Cytochrome P450 1a (CYP1A)-Knockout Javanese Medaka Fish Exhibit Diabetic Traits and Reduced Reproductive Capacity

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Source FASEB JOURNAL

View Journal Impact

Volume: 40 Issue: 12

DOI: 10.1096/fj.202502623R

Article Number e71935

Published JUN 22 2026

Indexed 2026-06-26

Document Type Article

Abstract

Cytochrome P450 1A (CYP1A) is an enzyme localized in the endoplasmic reticulum of liver cells. Although its roles in detoxification of exogenous substances have been investigated, its endogenous functions remain poorly understood. Here, we compared liver transcriptomes of CYP1A-knockout (KO) Javanese medaka (Oryzias javanicus) with those of wild-type (WT) fish to determine the physiological roles of CYP1A. We identified 508 differentially expressed genes (DEGs), including genes involved in glucose metabolism that were highly upregulated, such as insulin, glucagon, and somatostatin. KO fish exhibited elevated blood glucose levels, increased liver mass, and higher hepatic triglyceride levels, together with upregulation of glucose-regulatory genes, suggesting insulin resistance and a diabetic-like condition. In addition, some genes associated with reproduction, including zona pellucida sperm-binding proteins 1 and 3 (ZP1 and ZP3), were downregulated. Decreased spawning rates and fertilization rates confirmed reduced reproductive capacity in KO fish. Thus, this study demonstrates that CYP1A has endogenous functions in glucose homeostasis and reproduction. The CYP1A-KO strain is expected to serve as a model for investigating detailed physiological processes related to diabetes and reproductive mechanisms, as well as the relationship between these processes mediated by CYP1A.

Keywords

Author Keywords: genome editing; glucose metabolism; insulin resistance; PI3K-Akt signaling; zona pellucida

Keywords Plus: GLYCOGEN-METABOLISM; ARACHIDONIC-ACID; GENE-EXPRESSION; INSULIN; STRESS; METALLOTHIONEIN; INDUCTION; PANCREAS; MODEL

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Data availability statement Raw RNA sequencing data reported are available in the DDBJ Sequenced Read Archive under BioProject ID PRJDB19647.

Conflict of interest statement The authors declare no conflicts of interest.

Categories/ Classification Research Areas: Biochemistry & Molecular Biology; Life Sciences & Biomedicine - Other Topics; Cell Biology

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Funding

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Ministry of Education, Culture, Sports, Science and Technology, Japan (MEXT) Japan Society for the Promotion of Science	JPJSCCB20200009	Hide details
Appeared in source as: Japan Society for the Promotion of Science (JSPS)		
The Interdisciplinary Collaborative Research Program of Atmosphere and Ocean Research Institute, The University of Tokyo	JURCAOSIRG24-10	
The University of Tokyo FSI-Nippon		

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Journal information

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ISSN	0892-6638
eISSN	1530-6860
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Table of Contents	Current Contents Connect
Research Areas	Biochemistry & Molecular Biology; Life Sciences & Biomedicine - Other Topics; Cell Biology
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