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Areas of Expertise
Cell Signaling, Molecular Biology, Proteomics, Protein Kinase CK2, Cancer Biology, Epigenetics

Education, Research, and Professional Experience (Born in Tokyo, Japan)
MSc in Medical Science, Faculty of Medicine, The University of Tokyo
PhD in Medical Science, Dept. Biochemistry, Faculty of Medicine, The University of Tokyo
JSPS Fellowship for Japanese Junior Scientists
Research Associate at the Department of Hygiene and Oncology, Tokyo Medical and Dental University
Research Associate at the Department of Immunology, Fukushima Medical University School of Medicine
Research Associate at the Department of Biomolecular Sciences, Associate Professor at FMU
Visiting Scientist at University of Washington, Seattle (Professor Edwin G. Krebs, and Professor John D. Scott)
Visiting Scientist at University of Colorado, Boulder (Professor Natalie G. Ahn)
Fellow, Center for Research and Development / Japan Science and Technology Agent

Membership of Academic Societies:
The Japanese Biochemical Society (Councilor in Tohoku, 2009-2014)
The Molecular Biology Society of Japan (Secretory General, 2013-2016)
The Japanese Association for Cancer Research (Councilor, 2022-2024)
Japan Human Proteome Organization
Quantum Life Science Society Japan
The American Association for the Advancement of Science
The American Society for Biochemistry and Molecular Biology
The American Society for Pharmacology
Editorial Associate Board of *Molecular Pharmacology* (2016-)
Associate Editor of *Cancer Science* (2022-)

Awards:
Nissan Science Foundation
Yamada Science Foundation
The Japan Foundation for Aging and Health
The Society for Japanese Women Scientists, Promising Scientific Award
Fukushima Medical University School of Medicine, Faculty Encouragement Award

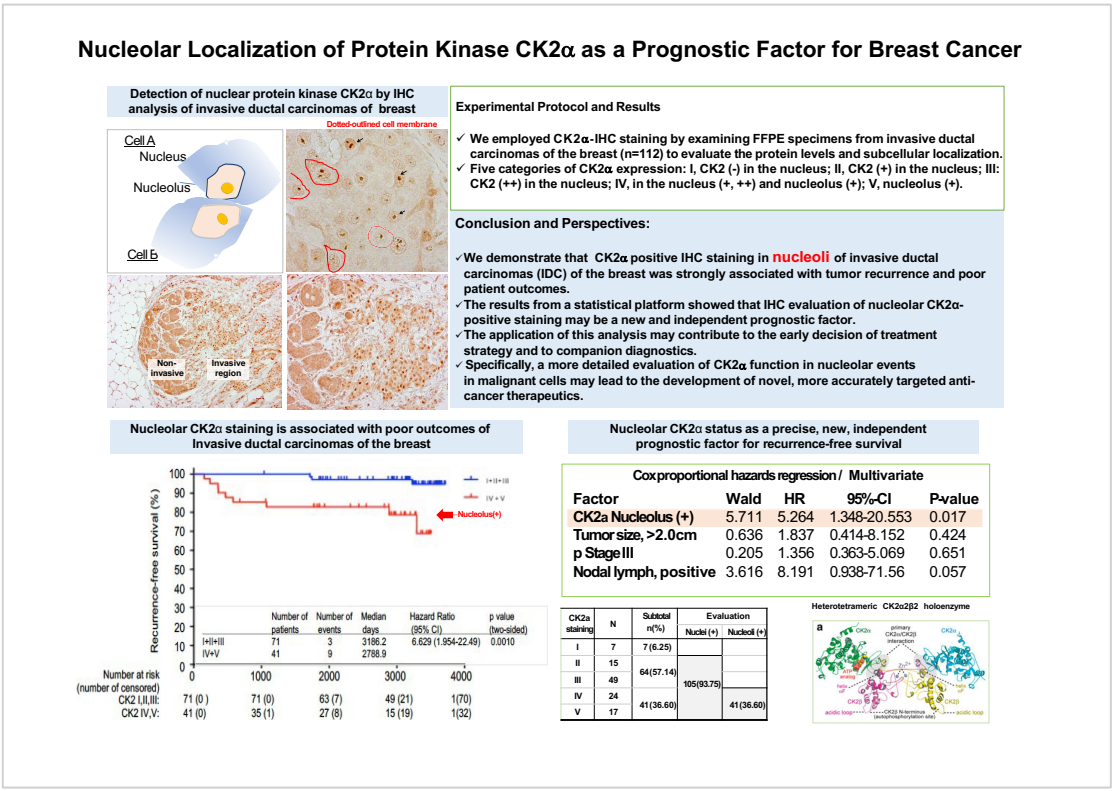
Related Links
FMU: https://www.fmu.ac.jp/kenkyu/html/157_en.html
Gender Equality Bureau Cabinet Office Japan: http://wwwb.cao.go.jp/yakuin/cor004/index/137
Organized Symposium on Gender Equality: https://www.gender.go.jp/public/event/2013/pdf/flyer_renkei0202.pdf
Unconscious Bias (March2019): https://www.djrenrakukai.org/doc_pdf/2019/UnconsciousBias_leaflet_eng.pdf
Career Girls: https://www.careergirls.org/role-models/medical-scientist-miwako-kato/?v=typical-day-japanese

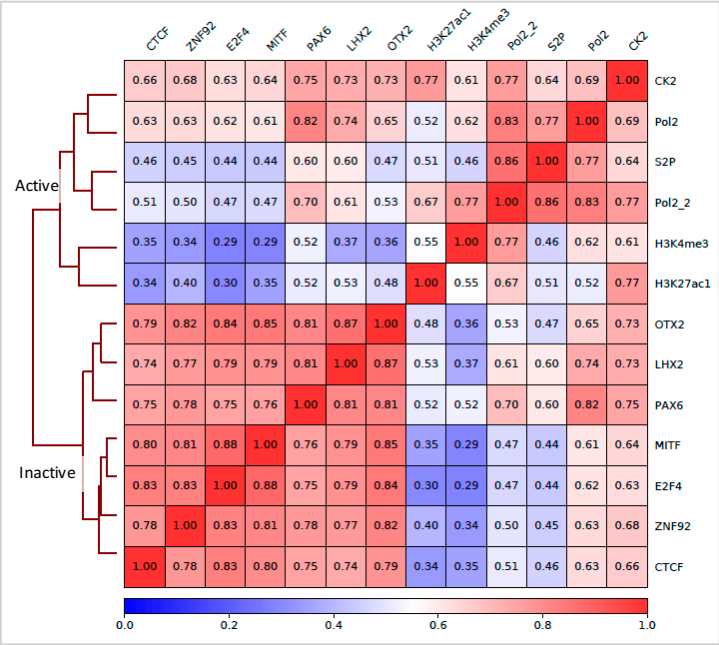
Research Focus and Objectives:

We have been studying intracellular signaling pathways, especially phosphorylation, in order to understand pathogenesis of various diseases. We have found that changes in activity and intracellular dynamics of protein kinase CK2 are associated with the prognosis of cancer recurrence, and are investigating underlying molecular mechanisms of CK2 using molecular biology, proteomics, and bioinformatics, as well as developing highly sensitive CK2 detection methods. Our goals are to discover target molecules that inhibit cancer recurrence due to malignant transformation, so as to clarify the scientific basis for translational research at the biomolecular level. We will also strive to nurture individuals who understand basic research and global trends, who will dedicate their lives to advancing original science, while adhering to the highest ethical principles.

Research Outline:

CK2 (Casein kinase 2/II), is a proliferation-related, serine/threonine kinase found in all eukaryotic cells and is essential for survival. Our group discovered that CK2 migrates from the cytoplasm to the nucleus when the cell cycle of normal fibroblasts synchronously progresses to the proliferative phase. We also found a growth stimulus-dependent increase in CK2 activity in both the cytoplasm and the nucleus. Furthermore, we ascretained that CK2 activity is regulated by *in vivo* interaction with APC protein, a tumor suppressor gene product. We learned that eIF5 (a eukaryotic translation initiation factor) is a CK2 target molecule during the proliferative phase, and also found that eIF5 contributes to normal cell cycle progression after it is phosphorylated by CK2. In addition, by analyzing human breast cancer surgical specimens, we discovered that an increase in CK2 expression in cancer cell nuclei and an accumulation of CK2 molecules in the nucleolus are associated with a poor prognosis (recurrence) of breast cancer. Statistical analysis of CK2 staining results revealed that CK2 nucleolar accumulation is the only independent variable that determines the length of recurrence-free survival (recurrence after several years). Therefore, we filed a patent application in 2019 and a PCT application in 2020 for CK2 as a novel marker for cancer prognosis, and we are now in the process of transferring the application to other countries. We are currently analyzing the relationship between CK2 nuclear accumulation and cancer recurrence in solid tumors other than breast cancer.





Furthermore, using ChIP-Seq analysis and other molecular biological methods to investigate CK2 function, we have revealed that CK2 is involved in epigenetic regulation of transcription in a cell cycle-dependent manner. Therefore, we are currently conducting molecular biological studies using various invasive cancer cell lines and clinical samples to determine how CK2 activates specific gene expression and translational processes, and consequently contributes to pathological conditions such as cancer progression (recurrence). We have also started to utilize multiplex-staining and tissue transparency techniques as well as integrative studies involving bioinformatics, proteomics, ChIP-Seq, single cell RNA, and spatial transcriptomics (spatial RNA expression analysis).

1. Development of biomarkers for cancer prognosis:

Prevention of cancer progression, such as tissue invasion and metastasis, which might be observed months after cancer resection, is important to maintain physiological functions for human well-being. We are conducting research to develop new biomarkers that are expected to be more sensitive and precise than current clinical staging and prognostic indicators, as well as to reveal intracellular functions of these markers.

(Homma, M.K., et al. *Cancer Science* 2021, Homma, M.K., et al. *Lancet Oncology (Abstract) 2022*)

2. Comprehensive analysis of phosphorylation signaling associated with proliferative diseases:

Follicular liver cancer (FL-HCC), a rare juvenile disease, is thought to be associated with a mutated gene, DNAJB1-PKAC, which consists of DNAJB1 fused to the catalytic site of protein kinase A (PKA) enzyme. We are analyzing oncogenic signals using a phospho-proteomics approach employing gene-expressing cell lines to identify cancer-driver gene-specific pathways.

(Kevin, M., et al. *Pediatrics* 2016)

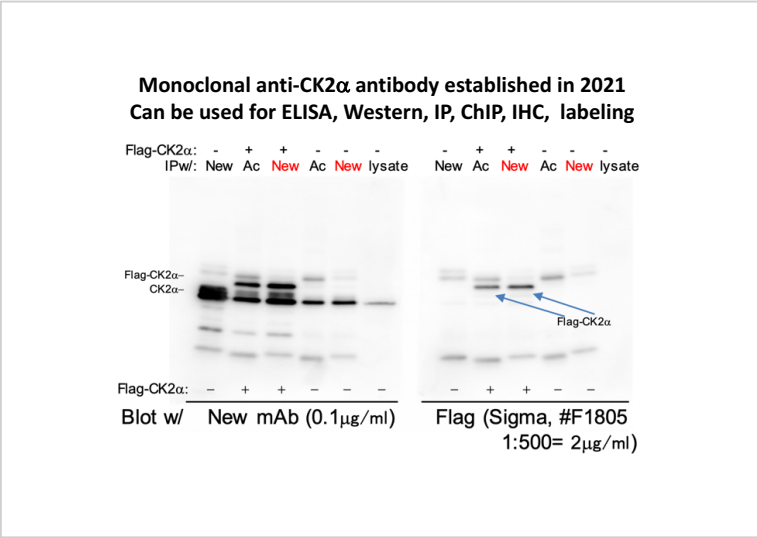
3. Cell signaling driven by protein kinases for progression of the cell cycle:

We have found that APC protein, the causative gene product of familial adenomatous polyposis (FAP), interacts with CK2 and that APC is an upstream regulator of CK2 catalytic activity. Furthermore, we revealed that CK2 phosphorylates eukaryotic translational initiation factor eIF5 during cell cycle progression as a downstream signaling molecule, and clarified the mechanism by which CK2 is involved in cell cycle progression. We recently published a study showing that phosphorylated CK2 translocates from the cytosol to the nucleus where CK2 is recruited to the active gene promoter locus.

(Homma, M.K., et al. *PNAS* 2002; Homma, M.K., *PNAS* 2005; Homma, M.K. *Life Science Alliance* 2023)

Message to students:

We expect graduate and undergraduate students who are interested in our projects, to become active researchers. We seek to encourage their scientific curiosity through interactions with colleagues and distinguished scientists overseas, and to conduct research ethically.



Our research is based on the connection between basic molecular science and pathological medicine, and we filed applications for patents in 2019 (methodology development, a PCT application in 2020) and 2022 (monoclonal antibodies, PCT application in 2023). We hope that all of you who pursue a career in medicine will develop the skill to read and write original papers in English, to have a broad and thorough understanding of life sciences, and to mature to contribute to the advancement of biomedical science. Scientific research can only be understood when you are engaged in it. We will strive to support you so that you will be able to work with full confidence.

Recruitment Requirements for the Graduate School of Medicine (Doctoral Program):

Focusing on proliferation associated protein kinase CK2, we have observed intracellular migration of CK2 to the nucleus during progression of the normal cell cycle *in vivo*. However, when we analyzed breast cancer specimens, we discovered extremely clear nucleolar accumulation of the kinase, CK2, that is associated with recurrence (poor prognosis) of invasive breast cancer. Statistical analysis of CK2-staining using surgical specimens revealed that it is the only independent variable that determines clinical outcome. Therefore, we filed a patent application in 2019 and a PCT application in 2020 for this novel marker for cancer prognosis. In addition, we are analyzing molecular and biochemical properties of nuclear accumulation of CK2 in human solid tumors.

We are currently conducting research to discover mechanisms of cancer progression. As we have shown by molecular biological methods that CK2 is involved in epigenetic transcriptional regulation, integrative bioinformatics tools such as RNA-seq, ChIP-seq, phospho-proteomic and single-cell RNA analysis are also being employed in order to learn how CK2 is involved in expression and translation of specific genes.

Research Publications (Selected):

1. Satoshi Muto, Miwako K. Homma, Yuichiro Kiko, Y Ozaki, M Watanabe, N Okabe, K Hamada, Yuko Hashimoto, Hiroyuki Suzuki. Nucleolar CK2α as a prognostic factor in patients with surgically resected early-stage lung adenocarcinoma ***Oncology Report*** November 6 https://doi.org/10.3892/or.2024.8837 (2024).
2. Miwako K. Homma, Ryuichiro Nakato, Atsushi Niida, Masashige Bando, Katusnori Fujiki, Naoko Yokota, So Yamamoto, Takeshi Shibata, Motoki Takagi, Junko Yamaki, Hiroko Kozuka-Hata, Masaaki Oyama, Katsuhiko Shirahige, Yoshimi Homma. Cell cycle-dependent gene networks for cell proliferation activated by nuclear CK2α complexes *Life Science Alliance* 7: e202302077 doi:10.26508/lsa.202302077 (2023).
3. Miwako K. Homma, Yuko Hashimoto, Yoshimi Homma, Tadashi Nomizu. CK2α as a prognostic factor in invasive ductal carcinomas of the breast: cancer recurrence prognosis by surgical sampling. *The Lancet Oncology* 23: S25 (Abstract) 2022. doi:10.1016/ s1470-2045(22)00424-7 (2022).
4. Miwako K. Homma, Yuichiro Kiko, Yuko Hashimoto, Miki Nagatsuka, Naoto Katagata, Sei-ichiro Masui, Yoshimi Homma, Tadashi Nomizu. Intracellular localization of CK2α as a prognostic factor in invasive breast carcinomas. *Cancer Science* 112 (2): 619-628 (2021).
5. Kevin M. Riggle, Kimberly J. Riehle, Heidi L. Kenerson, Rigney Turnham, Miwako K. Homma, Machiko Kazami, Bret Samelson, Renay Bauer, G. Stanley McKnight, John D. Scott and Reymond S. Yeung. Enhanced cAMP-stimulated protein kinase A activity in human fibrolamellar hepatocellular carcinoma. *Pediatric Res* 80 (1):110-8 (2016).
6. Miwako K. Homma, Takeshi Shibata, Toshiyuki Suzuki, Masato Ogura, Hiroko Kozuka-Hata, Masaaki Oyama and Yoshimi Homma. Role for protein kinase CK2 on cell proliferation: Assessing the components of the CK2 complex in the nucleus during the cell cycle progression. *Protein Kinase CK2 Cellular Function in Normal and Disease States, Advs in Biochemistry in Health and Disease, Vol 12, Eds. by Khalil Ahmed et al.,* Springer International Publishing Switzerland. P.197-226 (2015).
7. Toshiyuki Suzuki, Haruhisa Kikuchi, Masato Ogura, Miwako K. Homma, Yoshiteru Oshima and Yoshimi Homma. Weight loss by a novel small-molecule, Ppc-1, derived from slime mold. *PLOS One* 10(2): e0117088 (2015).
8. Masato Ogura, Junko Yamaki, Miwako K. Homma and Yoshimi Homma. Phosphorylation of flotillin-1 by mitochondorial c-Src is required to prevent the production of reactive oxgen species. *FEBS Letters,* 588 (17): 2837-43 (2014).
9. Miwako K. Homma, Reiko Motohashi, and Hisako Ohtsubo. Japan's lagging gender equality. *Science*, 340: 428- 429 (2013).
10. Masato Ogura, JunkoYamaki, Miwako K. Homma, and Yoshimi Homma. Mitochondrial c-Src regulates cell survival through phosphorylation of respiratory chain components. *Biochem J.*, 447 (2): 281-289 (2012).
11. Miwako K. Homma, Reiko Motohashi, and Hisako Ohtsubo. Maximizing the potential of scientists in Japan: Promoting equal participation for women scientists through leadership development. *Genes to Cells*, 18: 529-532 (2013).
12. Miwako K. Homma and Yoshimi Homma. Cell Cycle and activation of CK2. *Mol Cell Biochem* 316(1-2):49- 55 (2008).
13. Miwako K. Homma, Ikuo. Wada, Toshiyuki Suzuki, Junko Yamaki, Edwin G. Krebs and Yoshimi Homma. CK2 phosphorylation of eukaryotic translation initiation factor 5 potentiates cell cycle progression. *Proc Natl Acad Sci USA*, 102(43): 15688-15693 (2005).
14. Miwako K.Homma and Yoshimi Homma. Regulatory role of CK2 during the progression of cell cycle. *Mol Cell Biochem* 274(1-2): 46-52 (2005).
15. Miwako K. Homma, Dongxia Li, Edwin G. Krebs, and Yoshimi Homma. Association and regulation of

casein kinase 2 activity by adenomatous polyposis coli protein. *Proc Natl Acad Sci USA.,* 99(9): 5959-5964 (2002).

16. Miwako K. Homma, Motoo Yamasaki, Shinobu Ohmi-Imajoh, and Yoshimi Homma. Inhibition of phosphoinositide hydrolysis and cell growth of Swiss 3T3 cells by myristoylated phosphoinositide phospholipase C inhibitor peptides. *J Biochem* 122: 738-742 (1997).

17. Miwako K. Homma, Yoshimi Homma, Moto-o Yamasaki, Shinobu Ohmi-Imajoh, and Yasuhito Yuasa. Growth inhibition by phospholipase C inhibitor peptides of colorectal carcinoma cells derived from familial adenomatous polyposis. *Cell Growth & Differentiation* 7: 281-288 (1996).

18. Yoshio Terada, Kimio Tomita, Miwako K. Homma, Hiroshi Nonoguchi, Tianxin Yang, Takehisa Yamada, Yasuhito Yuasa, Edwin G. Krebs, and Fumiaki Marumo. Sequential activation of MAP kinase cascade by angiotensin II in opossum Kidney cells. *Kidney Internat* 48: 1801-1809 (1995).

19. Yoshio Terada, Kimio Tomita, Miwako K. Homma, Hiroshi Nonoguchi, Tiaxin Yang, Takehisa Yamada, Yasuhito Yuasa, Edwin G. Krebs, and Fumiaki Marumo. Sequential activation of Raf-1 kinase, MAP kinase kinase, MAP kinase, and S6 kinase by hyperosmolality in renal cells. *J Biol. Chem* 269: 312996-31301 (1994).

20. Miwako K. Homma, Yoshimi Homma, Masayoshi Namba, and Yasuhito Yuasa. Enhanced phosphoinositide metabolism in colorectal carcinoma cells derived from familial adenomatous polyposis patients. *J Cell Biochem* 55: 477-485 (1994).

21. Katrina C. Gause, Miwako K. Homma, Karen A. Licciardi, Rony Sager, Natalie G. Ahn, Marsha J. Peterson, Edwin G. Krebs, and Kathryn E. Meier. Effects of phorbor ester on mitogen-activated protein kinase activity in wild-type and phorbor ester-resistent EL4 thymoma cells. *J Biol Chem* 268: 16124-16129 (1993).

22. Miwako Kato and Tadaomi Takenawa. Purification and characterization of membrane-bound and cytosolic forms of diacylglycerol kinase from rat brain. *J Biol Chem* 265: 794-800 (1990).

23. Yasuhito Yuasa, Takashi Kamiyama, Miwako Kato, Takeo Iwama, Tatsuro Ikeuchi, and Akira Tonomura. Transforming genes from familial adenomatous polyposis patient cells detected by a tumorigenicity assay. *Oncogene* 5: 589-596 (1990).

24. Tadaomi Takenawa, Miwako Kato, and Akio Yamakawa. Phosphatidylinositol kinase and cell transformation., *Adv. Second Messenger and Phosphoprotein Research*, Edit. by Yasutomi Nishizuka, Raven Press Inc. p.317-322 (1989).

25. Miwako Kato, Sadaaki Kawai, and Tadaomi Takenawa. Dissapearance of phorbol acetate-induced translocation of diacylglycerol kinase in erbB-transformed cells. *FEBS Letters* 247: 247-250 (1989).

26. Miwako Kato, Tadaomi Takenawa, and Daniel R.Twardzik. Effect of transforming growth factor-alpha on inositol phospholipid metabolism in human epidermal carcinoma cells. *J Cell Biochem* 37: 339-346 (1988).

27. Miwako Kato, Sadaaki Kawai, and Tadaomi Takenawa. Altered signal transduction in erbB-transformed cells. An implication of enhanced inositol phospholipid metabolism in erbB-induced transformation. *J Biol Chem* 262: 5696-5704 (1987).

28. Miwako Kato, Yoshimi Homma, Yoshitaka Nagai and Tadaomi Takenawa. Epidermal growth factor stimulates diacylglycerol kinase activity in isolated plasma membrane vesicles from A431 cells. *Biochem Biophys Res Commun* 129: 375-380 (1985).

29. Tadaomi Takenawa, Jun-ichi Ishitoya, Yoshimi Homma, Miwako Kato, and Yoshitaka Nagai. Role of enhanced inositol phospholipid metabolism in neutrophil activation. *Biochem Pharmacol* 34: 1931-1936 (1985).

和文総説、等

1. 本間美和子「総説：プロテインキナーゼCK2核内機能について」***生化学***　日本生化学会 vol 96, no.5, pp662-675 (2024)
2. 山元想、本間美和子「核小体への分子集積を基盤とする癌予後マーカーの開発」***細胞***　ニューサイエンス社 vol 56, no.11, pp.822-824 (2024)
3. 山元想、本間美和子「癌予後マーカーの開発と高感度化へ資する独自抗体について」**月刊*BioIndustry***　シーエムシー出版 vol.41, No.7 (2024)