

Faculty members

Professor; Kenji IIZUKA, M.D., Ph.D.
 Associate Professor; Takuji MACHIDA, Ph.D.
 Assistant Professor; Sachiko HIRAIDE, Ph.D.

Outline and research fields

Major research projects of pathophysiology division have been focused on following two fields.

1) Smooth muscle and skeletal muscle pathophysiology & pharmacology

- * Effect of pressure stress on skeletal muscle and smooth muscle cell functions, particularly on production of vasodilating substances.
- * Protective roles of n-3 unsaturated fatty acids and their metabolites in the cardiovascular system.

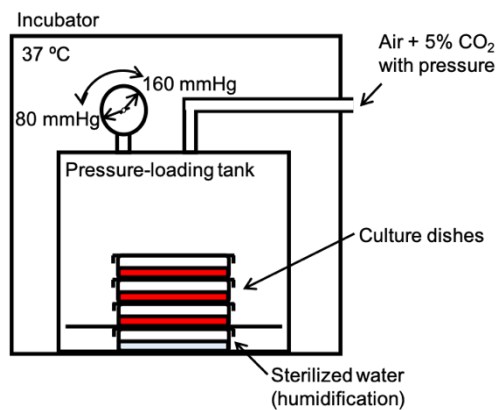


Fig. 1. Pulsatile pressure-loading apparatus

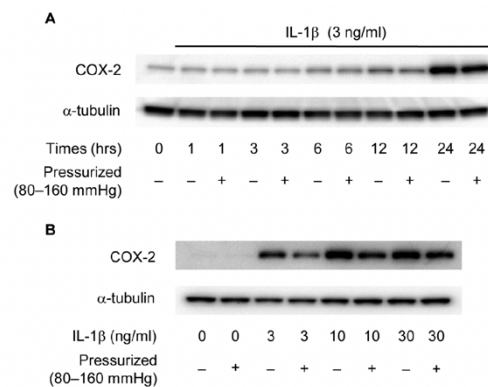


Fig. 2. Pulsatile pressure stress reduces COX-2 protein expression induced by IL-1β in rat vascular smooth muscle cells (Machida et al., 2021)

2) Gastrointestinal pathophysiology & pharmacology

- * Roles of 5-hydroxytryptamine and substance P in cancer chemotherapy-induced nausea and vomiting.

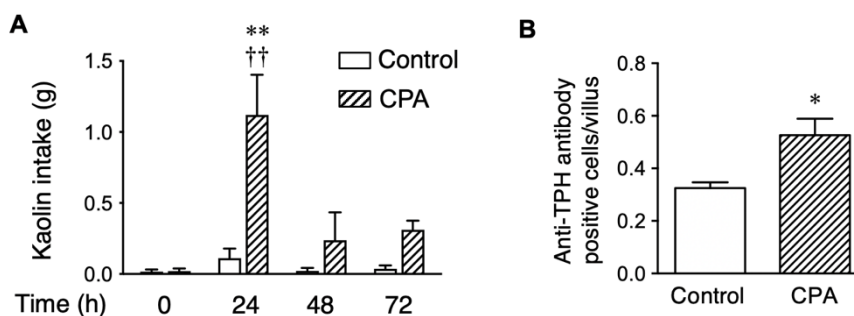


Fig. 3. Effect of cyclophosphamide (CPA) on pica behavior and the number of anti-tryptophan hydroxylase (TPH) antibody-positive cells in rat ileal tissue (Kamiya et al., 2021)

Current publications

Ferric citrate hydrate has little impact on hyperplasia of enterochromaffin cells in the rat small intestine compared to sodium ferrous citrate. Machida, T., Hiraide, S., Yamamoto, T., Shiga, S., Hasebe, S., Fujibayashi, A. & Iizuka K. *Pharmacology* in press, 2022.

Noradrenaline increases intracellular Ca²⁺ concentration in epithelial cells via α 2-adrenoceptors in isolated mouse ileal crypts. Kimyo, T., Machida, T., Iizuka K., Minami, M. & Hirafuji, M. *J Pharmacol Sci.* 148;337–341, 2022.

Methotrexate mediates the integrity of intestinal stem cells partly through nitric oxide-dependent Wnt/ β -catenin signaling in methotrexate-induced rat ileal mucositis. Machida, M., Machida, T., Kikuchi, M., Shimizu, A., Ida, S., Tawaraya, Y., Kato, R., Haramaki, K., Yama, K., Shiga, S., Hirafuji, M. & Iizuka, K. *J Pharmacol Sci.* 148;281–285, 2022.

Methotrexate induces hyperplasia of enterochromaffin cells in mouse jejunum. Machida, T., Tanaka, A., Kobayashi, M., Imai, K., Hirafuji, M. & Iizuka K. *BPB Reports.* 4:112–115, 2021.

Administration of cyclophosphamide to rats induces pica and potentiates 5-hydroxytryptamine synthesis in the intestine without causing severe intestinal injury. Kamiya, A., Machida, T., Hirano, M., Machida, M., Shiga, S., Hamaue, N., Hirafuji, M. & Iizuka K. *J Pharmacol Sci.* 147:251–259, 2021.

Abnormal pressure stress reduces interleukin-1 β -induced cyclooxygenase-2 expression in cultured rat vascular smooth muscle cells. Machida, T., Endo, H.E., Oyoshi, R., Yutani, M., Machida M., Shiga, S., Murakami, H., Hiraide, S., Hirafuji, M. & Iizuka K. *Biol Pharm Bull.* 44:853–860, 2021.

Effects of nafamostat mesilate on 5-hydroxytryptamine release from isolated ileal tissues induced by anti-cancer drugs in rats. Kikuchi, K., Hamaue, N., Machida, T., Iizuka K., Minami, M., & Hirafuji, M. *Biomed Res.* 41:253–257, 2020.

Role of nitric oxide in the change of 5-hydroxytryptamine synthesis in the intestine by a consecutive administration of methotrexate to rats. Machida, T., Inotani, A., Shiga, S., Kon, S., Yanada, T., Kobayashi, H., Hamaue, N., Hirafuji, M. & Iizuka K. *Pharmacology* 105:723–728, 2020.

The role of nitric oxide in small intestine differs between a single and a consecutive administration of methotrexate to rats. Shiga, S., Machida, T., Yanada, T., Machida, M., Hirafuji, M. & Iizuka K. *J Pharmacol Sci.* 143:30–38, 2020.

Nitric oxide plays a critical role in methotrexate-induced hyperplasia of enterochromaffin cells containing 5-hydroxytryptamine in rat small intestine. Takano, Y., Hirano, M., Machida, T., Obara, Y., Hamaue, N., Fujita, K., Taniguchi, M., Endo, T., Shiga, S., Machida, M., Iizuka K. & Hirafuji, M. *J Pharmacol Sci.* 141:32-40, 2019.

Potential of glucagon-like peptide-2 dynamics by methotrexate administration in rat small intestine. Machida, M., Shiga, S., Machida, T., Ohno, M., Iizuka, K. & Hirafuji, M. *Biol Pharm Bull.* 42:1733-40, 2019.

【 Education Field 】
Pharmacotherapeutics
Pharmacology
Pathophysiology

【 Research Field 】
Vascular pharmacology
Gastrointestinal pharmacology
Pathophysiology
Neuropsychopharmacology
Cardiology