

## 【*klotho*/Jclマウスおよび $\alpha$ -Klotho KOマウス参考文献リスト】

(※発行年度順。動物カタログのReferencesとは異なります。)

### 1995

Kuro-o M, Hanaoka K, Hiroi Y, Noguchi T, Fujimori Y, Takewaki S, Hayasaka M, Katoh H, Miyagishi A, Nagai R, Yazaki Y, Nabeshima Y. Salt-sensitive hypertension in transgenic mice overexpressing Na(+)-proton exchanger. *Circ Res.* 1995; 76(1): 148-53. [PMID: 8001273]

### 1997

Kuro-o M, Matsumura Y, Aizawa H, Kawaguchi H, Suga T, Utsugi T, Ohyama Y, Kurabayashi M, Kaname T, Kume E, Iwasaki H, Iida A, Shiraki-Iida T, Nishikawa S, Nagai R, Nabeshima YI. Mutation of the mouse *klotho* gene leads to a syndrome resembling ageing. *Nature.* 1997; 390: 45-51. [PMID: 9363890]

### 1998

Shiraki-Iida T, Aizawa H, Matsumura Y, Sekine S, Iida A, Anazawa H, Nagai R, Kuro-o M, Nabeshima Y. Structure of the mouse *klotho* gene and its two transcripts encoding membrane and secreted protein. *FEBS Lett.* 1998; 424(1-2): 6-10. [PMID: 9537505]

大山良雄, 宇都木敏浩, 大野富雄, 内山 強, 相澤宏樹, 松村 穰, 伴野祥一, 河津捷二, 岡 芳知, 黒尾 誠, 鍋島陽一, 永井良三. 老化抑制遺伝子(*klotho*)欠損マウスにおける糖代謝と膵内分泌機能の検討. *Diabetes Frontier.* 1998; 9(3): 363-4.

山下照仁, 黒尾 誠, 鍋島陽一, 野田政樹. 早期老化(*klotho*変異)マウスにおける骨の形態形成異常. *実験医学.* 1998; 16: 131-5.

Yamashita T, Nifuji A, Furuya K, Nabeshima Y, Noda M. Elongation of the epiphyseal trabecular bone in transgenic mice carrying a *klotho* gene locus mutation that leads to a syndrome resembling aging. *J Endocrinol.* 1998; 159(1): 1-8. [PMID: 9795335]

### 1999

Kawaguchi H, Manabe N, Miyaura C, Chikuda H, Nakamura K, Kuro-o M. Independent impairment of osteoblast and osteoclast differentiation in *klotho* mouse exhibiting low-turnover osteopenia. *J Clin Invest.* 1999; 104(3): 229-37. [PMID: 10430604]

鍋島 陽一. 個体老化の分子機構. *源流.* 1999; 1: 43-50.

### 2000

Kato Y, Arakawa E, Kinoshita S, Shirai A, Furuya A, Yamano

K, Nakamura K, Iida A, Anazawa H, Koh N, Iwano A, Imura A, Fujimori T, Kuro-o M, Hanai N, Takeshige K, Nabeshima Y. Establishment of the anti-Klotho monoclonal antibodies and detection of Klotho protein in kidneys. *Biochem Biophys Res Commun.* 2000; 267(2): 597-602. [PMID: 10631108]

Suga T, Kurabayashi M, Sando Y, Ohyama Y, Maeno T, Maeno Y, Aizawa H, Matsumura Y, Kuwaki T, Kuro-O M, Nabeshima Y, Nagai R. Disruption of the *klotho* gene causes pulmonary emphysema in mice. Defect in maintenance of pulmonary integrity during postnatal life. *Am J Respir Cell Mol Biol.* 2000; 22(1): 26-33. [PMID: 10615062]

Utsugi T, Ohno T, Ohyama Y, Uchiyama T, Saito Y, Matsumura Y, Aizawa H, Itoh H, Kurabayashi M, Kawazu S, Tomono S, Oka Y, Suga T, Kuro-o M, Nabeshima Y, Nagai R. Decreased insulin production and increased insulin sensitivity in the *klotho* mutant mouse, a novel animal model for human aging. *Metabolism.* 2000; 49(9): 1118-23. [PMID: 11016890]

Shiraki-Iida T, Iida A, Nabeshima Y, Anazawa H, Nishikawa S, Noda M, Kuro-o M, Nabeshima Y. Improvement of multiple pathophysiological phenotypes of *klotho* (*kl/kl*) mice by adenovirus-mediated expression of the *klotho* gene. *J Gene Med.* 2000; 2(4): 233-42. [PMID: 10953914]

### 2001

Morishita K, Shirai A, Kubota M, Katakura Y, Nabeshima Y, Takeshige K, Kamiya T. The progression of aging in *klotho* mutant mice can be modified by dietary phosphorus and zinc. *J Nutr.* 2001; 131(12): 3182-8. [PMID: 11739863]

### 2002

鍋島陽一. "IV加齢モデル. 1.老化モデルとしての*klotho*遺伝子変異マウス". ヒト型モデル動物. 井上 達, 他編. シュプリンガー・フェアラーク東京. 2002. p.85-94.

Nakamura T, Saito Y, Ohyama Y, Masuda H, Sumino H, Kuro-o M, Nabeshima Y, Nagai R, Kurabayashi M. Production of nitric oxide, but not prostacyclin, is reduced in *Klotho* mice. *Jpn J Pharmacol.* 2002; 89(2): 149-56. [PMID: 12120757]

### 2003

Nagai T, Yamada K, Kim HC, Kim YS, Noda Y, Imura A,

Nabeshima Y, Nabeshima T. Cognition impairment in the genetic model of aging *klotho* gene mutant mice: a role of oxidative stress. *FASEB J*. 2003; 17(1): 50-2. [PMID: 12475907]

Klotho遺伝子変異マウスの学習障害と酸化ストレス. 永井拓, 山田清文, Hyoung-Chun Kim, 野田幸裕, 鍋島陽一, 鍋島俊隆. *日本神経精神薬理学雑誌*. 2003; 23: 211-7. [PMID: 14653227]

Tsujikawa H, Kurotaki Y, Fujimori T, Fukuda K, Nabeshima Y. *Klotho*, a gene related to a syndrome resembling human premature aging, functions in a negative regulatory circuit of vitamin D endocrine system. *Mol Endocrinol*. 2003; 17(12): 2393-403. [PMID: 14528024]

## 2004

Takeshita K, Fujimori T, Kurotaki Y, Honjo H, Tsujikawa H, Yasui K, Lee JK, Kamiya K, Kitaichi K, Yamamoto K, Ito M, Kondo T, Iino S, Inden Y, Hirai M, Murohara T, Kodama I, Nabeshima Y. Sinoatrial node dysfunction and early unexpected death of mice with a defect of *klotho* gene expression. *Circulation*. 2004; 109(14): 1776-82. [PMID: 15037532]

Tohyama O, Imura A, Iwano A, Freund JN, Henrissat B, Fujimori T, Nabeshima Y. *Klotho* is a novel  $\beta$ -glucuronidase capable of hydrolyzing steroid  $\beta$ -glucuronides. *J Biol Chem*. 2004; 279(11): 9777-84. [PMID: 14701853]

Shimada T, Takeshita Y, Murohara T, Sasaki K, Egami K, Shintani S, Katsuda Y, Ikeda H, Nabeshima Y, Imaizumi T. Angiogenesis and vasculogenesis are impaired in the precocious-aging *klotho* mouse. *Circulation*. 2004; 110(9): 1148-55. [PMID: 15302783]

Li SA, Watanabe M, Yamada H, Nagai A, Kinuta M, Takei K. Immunohistochemical localization of *Klotho* protein in brain, kidney, and reproductive organs of mice. *Cell Struct Funct*. 2004; 29(4): 91-9. [PMID: 15665504]

Funada Y, Nishimura Y, Yokoyama M. Imbalance of matrix metalloproteinase-9 and tissue inhibitor of matrix metalloproteinase-1 is associated with pulmonary emphysema in *Klotho* mice. *Kobe J Med Sci*. 2004; 50(3-4): 59-67. [PMID: 15864012]

鍋島陽一. *Klotho*遺伝子欠損マウス. モデル動物の作製と維持 (森脇和郎, 山村研一, 米川博通編), (株)エル・アイ・シー, 東京, 938-48, 2004.

## 2005

Sato I, Miyado M, Sunohara M. NADH dehydrogenase activity and expression of mRNA of complex I (ND1, 51kDa, and 75kDa) in heart mitochondria of *klotho* mouse.

*Okajimas Folia Anat Jpn*. 2005; 82(2): 49-56. [PMID: 16212276]

Suzuki H, Amizuka N, Oda K, Li M, Yoshie H, Ohshima H, Noda M, Maeda T. Histological evidence of the altered distribution of osteocytes and bone matrix synthesis in *klotho*-deficient mice. *Arch Histol Cytol*. 2005; 68(5): 371-81. [PMID: 16505583]

## 2006

Suzuki H, Amizuka N, Noda M, Amano O, Maeda T. Histological and immunohistochemical changes in the submandibular gland in *klotho*-deficient mice. *Arch Histol Cytol*. 2006; 69(2): 119-28. [PMID: 16819151]

Toyama R, Fujimori T, Nabeshima Y, Itoh Y, Tsuji Y, Osamura RY, Nabeshima Y. Impaired regulation of gonadotropins leads to the atrophy of the female reproductive system in *klotho*-deficient mice. *Endocrinology*. 2006; 147(1): 120-9. [PMID: 16179415]

Urakawa I, Yamazaki Y, Shimada T, Iijima K, Hasegawa H, Okawa K, Fujita T, Fukumoto S, Yamashita T. *Klotho* converts canonical FGF receptor into a specific receptor for FGF23. *Nature*. 2006; 444(7120): 770-4. [PMID:17086194]

## 2007

Sato A, Hirai T, Imura A, Kita N, Iwano A, Muro S, Nabeshima Y, Suki B, Mishima M. Morphological mechanism of the development of pulmonary emphysema in *klotho* mice. *Proc Natl Acad Sci USA*. 2007; 104(7): 2361-5. [PMID: 17284608]

Imura A, Tsuji Y, Murata M, Maeda R, Kubota K, Iwano A, Obuse C, Togashi K, Tominaga M, Kita N, Tomiyama K, Iijima J, Nabeshima Y, Fujioka M, Asato R, Tanaka S, Kojima K, Ito J, Nozaki K, Hashimoto N, Ito T, Nishio T, Uchiyama T, Fujimori T, Nabeshima Y.  $\alpha$ -*Klotho* as a regulator of calcium homeostasis. *Science*. 2007; 316(5831): 1615-8. [PMID: 17569864]

Segawa H, Yamanaka S, Ohno Y, Onitsuka A, Shiozawa K, Aranami F, Furutani J, Tomoe Y, Ito M, Kuwahata M, Imura A, Nabeshima Y, Miyamoto K. Correlation between hyperphosphatemia and type II Na-Pi cotransporter activity in *klotho* mice. *Am J Physiol Renal Physiol*. 2007; 292(2): 769-79. [PMID: 16985213]

宮本賢一, 瀬川博子, 伊藤美紀子, 辰巳佐和子.  $\alpha$ -*Klotho*とリン代謝. *CLINICAL CALCIUM*. 2007; 17(5): 698-703. [PMID: 17470998]

鍋島陽一. カルシウム恒常性制御における $\alpha$ -*Klotho*の機能. *医学のあゆみ*. 2007; 222(3): 225-31.

## 2008

Suzuki H, Amizuka N, Oda K, Noda M, Ohshima H, Maeda T. Histological and elemental analyses of impaired bone mineralization in klotho-deficient mice. *J Anat.* 2008; 212(3): 275-85. [PMID: 18248363]

鍋島陽一.  $\alpha$ -Klotho, FGF23の発見がもたらしたカルシウム・リン制御の新たなコンセプト. *CLINICAL CALCIUM.* 2008; 18(7): 923-34. [PMID: 18591743]

鍋島陽一.  $\alpha$ -Klothoの分子機能と老化についての一考察. *医学のあゆみ.* 2008; 227(8): 574-9.

Ishii M, Yamaguchi Y, Yamamoto H, Hanaoka Y, Ouchi Y. Airspace enlargement with airway cell apoptosis in klotho mice: a model of aging lung. *J Gerontol A Biol Sci Med Sci.* 2008; 63(12):1289-98. [PMID: 19126841]

## 2009

Bai X, Dinghong Q, Miao D, Goltzman D, Karaplis AC. Klotho ablation converts the biochemical and skeletal alterations in FGF23 (R176Q) transgenic mice to a Klotho-deficient phenotype. *Am J Physiol Endocrinol Metab.* 2009; 296(1): E79-88. [PMID: 18984852]

Nabeshima Y. Discovery of  $\alpha$ -Klotho unveiled new insights into calcium and phosphate homeostasis. *Proc Jpn Acad, Ser B.* 2009; 85(3): 125-41. [PMID: 19282648]

## 2010

Tomiyama K, Maeda R, Urakawa I, Yamazaki Y, Tanaka T, Ito S, Nabeshima Y, Tomita T, Odori S, Hosoda K, Nakao K, Imura A, Nabeshima Y. Relevant use of Klotho in FGF19 subfamily signaling system in vivo. *Proc Natl Acad Sci U S A.* 2010; 107(4): 1666-71. [PMID: 20080590]

## 2011

坂部 勇, 他. "32章 老化促進モデル.  $\alpha$ -Klothoマウス". 完全版マウス・ラット疾患モデル動物活用ハンドブック. 秋山 徹他編. 羊土社. 2011. p.510-2.

Satoko Shimasaki, Midori Kubota, Makiko Yoshitomi, Kyoko Takagi, Kazuma Suda, Katsumi Mera, Yukio Fujiwara, Ryoji Nagai. N $\omega$ -(carboxymethyl)arginine Accumulates in Glycated Collagen and Klotho-deficient Mouse Skin. *ANTI-AGING MEDICINE.* 2011; 8(6): 82-7.

Iida RH, Kanko S, Suga T, Morito M, Yamane A. Autophagic-lysosomal pathway functions in the masseter and tongue muscles in the klotho mouse, a mouse model for aging. *Mol Cell Biochem.* 2011; 348(1-2): 89-98. [PMID: 21082218]

Amano I, Imaizumi Y, Kaji C, Kojima H, Sawa Y. Expression

of podoplanin and classical cadherins in salivary gland epithelial cells of klotho-deficient mice. *Acta Histochem Cytochem.* 2011; 44(6): 267-76. [PMID: 22282587]

## 2012

Takahashi M, Eda A, Fukushima T, Hohjoh H. Reduction of type IV collagen by upregulated miR-29 in normal elderly mouse and klotho-deficient, senescence-model mouse. *PLoS One.* 2012; 7(11): e48974. [PMID: 23139829]

Sugiura H, Yoshida T, Shiohira S, Kohei J, Mitobe M, Kurosu H, Kuro-o M, Nitta K, Tsuchiya K. Reduced Klotho expression level in kidney aggravates renal interstitial fibrosis. *Am J Physiol Renal Physiol.* 2012; 302(10): 1252-64. [PMID: 22338084]

## 2013

Asada N, Katayama Y, Sato M, Minagawa K, Wakahashi K, Kawano H, Kawano Y, Sada A, Ikeda K, Matsui T, Tanimoto M. Matrix-embedded osteocytes regulate mobilization of hematopoietic stem/progenitor cells. *Cell Stem Cell.* 2013 Jun 6; 12 (6):737-47. [PMID: 23746979]

Kawai M, Kinoshita S, Kimoto A, Hasegawa Y, Miyagawa K, Yamazaki M, Ohata Y, Ozono K, Michigami T. FGF23 suppresses chondrocyte proliferation in the presence of soluble  $\alpha$ -Klotho both in vitro and in vivo. *J Biol Chem.* 2013 Jan 25;288(4):2414-27. [PMID: 23235154]

Inoue S, Sato T, Suzuki-Utsunomiya K, Komori Y, Hozumi K, Chiba T, Yahata T, Nakai K, Inokuchi S. Sepsis-induced hypercytokinemia and lymphocyte apoptosis in aging-accelerated Klotho knockout mice. *Shock.* 2013 Mar;39 (3):311-6. [PMID: 23364432]

Sasaki M, Hasegawa T, Yamada T, Hongo H, de Freitas PH, Suzuki R, Yamamoto T, Tabata C, Toyosawa S, Yamamoto T, Oda K, Li M, Inoue N, Amizuka N. Altered distribution of bone matrix proteins and defective bone mineralization in *klotho*-deficient mice. *Bone.* 2013 Nov; 57(1):206-19. [PMID: 23954506]

## 2014

Yamashita, K., Yotsuyanagi, T., Yamauchi, M., & Young, D. M. (2014). Klotho Mice: A Novel Wound Model of Aged Skin. *Plastic and Reconstructive Surgery-Global Open*, 2(1), e101.

Maruyama N, Shibata Y, Mochizuki A, Miyazaki T, Inoue T, Maki K. Age-related degradation of mouse cortical bone: implications for the  $\alpha$ -klotho gene responsible for bone mechanical integrity in a series of nanoindentation experiments. *Recent Advances in Structural Integrity*

Analysis - Proceedings of the International Congress (APCF/SIF-2014) Pages 300–304

Sun Y, Zhou G, Gui T, Shimokado A, Nakanishi M, Oikawa K, Sato F, Muragaki Y. Elevated serum 1,25(OH)<sub>2</sub>-vitamin D<sub>3</sub> level attenuates renal tubulointerstitial fibrosis induced by unilateral ureteral obstruction in kl/kl mice. *Sci Rep*. 2014 Oct 9;4:6563. doi: 10.1038/srep06563. [PMID: 25297969]

## 2015

Maruyama N, Shibata Y, Mochizuki A, Yamada A, Maki K, Inoue T, Kamijo R, Miyazaki T. Bone micro-fragility caused by the mimetic aging processes in  $\alpha$ -klotho deficient mice: in situ nanoindentation assessment of dilatational bands. *Biomaterials*. 2015 Apr;47:62-71. [PMID: 25682161]

Sato S, Kawamata Y, Takahashi A, Imai Y, Hanyu A, Okuma A, Takasugi M, Yamakoshi K, Sorimachi H, Kanda H, Ishikawa Y, Sone S, Nishioka Y, Ohtani N, Hara E. Ablation of the p16(INK4a) tumour suppressor reverses ageing phenotypes of klotho mice. *Nat Commun*. 2015 Apr 29;6:7035. doi: 10.1038/ncomms8035. [PMID: 25923845]

## 2016

Takenaka T, Inoue T, Miyazaki T, Hayashi M, Suzuki H. Xeno-Klotho Inhibits Parathyroid Hormone Signaling. *J Bone Miner Res*. 2016 Feb;31(2):455-62.[PMID: 26287968]

Jin J, Jin L, Lim SW, Yang CW. Klotho Deficiency Aggravates Tacrolimus-Induced Renal Injury via the Phosphatidylinositol 3-Kinase-Akt-Forkhead Box Protein O Pathway. *Am J Nephrol*. 2016;43(5):357-65. [PMID: 27174564]

Yamauchi M, Hirohashi Y, Torigoe T, Matsumoto Y, Yamashita K, Kayama M, Sato N, Yotsuyanagi T. Wound healing delays in  $\alpha$ -Klotho-deficient mice that have skin appearance similar to that in aged humans - Study of delayed wound healing mechanism. *Biochem Biophys Res Commun*. 2016 May 13;473(4):845-52. [PMID: 27037022]

## 2017

Fujino Y, Minamizaki T, Hayashi I, Kawakami A, Miyaji T, Sakurai K, Yoshioka H, Kozai K, Okada M, Yoshiko Y. Comparative proteome analysis of wild-type and klotho-knockout mouse kidneys using a combination of MALDI-IMS and LC-MS/MS. *Proteomics Clin Appl*. 2017 Mar 8. [PMID: 28276159]

Nakamura K, Miura D, Saito Y, Yunoki K, Koyama Y, Satoh M, Kondo M, Osawa K, Hatipoglu OF, Miyoshi T, Yoshida M, Morita H, Ito H. Eicosapentaenoic acid prevents arterial

calcification in klotho mutant mice. *PLoS One*. 2017 Aug 3;12(8):e0181009.[PMID: 28771600]

Hasegawa Y, Hayashi K, Takemoto Y, Cheng C, Takane K, Lin B, Komohara Y, Kim-Mitsuyama S. DPP-4 inhibition with linagliptin ameliorates the progression of premature aging in klotho<sup>-/-</sup> mice. *Cardiovasc Diabetol*. 2017 Dec 1;16(1):154.

Hikone K, Hasegawa T, Tsuchiya E, Hongo H, Sasaki M, Yamamoto T, Kudo A, Oda K, Haraguchi M, de Freitas PH, Li M, Iida J, Amizuka N. Histochemical Examination on Periodontal Tissues of Klotho-Deficient Mice Fed With Phosphate-Insufficient Diet. *J Histochem Cytochem*. 2017 Apr;65(4):207-221.[PMID: 28122194]

## 2018

## 2019

## 2020

Keiko Akasaka-Manyá, Hiroshi Manyá, Satomi Nadanaka, Hiroshi Kitagawa, Yoshitaka Kondo, Akihito Ishigami, Tamao Endo. Decreased ADAM17 Expression in the Lungs of  $\alpha$ -Klotho Reduced Mouse *J Biochem*. 2020 May 1;167(5):483-493. [PMID: 31951006]

Wakako Kawarazaki, Risuke Mizuno, Mitsuhiro Nishimoto, Nobuhiro Ayuzawa, Daigoro Hirohama, Kohei Ueda, Fumiko Kawakami-Mori, Shigeyoshi Oba, Takeshi Marumo, Toshiro Fujita. Salt Causes Aging-Associated Hypertension via Vascular Wnt5a Under Klotho Deficiency. *J Clin Invest*. 2020 Jun 29;134431 [PMID: 32597829]

(2021.3)