSC), which exist near adipocytes in adipose tissue, have been used as a potential tool of regenerative medicine. Lipid chaperones, fatty acid-binding protein 4 (FABP4) and 5 (FABP5), are abundantly expressed in adipocytes. FABP4 has recently been shown to be secreted from adipocytes during lipolysis in a non-classical pathway and may act as an adipokine. Here, we investigated the role of exogenous FABP4 and FABP5 in

transcriptional and metabolic regulation in ADSC. FABP4 and FABP5 were not expressed in ADSC. However, both FABP4 and FABP5 were significantly induced after adipocyte differentiation of ADSC and were secreted from the differentiated adipocytes. Analysis of microarray data, including gene ontology enrichment analysis and cascade analysis of the protein-protein interaction network using a transcription factor binding site search, demonstrated that treatment of ADSC with FABP4 or FABP5 affected several kinds of genes related to inflammatory and metabolic responses and the process of cell differentiation. Notably, myogenic factors, including myocyte enhancer factors, myogenic differentiation 1 and myogenin, were modulated by treatment of ADSC with FABP4, indicating that exogenous FABP4 treatment is partially associated with myogenesis in ADSC. Metabolome analysis showed that treatment of ADSC with FABP4 and with FABP5 similarly, but differently in extent, promoted hydrolysis and/or uptake of lipids, consequentially together with enhancement of β oxidation , inhibition of downstream of the glycolysis pathway, accumulation of amino acids, reduction of nucleic acid components and increase in the ratio of reduced and oxidized nicotinamide adenine dinucleotide phosphates ($NADPH/NADP^+$), an indicator of reducing power, and the ratio of adenosine triphosphate and adenosine monophosphate (ATP/AMP), an indicator of the energy state, in ADSC. In conclusion, secreted FABP4 and FABP5 from adipocytes as adipokines differentially affect transcriptional and metabolic regulation in ADSC near adipocytes. The adiposity condition in the host of regenerative medicine may affect characteristics of ADSC by exposure of the balance of FABP4 and FABP5.

Research Background

Adipocyte-derived stem cells (ADSC), which exist near adipocytes in adipose tissue, have been used as a potential tool of regenerative medicine. Lipid chaperones, fatty acid-binding protein 4 (FABP4) and 5 (FABP5), are abundantly expressed in adipocytes. FABP4 has recently been shown to be secreted from adipocytes during lipolysis in a non-classical pathway and may act as an adipokine.

Research Results

FABP4 and FABP5 were not expressed in ADSC. However, both FABP4 and FABP5 were significantly induced after adipocyte differentiation of ADSC and were secreted from the differentiated adipocytes. Analysis of microarray data, including gene ontology enrichment analysis and cascade analysis of the protein-protein interaction network using a transcription factor binding site search, demonstrated that treatment of ADSC with FABP4 or FABP5 affected several kinds of genes related to inflammatory and metabolic responses and the process of cell differentiation. Notably, myogenic factors, including myocyte enhancer factors, myogenic differentiation 1 and myogenin, were modulated by treatment of ADSC with FABP4, indicating that exogenous FABP4 treatment is partially associated with myogenesis in ADSC. Metabolome analysis showed that treatment of ADSC with FABP4 and with FABP5 similarly, but differently in extent, promoted hydrolysis and/or uptake of lipids, consequentially together

with enhancement of β xidation, inhibition of downstream of the glycolysis pathway, accumulation of amino acids, reduction of nucleic acid components and increase in the ratio of reduced and oxidized nicotinamide adenine dinucleotide phosphates (NADPH/$NADP^+$), an indicator of reducing power, and the ratio of adenosine triphosphate and adenosine monophosphate (ATP/AMP), an indicator of the energy state, in ADSC. In conclusion, secreted FABP4 and FABP5 from adipocytes as adipokines differentially affect transcriptional and metabolic regulation in ADSC near adipocytes.

Research Summary and Future Perspective

The adiposity condition in the host of regenerative medicine may affect characteristics of ADSC by exposure of the balance of FABP4 and FABP5.

Publication

YamamotoT, Furuhashi M, Sugaya T, Oikawa T, Matsumoto M, Funahashi Y,Mastukawa Y, Gotoh M, Miura T. Transcriptome and metabolome analyses in exogenous FABP4- and FABP5-treated adipocyte-derived stem cells, *PLOS One*, Dec. 9,2016.

Japanese ver.

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