

Shigehiro A. Kawashima, Ph. D.

male (born in 1980)

Project Lecturer

Graduate School of Pharmaceutical Sciences

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Education/Career

2003(H.15) **B.Sc.** in Department of Biophysics & Biochemistry

The University of Tokyo (Prof. Masayuki Yamamoto)

2005(H.17) **M.Sc.** in Graduate School of Science, Biophysics & Biochemistry

The University of Tokyo (Prof. Yoshinori Watanabe)

2008(H.20) **Ph.D. (Science)**

Graduate School of Science, Biophysics & Biochemistry

The University of Tokyo (Prof. Yoshinori Watanabe)

2008(H.20)-2009(H.21) **Postdoctoral Associate**

Institute of Molecular and Cellular Biosciences,

The University of Tokyo (Prof. Yoshinori Watanabe)

2009(H.21)- 2012(H.24) **Postdoctoral Fellow**

Laboratory of Chemistry & Cell Biology

The Rockefeller University (Prof. Tarun Kapoor)

2012(H.24)-2018(H.30) **ERATO project Group Leader**

Graduate School of Pharmaceutical Sciences

ERATO Kanai Life-Science Catalysis Project (Prof. Motomu Kanai)

The University of Tokyo

2016(H.24)-present **Project Lecturer**

Graduate School of Pharmaceutical Sciences

The University of Tokyo (Prof. Motomu Kanai)

Fellowships & Grants

2005-2008 JSPS Research Fellowship for Young Scientists (DC1)

2009-2011 JSPS Postdoctoral Fellow for Research Abroad

2011 Marie-Josée and Henry Kravis Fellowship Postdoctoral Fellowship

2012 The Uehara Memorial Foundation, research fellowship

2014-2018 Grant-in-Aid for Young Scientists (A) #26711001

2016-2018 Grant-in-Aid for Scientific Research on Innovative Areas #16H01300

2017 薬学振興会 平成 29 年度海外派遣研究者等旅費助成 [travel expenses grant]

2017 The Naito Foundation, 2017 年度 内藤記念特定研究助成金
2018 The Uehara Memorial Foundation, 平成 29 年度 研究奨励金
2018-2019 Grant-in-Aid for Challenging Exploratory Research # 18K19138

Awards

2010 Inoue Research Award for Young Scientists
2016 優秀ポスター賞 (第 39 回日本分子生物学会年会)
2019 平成 31 年度科学技術分野の文部科学大臣表彰 若手科学者賞

Publication List (*Corresponding author)

1. Hamajima W, Fujimura A, Fujiwara Y, Yamatsugu K*, **Kawashima SA***, Kanai M*. Site-Selective Synthetic Acylation of a Target Protein in Living Cells Promoted by a Chemical Catalyst/Donor System. *ACS Chemical Biology*, X:XXXX (2019).
2. Kobayashi Y, **Kawashima SA***. Bub1 kinase- and H2A phosphorylation-independent regulation of Shugoshin proteins under glucose-restricted conditions. *Scientific Reports*, 9:2826 (2019).
3. Chen Z, Suzuki H, Kobayashi Y, Wang AC, DiMaio F, **Kawashima SA**, Walz T, & Kapoor TM. Structural Insights into Mdn1, an Essential AAA Protein Required for Ribosome Biogenesis. *Cell*, 175, 822-834 (2018).
4. Yamatsugu K, Furuta M, Xi S, Amamoto Y, Liu J, **Kawashima SA**, Kanai M. Kinetic analyses and structure-activity relationship studies of synthetic lysine acetylation catalysts. *Bioorganic & Medicinal Chemistry*, 26:5359-5367 (2018).
5. Ishiguro T, Tanabe K, Kobayashi Y, Mizumoto S, Kanai M, **Kawashima SA***. Malonylation of histone H2A at lysine 119 inhibits Bub1-dependent H2A phosphorylation and chromosomal localization of shugoshin proteins. *Scientific Reports*, 8:7671 (2018).
6. Yamatsugu K*, **Kawashima SA***, Kanai M*. Leading Approaches in Synthetic Epigenetics for Novel Therapeutic Strategies. *Current Opinion in Chemical Biology*, 46:10-17 (2018).
7. Tanabe K, Liu J, Kato D, Kurumizaka H, Yamatsugu K, Kanai M*, **Kawashima SA***. LC-MS/MS-based quantitative study of the acyl group- and site-selectivity of human sirtuins to acylated nucleosomes. *Scientific Reports*, 8:2656 (2018).
8. Ishiguro T, Amamoto Y, Tanabe K, Liu J, Kajino H, Fujimura A, Aoi Y, Osakabe A, Horikoshi N, Kurumizaka H, Yamatsugu K, **Kawashima SA***, Kanai M*. Synthetic chromatin acylation by

artificial catalyst system. *Chem*, 2:840-859 (2017).

9. Amamoto Y, Aoi Y, Nagashima N, Suto H, Yoshidome, Arimura Y, Osakabe A, Kato D, Kurumizaka H, **Kawashima SA***, Yamatsugu K*, Kanai M*. Synthetic Posttranslational Modifications: Chemical Catalyst-Driven Regioselective Histone Acylation of Native Chromatin. *Journal of the American Chemical Society*, 139(22):7568-7576 (2017).

10. **Kawashima SA*****, Chen Z**, Aoi Y, Patgiri A, Kobayashi Y, Nurse P, Kapoor TM*. Potent, Reversible, and Specific Chemical Inhibitors of Eukaryotic Ribosome Biogenesis. *Cell*, 167(2):512-524 (2016). (**Equal contribution)

11. Takemoto A, **Kawashima SA**, Li JJ, Jeffery L, Yamatsugu K, Elemento O, Nurse P. Nuclear envelope expansion is crucial for proper chromosomal segregation during a closed mitosis. *Journal of Cell Science*, 129(6):1250-1259 (2016).

12. Kimura Y, Saito N, Hanada K, Liu J, Okabe T, **Kawashima SA***, Yamatsugu K*, Kanai M*. Supramolecular Ligands for Histone Tails by Employing a Multivalent Display of Trisulfonated Calix[4]arenes. *Chembiochem*, 16(18):2599-2604 (2015).

13. Chang F, **Kawashima SA**, Brady S. Mutations in the proteolipid subunits of the vacuolar H⁺-ATPase provide resistance to indolotryptoline natural products. *Biochemistry*, 53(45):7123-7131 (2014).

14. Aoi Y**, **Kawashima SA****, Simanis V, Yamamoto M, Sato M. Optimization of the analogue-sensitive Cdc2/Cdk1 mutant by in vivo selection eliminates physiological limitations to its use in cell cycle analysis. *Open Biology*, 4(7) (2014). (**Equal contribution)

15. Aoi Y, Sato M, Sutani T, Shirahige K, Kapoor TM, **Kawashima SA***. Dissecting the first and the second meiotic divisions using a marker-less drug-hypersensitive fission yeast. *Cell Cycle*, 13(8):1327-1334 (2014).

16. Komatsu H, Shindo Y, **Kawashima SA**, Yamatsugu K, Oka K, Kanai M. Intracellular activation of acetyl-CoA by an artificial reaction promoter and its fluorescent detection. *Chemical Communications*, 49(28):2876-2878 (2013).

17. **Kawashima SA**, Takemoto A, Nurse P, Kapoor TM. A chemical biology strategy to analyze rheostat-like protein kinase-dependent regulation. *Chemistry & Biology*, 20(2):262-271 (2013).

18. Li X, Foley EA, **Kawashima SA**, Molloy KR, Li Y, Chait BT, Kapoor TM. Examining post-translational modification-mediated protein-protein interactions using a chemical proteomics approach. *Protein Science*, 22(3):287-295 (2012).
19. **Kawashima SA**, Takemoto A, Nurse P, Kapoor TM. Analyzing fission yeast multidrug resistance mechanisms to develop a genetically tractable model system for chemical biology. *Chemistry & Biology*, 19(7):893-901 (2012).
20. **Kawashima SA**, Yamagishi Y, Honda T, Ishiguro K, Watanabe Y. Phosphorylation of H2A by Bub1 prevents chromosomal instability through localizing shugoshin. *Science*. 327(5962):172-177 (2010).
21. Hauf S, Biswas A, Langeegger M, **Kawashima SA**, Tsukahara T, Watanabe Y. Aurora controls sister kinetochore mono-orientation and homolog bi-orientation in meiosis-I. *The EMBO Journal*, 26(21):4475-4486 (2007).
22. **Kawashima SA**, Tsukahara T, Langeegger M, Hauf S, Kitajima TS, Watanabe Y. Shugoshin enables tension-generating attachment of kinetochores by loading Aurora to centromeres. *Genes & Development*, 21(4):420-435 (2007).
23. Kitajima TS, Sakuno T, Ishiguro K, Iemura S, Natsume T, **Kawashima SA**, Watanabe Y. Shugoshin collaborates with protein phosphatase 2A to protect cohesin. *Nature*, 441(7089):46-52 (2006).
24. Kitajima TS, **Kawashima SA**, Watanabe Y. The conserved kinetochore protein shugoshin protects centromeric cohesion during meiosis. *Nature*, 427(6974):510-517 (2004).

Selected Presentation List (International meetings)

(Invited Talk)

1. **Shigehiro Kawashima**, 「Developing artificial catalyst systems for synthetic epigenetics」『The 21st iCeMS International Symposium』, Kyoto, Japan, (June 2016)

(Oral Presentations)

2. **Shigehiro Kawashima**, Yoshifumi Amamoto, Tadashi Ishiguro, Kana Tanabe, Nozomu Nagashima, Yuki Aoi, Jiaan Liu, Hitoshi Kurumizaka, Kenzo Yamatsugu, Motomu Kanai, 「Developing artificial catalyst systems for synthetic histone acylation」『Cold Spring harbor laboratory meeting: EPIGENETICS & CHROMATIN』, Cold Spring Harbor, USA, (Sep. 2016)

3. **Shigehiro Kawashima**, Ai Takemoto, Paul Nurse, Tarun Kapoor, 「Developing fission yeast for chemical biology」『7th International Fission Yeast Meeting』, London, United Kingdom, (June 2013)

(Poster Presentations)

4. **Shigehiro Kawashima**, Akiko Fujimura, Wataru Hamajima, Kenzo Yamatsugu, and Motomu Kanai, 「Developing artificial catalyst systems for epigenome manipulation」『11th AACR-JCA Joint Conference on Breakthroughs in Cancer Research: Biology to Precision Medicine』, Maui, USA, (Feb 2019)

5. **Shigehiro Kawashima**, Zhen Chen, Yuki Aoi, Yuki Kobayashi, Paul Nurse, Tarun M. Kapoor, 「Discovery of Potent, Reversible, and Specific Chemical Inhibitors of Eukaryotic Ribosome Biogenesis using Drug-hypersensitive Fission Yeast」『9th International Fission Yeast Meeting』, Alberta, Canada, (May 2017)

6. **Shigehiro Kawashima**, Zhen Chen, Yuki Aoi, Yuki Kobayashi, Paul Nurse, Tarun M. Kapoor, 「Identifying a potent small-molecule inhibitor of Midasin, a AAA+ ATPase required for eukaryotic ribosome biogenesis, using drug-hypersensitive fission yeast」『8th International Fission Yeast Meeting』, Kobe, Japan, (June 2017)

7. **Shigehiro Kawashima**, Yoshifumi Amamoto, Tadashi Ishiguro, Kana Tanabe, Hiroki Suto, Yuki Aoi, Haiyan Zhu, Akihisa Osakabe, Naoki Horikoshi, Yasuhiro Arimura, Hitoshi Kurumizaka, Kenzo Yamatsugu, Motomu Kanai, 「Synthetic epigenetics by artificial catalyst systems」『The 40th Naito Conference on “Epigenetics—From Histone Code to Therapeutic Strategy”』, Sapporo, Japan, (Sep. 2015)

8. **Shigehiro Kawashima**, Haiyan Zhu, Yoshifumi Amamoto, Kenzo Yamatsugu, Motomu Kanai, 「Synthetic chromatin acetylation promoted by artificial catalyst induces p53-dependent cell cycle arrest in tumor cells」『Cold Spring harbor laboratory meeting: EPIGENETICS & CHROMATIN』, Cold Spring Harbor, USA, (Sep. 2014)

9. **Shigehiro Kawashima**, Anupam Patgiri, Paul Nurse, Tarun M. Kapoor, 「Identifying a novel small-molecule inhibitor of Midasin-dependent 60S ribosome biogenesis using drug-hypersensitive fission yeast」『Cold Spring harbor laboratory meeting: CELL BIOLOGY OF YEASTS』, Cold Spring Harbor, USA, (Nov. 2013)

10. **Shigehiro Kawashima**, Paul Nurse, Tarun M. Kapoor, 「Developing fission yeast-based approaches for drug discovery and target identification」『The LXXV Cold Spring Harbor Symposium on Quantitative Biology』, Cold Spring Harbor, USA, (June 2010)

11. **Shigehiro Kawashima**, Tatsuya Tsukahara, Maria Langedger, Silke Hauf, Tomoya S. Kitajima, Yoshinori Watanabe, 「Shugoshin enables tension-generating attachment of kinetochores by loading Aurora to centromeres」『4th international fission yeast meeting』, Copenhagen, Danmark, (June 2007)

Selected Presentation List (Japanese meetings)

(Invited Talks)

1. **川島茂裕**, 「ヒストン翻訳後修飾を導入する人工触媒システムの開発」『第 11 回日本エピジェネティクス研究会年会』, 東京, 2017 年 5 月
2. **川島茂裕**, 山次健三, 「触媒医療の実現に向けて: 人工触媒システムによる ヒストンの合成的アシル化(1)」『日本薬学会第137年会』, 仙台, 2017 年 3 月
3. **川島茂裕**, 「薬剤感受性分裂酵母を用いた化学遺伝学的スクリーニング系の構築と新規低分子阻害剤の同定」, 広島大学, 広島, 2016 年 12 月
4. **川島茂裕**, 「Developing fission yeast for chemical biology」『2016 酵母ルネッサンス』, 東京, 2016 年 11 月
5. **川島茂裕**, 「人工触媒システムを用いたクロマチン修飾」『第 16 回日本蛋白質科学会』, 福岡, 2016 年 6 月
6. **川島茂裕**, 「Toward synthetic epigenetics by artificial catalyst systems」『生物物理学会 第 53 回年会』, 福岡, 2015 年 9 月
7. **川島茂裕**, 「生物と化学の融合による染色体研究のブレークスルーを目指して」『新学術領域研究「クロマチン動構造」若手の会 第三回ワークショップ』, 2015 年 7 月

(Oral Presentations)

8. **川島茂裕**, 小林由紀, 「Bub1 および H2A リン酸化に依存しないシュゴシンの染色体局在化」『第 36 回染色体ワークショップ第 17 回核ダイナミクス研究会』, 2019 年 1 月
9. **川島茂裕**, 青井勇樹, Zhen Chen, Tarun M. Kapoor 「薬剤感受性分裂酵母を用いた化学遺伝学スクリーニングによるリボソーム生合成を標的にした新規低分子阻害剤の同定」『日本ケミカルバイオロジー学会第 12 回年会』, 2017 年 6 月
10. **川島茂裕**, 天本義史, 須藤宏城, 永島臨, 青井勇樹, 越阪部晃永, 有村泰宏, 胡桃坂仁志,

山次健三、金井求、「生体内 HAT 代替を目指した人工触媒システムの開発」『第 33 回染色体ワークショップ第 14 回核ダイナミクス研究会』、2016 年 1 月

13. 川島茂裕、朱海燕、天本義史、石黒伸茂、田辺佳奈、越阪部晃永、堀越直樹、胡桃坂仁志、山次 健三、金井求、「染色体を標的にした新規人工触媒システムによるヒストンの合成的アセチル化」『第 32 回染色体ワークショップ第 13 回核ダイナミクス研究会』、2014 年 12 月

11. 川島茂裕、朱海燕、天本義史、山次健三、金井求、「人工触媒システムによる染色体の合成的アセチル化」『第 37 回日本分子生物学会年会』、2014 年 11 月

12. 川島茂裕、竹本愛、Paul Nurse、Tarun Kapoor、「分裂酵母ケミカルジェネティクスを用いたダイナミックな染色体分配機構への新たなアプローチ」『第 35 回日本分子生物学会年会』、2012 年 12 月

(Selected Poster Presentations)

13. 川島茂裕、藤村 亜紀子、濱島 航、山次健三、金井求、「Developing artificial catalyst systems for epigenome manipulation」『第 13 回エピジェネティクス研究会年会』、2019 年 5 月

14. 川島茂裕、小林由紀、「Bub1 および H2A リン酸化に依存しないシュゴシンの染色体局在化機構」『酵母遺伝学フォーラム第 51 回研究報告会』、2018 年 9 月

15. 川島茂裕、石黒伸茂、田辺佳奈、小林由紀、堀越直樹、胡桃坂仁志、山次 健三、金井求、「ヒストン H2A リジン 119 番のマロニル化は Bub1 による H2A リン酸化及びシュゴシタンパク質の染色体局在化を阻害する」『第 12 回日本エピジェネティクス研究会年会』、2018 年 5 月

16. 川島茂裕、Zhen Chen、青井勇樹、小林由紀、Paul Nurse、Tarun M. Kapoor、「リボソーム生合成に必須な AAA+タンパク質ミダシンの特異的かつ可逆的低分子阻害剤の発見」『第 39 回日本分子生物学会年会』、2016 年 11 月

Patent List

1. 特許出願 (国際):「選択的な染色体タンパク質のアシル化を行うための人工触媒システム」金井求、川島茂裕、山次健三、天本義史、青井勇樹、須藤宏樹、胡桃坂仁志、越阪部是永、有村泰宏、特願 PCT/JP2016/075183 号

2. 特許出願 (国際):「生体内の酵素機能と置き換えられる人工触媒システム」金井求、川島茂裕、山次健三、朱海燕、天本義史、田辺佳奈、石黒伸茂、劉家安、特願 PCT/JP2015/66179 号

3. 特許出願 (国内):「選択的な染色体タンパク質のアシル化を行うための人工触媒システム」金井求、川島茂裕、山次健三、天本義史、青井勇樹、須藤宏樹、胡桃坂仁志、越阪部是永、有村泰宏、特願 2015-169448 号

4. 特許出願 (国内):「生体内の酵素機能と置き換えられる人工触媒システム」金井求、川島茂裕、山次健三、朱海燕、天本義史、特願 2014-115494 号