

## The Research Outputs of the fiscal year of 2023

### Center for Metabolic Regulation of Healthy Aging (CMHA), Faculty of Life Sciences, Kumamoto University

#### ● Division of Metabolic and Cardiovascular Research

##### 1) Department of Medical Biochemistry

1. Yamazaki M, Hino S, Usuki S, Miyazaki Y, Oda T, Nakao M, Ito T, Yamagata K: YAP/BRD4-controlled ROR1 promotes tumor-initiating cells and hyperproliferation in pancreatic cancer. *EMBO J* e112614, 2023
2. Tsuyama T, Sato Y, Yoshizawa T, Matsuoka T, Yamagata K: Hypoxia causes pancreatic b-cell dysfunction and impairs insulin secretion by activating the transcriptional repressor BHLHE40. *EMBO reports* e56227, 2023
3. Guo X, Tan S, Wang T, Sun R, Li S, Tian P, Li M, Wang Y, Zhang Y, Yan Y, Dong Z, Yan L, Yue X, Wu Z, Li C, Yamagata K, Gao L, Ma C, Li T, Liang X: NAD<sup>+</sup> salvage governs mitochondrial metabolism invigorating NK cell anti-immunity. *Hepatology* 78: 468-485, 2023
4. Yamagata K, Mizumoto T, Yoshizawa T: The emerging role of SIRT7 in glucose and lipid metabolism. *Cells* 13: 48, 2023

##### 2) Department of Molecular Genetics

1. Morinaga J, Kashiwabara K, Torigoe D, Okadome Y, Aizawa K, Uemura K, Kurashima A, Matsunaga E, Fukami H, Horiguchi H, Sato M, Sugizaki T, Miyata K, Kadomatsu T, Mukoyama M, Miyauchi K, Hokimoto S, Fukumoto Y, Hiro T, Hibi K, Nakagawa Y, Sakuma I, Ozaki Y, Iwata H, Iimuro S, Daida H, Shimokawa H, Kimura T, Matsuzaki M, Saito Y, Matsuyama Y, Nagai R, Oike Y: Plasma ANGPTL8 levels and risk for secondary cardiovascular events in Japanese patients with stable coronary artery disease receiving statin therapy. *Arterioscler Thromb Vasc Biol* 43: 1549-1559, 2023
2. Kadomatsu T, Hara T, Kurahashi R, Horiguchi H, Morinaga J, Miyata K,

Kurano S, Kanemaru H, Fukushima S, Araki K, Baba M, Linehan M W, Kamba T, Oike Y: ANGPTL2-mediated epigenetic repression of MHC-I in tumor cells accelerates tumor immune evasion. *Mol Oncol* 17:2637-2658, 2023

3. Horiguchi H, Kadomatsu T, Yamashita T, Yumoto S, Terada K, Sato M, Morinaga J, Miyata K, Oike Y: ANGPTL2 promotes immune checkpoint inhibitor-related murine autoimmune myocarditis. *Commun Biol* 6:965, 2023
4. Fukami H, Morinaga J, Nakagami H, Hayashi H, Okadome Y, Matsunaga E, Kadomatsu T, Horiguchi H, Sato M, Sugizaki T, Miyata K, Torigoe D, Mukoyama M, Morishita R, Oike Y: Efficacy and safety in mice of repeated, lifelong administration of an ANGPTL3 vaccine. *npj Vaccines* 8:168, 2023
5. Okadome Y, Morinaga J, Yamanouchi Y, Matsunaga E, Fukami H, Kadomatsu T, Horiguchi H, Sato M, Sugizaki T, Hayata M, Sakaguchi T, Hirayama R, Ishimura T, Kuwabara T, Usuku K, Yamamoto T, Mukoyama M, Suzuki R, Fukui T, Oike Y: Increased numbers of pre-operative circulating monocytes predict risk of developing cardiac surgery-associated acute kidney injury in conditions requiring cardio pulmonary bypass. *Clin Exp Nephrol* 27:329-339, 2023
6. Terada K, Endo M, Kiyonari H, Takeda H, Oike Y: Loss of Dj2 accompanies pH deviation in lysosomes and lysosome-related organelles. *J Cell Physiol*, 2023 Online ahead of print
7. Horiguchi H, Kadomatsu T, Yamashita T, Yumoto S, Horino T, Sato M, Terada K, Miyata K, Ichigozaki Y, Kimura T, Fukushima S, Moroishi T, Oike Y: Tumor stroma-derived ANGPTL2 potentiates immune checkpoint inhibitor efficacy. *Cancer Gene Ther* doi: 10.1038/s41417-024-00757-9. Online ahead of print, 2024.

### 3) Department of Metabolic Medicine

1. Araki H, Matsumura T, Furukawa N, Araki E. Updates of incretin-related drugs for the treatment of type 2 diabetes. *Journal of Diabetes Investigation*. 14(2):189-192. 2023.
2. Araki H, Hino S, Anan K, Kuribayashi K, Etoh K, Seko D, Takase R, Kohroggi K, Hino Y, Ono Y, Araki E, Nakao M. LSD1 defines the fiber type-selective responsiveness to environmental

stress in skeletal muscle. *eLife* 12: e84618, 2023.

3. Matsushima-Nagata K, Matsumura T, Kondo Y, Anraku K, Fukuda K, Yamanaka M, Manabe M, Irie T, Araki E, Sugiuchi H. Significance of Circulating Remnant Lipoprotein Cholesterol Levels Measured by Homogeneous Assay in Patients with Type 2 Diabetes. *Biomolecules*. 13(3):468. 2023.
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5. Basile G, Vetere A, Hu J, Ijaduola O, Zhang Y, Liu KC, Eltony AM, De Jesus DF, Fukuda K, Doherty G, Leech CA, Chepurny OG, Holz GG, Yun SH, Andersson O, Choudhary A, Wagner BK, Kulkarni RN. Excess pancreatic elastase alters acinar- $\beta$  cell communication by impairing the mechano-signaling and the PAR2 pathways. *Cell Metab*. 11;35(7):1242-1260.e9. 2023.
6. Murata Y, Haneda M, Miyakawa N, Nishida S, Kajihara N, Maeda S, Ono K, Hanatani S, Igata M, Takaki Y, Motoshima H, Kishikawa H, Araki E. A Case of Autoimmune Polyglandular Syndrome Type 3 Complicated with IgG4-related Disease. *Intern Med*. 2023. In press.
7. Toma T, Miyakawa N, Tateishi M, Todaka M, Kondo T, Fujita M, Otsuka M, Araki E, Tateishi H. An ADAM17 selective inhibitor promotes glucose uptake by activating AMPK. *J Pharmacol Sci*. 154(1):37-46. 2024.

#### 4) Department of Cardiovascular Medicine

1. Kawahara Y, Kanazawa H, Takashio S, Tsuruta Y, Sumi H, Kiyama T, Kaneko S, Ito M, Hoshiyama T, Hirakawa K, Ishii M, Tabata N, Yamanaga K, Fujisue K, Hanatani S, Sueta D, Arima Y, Araki S, Usuku H, Nakamura T, Yamamoto E, Soejima H, Matsushita K, Kawano H, Tsujita K. Clinical, electrocardiographic, and echocardiographic parameters associated with the development of pacing and implantable cardioverter-defibrillator indication in patients with transthyretin amyloid cardiomyopathy. *Europace*. (in press), 2023
2. Kuyama N, Takashio S, Nagakura T, Imamura M, Takamatsu K, Takae M, Hirakawa K, Yamanaga K, Hanatani S, Yamamoto E, Matsushita K, Ueda M, Tsujita K. Anti-Kv1.4 Antibody Without Myasthenia Gravis: A Rare Cause of Autoimmune Myocarditis and Myositis. *JACC*

*Case Rep.* 9:101734, 2023

3. Soejima H, Ogawa H, Morimoto T, Okada S, Matsumoto C, Nakayama M, Masuda I, Jinnouchi H, Waki M, Saito Y. Kidney function deterioration is dependent on blood pressure levels: 11.2year follow-up in diabetic patients. *Heart Vessels*.37(11):1873-1881, 2022
4. Sumi H, Hoshiyama T, Morihisa K, Noda K, Kaneko S, Kanazawa H, Ishii M, Fujisue K, Sueta D, Takashio S, Usuku H, Matsushita K, Tsujita K. Effect of Contact Vector Direction on Achieving Cavotricuspid Isthmus Block. *Sci Rep.* 13(1):2579, 2023
5. Takashio S, Morioka M, Ishii M, Morikawa K, Hirakawa K, Hanatani S, Oike F, Usuku H, Kidoh M, Oda S, Yamamoto E, Matsushita K, Ueda M, Tsujita K. Clinical characteristics, outcome, and therapeutic effect of tafamidis in wild-type transthyretin amyloid cardiomyopathy. *ESC Heart Fail.* (in press), 2023
6. Takashio S, Kato T, Tashima H, Irie H, Komohara Y, Oguni T, Morikawa K, Kuyama N, Tabata N, Hanatani S, Yamamoto E, Matsushita K, Ueda M, Tsujita K. Prevalence of cardiac amyloidosis in patients undergoing carpal tunnel release with amyloid deposition. *Circ J.* (in press), 2023
7. Usuku H, Yamamoto E, Sueta D, Noguchi M, Fujisaki T, Egashira K, Oike F, Fujisue K, Hanatani S, Arima Y, Takashio S, Kawano Y, Oda S, Kawano H, Matsushita K, Ueda M, Matsui H, Matsuoka M, Tsujita K. Prognostic value of right ventricular global longitudinal strain in patients with immunoglobulin light-chain cardiac amyloidosis. *Eur Heart J Open.* (in press), 2023

## 5) Department of Cell Pathology

1. Anami T, Ibe Y, Li L, Komohara Y, Hirao H, Harada M, Yano H, Fujiwara Y, Motoshima T, Yatsuda J, Hibi T, Kamba T. Overexpression of SerpinB9 in non-seminomatous germ cell tumors. *Med Mol Morphol.* 2023
2. Anami T, Pan C, Fujiwara Y, Komohara Y, Yano H, Saito Y, Sugimoto M, Wakita D, Motoshima T, Murakami Y, Yatsuda J, Takahashi N, Suzu S, Asano K, Tamada K, Kamba T. Dysfunction of sinus macrophages in tumor-bearing host induces resistance to immunotherapy. *Cancer Sci.* 2023
3. Matsubara E, Shinchi Y, Komohara Y, Yano H, Pan C, Fujiwara Y, Ikeda K, Suzuki M. PD-L2 overexpression on tumor-associated macrophages is one of the predictors for better prognosis in lung adenocarcinoma. *Med Mol Morphol.* 56:250-256, 2023
4. Oguro A, Fujiyama T, Ishihara Y, Kataoka C, Yamamoto M, Eto K, Komohara Y, Imaoka S, Sakuragi T, Tsuji M, Shibata E, Kotake Y, Yamazaki T. Maternal DHA intake in mice increased DHA metabolites in the pup brain and ameliorated MeHg-induced behavioral disorder. *J Lipid Res.* 64:100458, 2023.

5. Yamada R, Ohnishi K, Pan C, Yano H, Fujiwara Y, Shiota T, Mikami Y, Komohara Y. Expression of macrophage/dendritic cell-related molecules in lymph node sinus macrophages. *Microbiol Immunol.* 67:490-500, 2023
6. Takashio S, Kato T, Tashima H, Irie H, Komohara Y, Oguni T, Morikawa K, Kuyama N, Tabata N, Hanatani S, Yamamoto E, Matsushita K, Ueda M, Tsujita K. Prevalence of Cardiac Amyloidosis in Patients Undergoing Carpal Tunnel Release With Amyloid Deposition. *Circ J.* 87:1047-1055, 2023
7. Panawan O, Silsirivanit A, Chang CH, Putthisen S, Boonnate P, Yokota T, Nishiyama-Ikeda Y, Detarya M, Sawanyawisuth K, Kaewkong W, Muisuk K, Luang S, Vaeteewoottacharn K, Kariya R, Yano H, Komohara Y, Ohta K, Okada S, Wongkham S, Araki N. Establishment and characterization of a novel cancer stem-like cell of cholangiocarcinoma. *Cancer Sci.* 114:3230-3246, 2023
8. Miura Y, Motoshima T, Anami T, Yano H, Mito R, Pan C, Urakami S, Kinowaki K, Tsukamoto H, Kurahashi R, Murakami Y, Yatsuda J, Fujiwara Y, Kamba T, Komohara Y. Predictive value of CXCL10 for the occurrence of immune-related adverse events in patient with renal cell carcinoma. *Microbiol Immunol.* 67:345-354, 2023
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10. Adawy A, Li L, Hirao H, Irie T, Yoshii D, Yano H, Fujiwara Y, Esumi S, Honda M, Suzu S, Komohara Y, Hibi T. Potential involvement of IL-32 in cell-to-cell communication between macrophages and hepatoblastoma. *Pediatr Surg Int.* 39:275, 2023.
11. Tatetsu H, Watanabe M, Liu J, Tokunaga K, Iwanaga E, Komohara Y, Thrash E, Bassal MA, Matsuoka M, Tenen DG, Chai L. Dissecting the cell of origin of aberrant SALL4 expression in myelodysplastic syndrome. *Clin Transl Med.* 13:e1327, 2023.
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17. Nakamura E, Maekawa K, Saito Y, Matsumoto T, Ogawa M, Komohara Y, Asada Y, Yamashita A. Altered choline level in atherosclerotic lesions: Upregulation of choline transporter-like protein 1 in human coronary unstable plaque. *PLoS One.* 18:e0281730, 2023.
18. Matsuzaki H, Komohara Y, Yano H, Fujiwara Y, Kai K, Yamada R, Yoshii D, Uekawa K, Shinojima N, Mikami Y, Mukasa A. Macrophage colony stimulating factor potentially induces recruitment and maturation of macrophages in recurrent pituitary neuroendocrine tumors. *Microbiol Immunol.* 67:90-98, 2023.
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22. Honda M, Kadohisa M, Yoshii D, Komohara Y, Hibi T. Intravital imaging of immune responses in intestinal inflammation. *Inflamm Regen*. 43:9, 2023.
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## 6) Department of Medical Cell Biology

1. Kuwayama N, Kujirai T, Kishi Y, Hirano R, Echigoya K, Fang L, Watanabe S, Nakao M, Suzuki Y, Ishiguro K, Kurumizaka H, and Gotoh Y. HMGA2 directly mediates chromatin condensation in association with neuronal fate regulation. *Nature Commun.* 14: 6420, 2023.
2. Ikeda R, Noshiro D, Morishita H, Takada S, Kagaeyama S, Fujioka Y, Funakoshi T, Komatsu-Hirota S, Arai R, Ryzhii E, Abe M, Koga T, Nakao M, Sakimura K, Horii A, Waguri S, Ichimura Y, Noda N, and Komatsu M. Phosphorylation of phase-separated p62 bodies by ULK1 activates a redox-independent stress response. *EMBO J.* e113349, 2023.
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## 7) Laboratory of Developmental Cardiology

1. Wenjuan Ma, Shah Adil Ishtiyahq Ahmad, Michihiro Hashimoto, Ahad Khalilnezhad, Miho Kataoka, Yuichiro Arima, Yosuke Tanaka, Shigeru Yanagi, Terumasa Umemoto, Toshio Suda. MITOL deficiency triggers hematopoietic stem cell apoptosis via ER stress response. *The EMBO Journal* 43(3) 339-361, 2024
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3. Kaoru Mizukami, Hiroki Higashiyama, Yuichiro Arima, Koji Ando, Norihiro Okada, Katsumi Kose, Shigehito Yamada, Jun K Takeuchi, Kazuko Koshiba-Takeuchi, Shigetomo Fukuhara, Sachiko Miyagawa-Tomita, Hiroki Kurihara. Coronary artery established through amniote evolution. *eLife* 12:e83005, 2023



4. Kush Ketan Patel, Cynthia Venkatesan, Habiba Abdelhalim, Saman Zeeshan, Yuichiro Arima, Suvi Linna-Kuosmanen, Zeeshan Ahmed. Genomic approaches to identify and investigate genes associated with atrial fibrillation and heart failure susceptibility. *Human genomics* 17(1) 47-47, 2023

## 8) Department of Nephrology

1. Deng QY, Kakizoe Y, Iwata Y, Nakagawa T, Miyasato Y, Nakagawa M, Nishiguchi K, Nagayoshi Y, Adachi M, Narita Y, Izumi Y, Kuwabara T, Tsuda Y, Mukoyama M: The serine protease plasmin plays detrimental roles in epithelial sodium channel activation and podocyte injury in Dahl salt-sensitive rats. *Hypertens Res* 46 (1): 50-62, 2023.
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4. Izumi Y, Date R, Mizumoto T, Nakagawa T, Kakizoe Y, Adachi M, Kuwabara T, Mukoyama M: A case of chyluria with nephrotic-range proteinuria caused by lymphatic malformation, leading to a diagnosis of Klippel-Trenaunay syndrome. *CEN Case Rep* 12 (2): 205-209. 2023.
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9. Miyasato Y, Hanna RM, Moringa J, Mukoyama M, Kalantar-Zadeh K: Prognostic nutritional index as a predictor of mortality in 101,616 patients undergoing hemodialysis. *Nutrients* **15** (2): 311, 2023.
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## ○Data Science/Omics Analysis Research and Support Division

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