

# 研究開発部門

Department of Research and Development

## 資源開発分野

Division of Medicinal Resources

### 天然物創薬学領域

Section of Natural Products & Drug Discovery

#### 天然物化学ユニット

Natural Products Chemistry

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#### ◆ 原 著

- 1) Lee Y\*, Nakashima Y, Kodama T, Chen X, Morita H. Dual engineering of olivetolic acid cyclase and tetraketide synthase to generate longer alkyl-chain olivetolic acid analogs. *Org lett.* 2022 Jan 14; 24(1): 410-414. doi: 10.1021/acs.orglett.1c04089.
- 2) Wang X#, Gao B#, Nakashima Y#, Mori T, Zhang Z, Kodama T, Lee Y, Zhang Z, Wong CP, Liu Q, Qi B, Wang J, Li J, Liu X, Abe I, Morita H, Tu P, Shi SP. (# equal contribution). Identification of a diarylpentanoids-producing plant polyketide synthase revealing an unusual biosynthetic pathway of 2-(2-phenylethyl)chromones in Agarwood. *Nat Commun.* 2022 Jan 17; 13(1): 348. doi: 10.1038/s41467-022-27971-z.
- 3) Muslimin R, Nishiura N, Teshima A, Do KM, Kodama T, Morita H, Lewis CW, Chan G, Ayoub AT, Arakawa K. Chemoenzymatic synthesis, computational investigation, and antitumor activity of monocyclic lankacidin derivatives. *Bioorg Med Chem.* 2022 Jan 1; 53: 116551. doi: 10.1016/j.bmc.2021.116551.
- 4) Takashima K, Okada T, Kato A, Yamasaki Y, Akanuma S, Kubo Y, Hosoya K, Morita H, Ito T, Kodama T, Tanabe G, Toyooka N. Divergent synthesis of decahydroquinoline-type poison-frog alkaloids. *ChemistrySelect.* 2022 Feb 3; 7: e202104533. doi: 10.1002/slct.202004825.
- 5) Do KM\*, Kodama T, Shin MK, Nu LHT, Nguyen HM, Dang SV, Shiokawa K, Hayakawa Y, Morita H. Marginols A-H, unprecedented pimarane diterpenoids from *Kaempferia marginata* and their NO inhibitory activities. *Phytochemistry.* 2022 Apr; 196: 113109. doi: 10.1016/j.phytochem.2022.113109.
- 6) Nguyen QP, Hue BTB, Do KM, Quy HTK, De TQ, Quoc NC, Phuong NB, Trang PC, Morita H. Design, synthesis and cytotoxicity evaluation of substituted benzimidazole conjugated 1,3,4-oxadiazoles. *Chem Pharm Bull.* 2022; 70(6): 448-453. doi: 10.1248/cpb.c22-00162.
- 7) Hamdy SA\*, Kodama T, Nakashima Yu, Han X, Matsui T, Morita H. Enzymatic formation of a prenyl β-carboline by using a fungal indole prenyltransferase. *J Nat Med.* 2022 Sep; 76(4): 873-879. doi: 10.1007/s11418-022-01635-0.
- 8) Do KM\*, Shin M, Kodama T, Win NN, Prema, Nguyen HM, Hayakawa Y, Morita H. Flavanols and flavanes from *Crinum asiaticum* and their effects on LPS signaling pathway through the inhibition of NF- κ B activation. *Planta Med.* 2022 Sep; 88(11): 913-920. doi: 10.1055/a-1585-5877.
- 9) Ayoub AT, Nishiura N, Teshima A, Elrefaiy MA, Muslimin R, Do KM, Kodama T, Lewis CW, Chan G, Morita H, Arakawa K. Bio-inspired computational design of lankacidin derivatives for the improvement of antitumor activity. *Future Med Chem.* 2022 Oct; 14(19): 1349-1360. doi: 10.4155/fmc-2022-0134.
- 10) Hamdy SA\*, Kodama T, Nakashima Y, Han X, Morita H. Catalytic potential of a fungal indole prenyltransferase toward β-carbolines, harmine and harman, and their prenylation effect on antibacterial activities. *J Biosci Bioeng.* 2022 Oct; 134(4): 311-317. doi: 10.1016/j.jbiosc.2022.07.004.
- 11) Mori T, Nakashim Y, Morita H, Abe I. Structure, function, and engineering of plant polyketide synthases. *Methods in Enzymology.* 2022; 676: 3-48. doi: 10.1016/bs.mie.2022.06.003.

- 12) Htoo ZP\*, Kodama T, Win NN, Ikumi N, Shiokawa K, Morita H. A new sterol from the polypore fungus *Ganoderma luteomarginatum* and its cytotoxic activities. *Nat Prod Commun.* 2022; 17(5): 1-6. doi: 10.1177/1934578X221098852.

#### ◆ 総 説

- 1) 中嶋優. 沈香の香り成分の生産に関する酵素の発見. ファルマシア. 2022 Dec 1; 58(12): 1110-1114.
- 2) 森田洋行. 人工沈香の開発に繋がる「沈香の香り成分生合成」に関する鍵酵素. においてかおり環境学会誌. 2022 Jul 25; 53(284): 242-253.

#### ◆ 学会報告

- 1) Yuan-E Lee\*, Yu Nakashima, Takeshi Kodama, Xinrui Chen, Hiroyuki Morita. Dual engineering of olivetolic acid cyclase and tetraketide synthase to generate longer alkyl-chain olivetolic acid analogs. *Active Enzyme Molecule* 2022; 2022 Sep 30-Oct 1; 富山.
- 2) Yu Nakashima, Lennart Brewitz, Anthony Tumber, Eidarus Salah, and Christopher J. Schofield. Structural-based design of selective enhancement or inhibition of human 2-oxoglutarate dependent oxygenases. *JNU-UTokyo Joint Seminar on Natural Product Biosynthesis*; 2022 Jun 12; オンライン. (Invited lecture)
- 3) Hiroyuki Morita. Engineering of biosynthetic enzymes to synthesize unnatural compounds. 2022 International Symposium of Natural Products Research Institute; 2022 Dec 23; 名古屋 (オンライン). (Invited lecture)
- 4) 中嶋優, Hamdy Sherif, 内山駿, 丸山千登勢, 浜野吉十, 森田洋行. X線結晶構造解析に基づく抗生物質glycylthricin生合成酵素に見られる基質特異性の解明. 日本薬学会第142年会; 2022 Mar 25-28; 名古屋 (オンライン).
- 5) Yuan-E Lee\*, Yu Nakashima, Takeshi Kodama, Xinrui Chen, Hiroyuki Morita. Dual engineering of olivetolic acid cyclase and tetraketide synthase to generate longer alkyl-chain olivetolic acid analogs. 日本薬学会第142年会; 2022 Mar 25-28; 名古屋 (オンライン).
- 6) Kiep Minh Do\*, Takeshi Kodama, Min-Kyoung Shin, Lien Huong Ton Nu, Hien Minh Nguyen, Son Van Dang, Ken-ichi Shiokawa, Yoshihiro Hayakawa, Hiroyuki Morita. Four unprecedented pimarane diterpenoids from *Kaempferia marginata* and their NO inhibitory activities. 日本薬学会第142年会; 2022 Mar 25-28; 名古屋 (オンライン).
- 7) Saw Yu Yu Hnin, Yu Nakashima, Takeshi Kodama, Hiroyuki Morita. Crystal structure analysis of norbelladine-4'-O-methyltransferase. 日本薬学会第142年会; 2022 Mar 25-28; 名古屋 (オンライン).
- 8) 中嶋優, 川上篤士, 小笠原泰志, 大利徹, 森田洋行. ラッソペプチド生合成を担うエピメリ化酵素MsIHのX線結晶構造解析. 日本生薬学会第68回年会; 2022 Sep 10-11; 松山 (オンライン).
- 9) Kiep Minh Do\*, Takeshi Kodama, Min-Kyoung Shin, Lien Huong Ton Nu, Hien Minh Nguyen, Son Van Dang, Ken-ichi Shiokawa, Yoshihiro Hayakawa, Hiroyuki Morita. Four new pimarane diterpenoids from *Kaempferia marginata* and their NO production inhibitory activities. 日本生薬学会第68回年会; 2022 Sep 10-11; 松山 (オンライン).
- 10) Saw Yu Yu Hnin, Yu Nakashima, Takeshi Kodama, Hiroyuki Morita. Structural-based engineering of norbelladine-O-methyltransferase. 日本生薬学会第68回年会; 2022 Sep 10-11; 松山 (オンライン).
- 11) 川上篤士, 中嶋優, 森田洋行, 小笠原泰志, 大利徹. 新規ペプチドエピメラーゼMsIHの反応機構解析. 第36回日本放線菌学会大会; 2022 Sep 14-16, 福井.
- 12) 中嶋優. X線結晶構造に基づく2OG依存性酸化酵素の機能解析. 第9回食品薬物シンポジウム; 2022 Oct 15-16; 富山 (ハイブリッド). (招待講演)

#### ◆ その他

- 1) 中嶋優. 2-オキソグルタル酸依存性酸化酵素の選択的阻害剤の開発. 富山大学和漢医薬学総合研究所・長崎大学熱帯医学研究所 第11回交流セミナー; 2022 Jan 27; 長崎 (オンライン). (招待講演)