### フロンティア医科学専攻 **発生遺伝学研究室** 生存ダイナミクス研究センター 生理ダイナミクス

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## 様々な生命現象に関与する液性因子 (神経伝達物質・ホルモン・毒)の研究

多細胞からなる動物の体の機能の維持には、自律神経系が産生する神経伝達物質や、各種臓器が産生するホルモンが重要な役割を担います。特に近年、様々な臓器の間でこれらの液性因子を介した信号が交されること(臓器連環)の重要性が認識され、その破綻はがんなどの病気に直結することも提唱されています。一方、自然界を見渡せば、ある個体が別の個体を撹乱するような毒も、生態系の中で重要な役割を持つ液性因子として存在しています。しかし、これらの内在性あるいは外来の液性因子の作用機序には多くの未解明の課題が残されています。

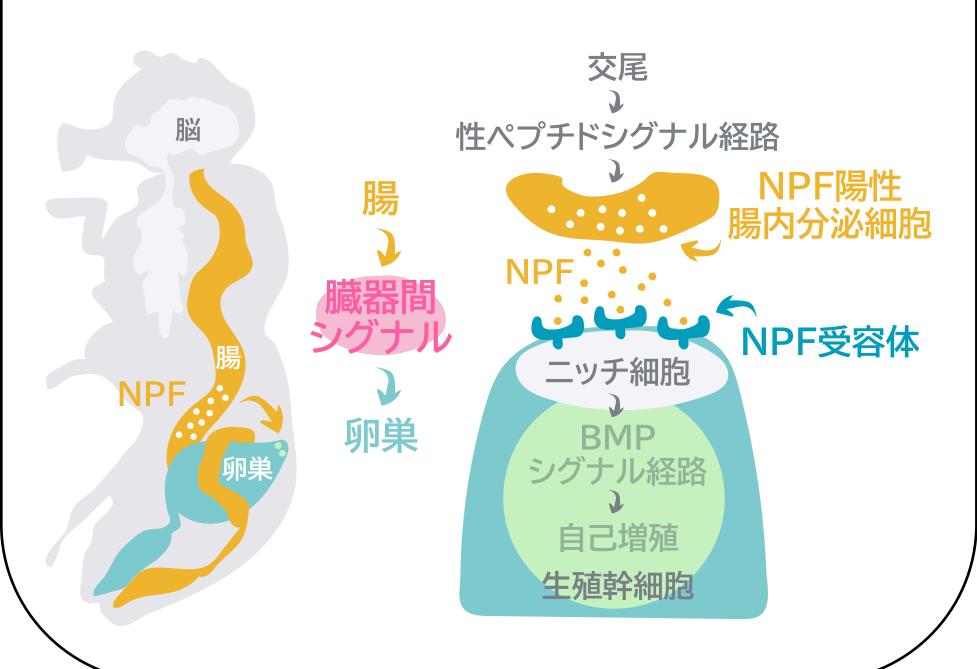
私たちは、ショウジョウバエと寄生蜂を主な材料として、 ホルモン、神経伝達物質、そして毒の作用を追究し、 ヒトにまで敷衍できるメカニズムの解明を目指します。



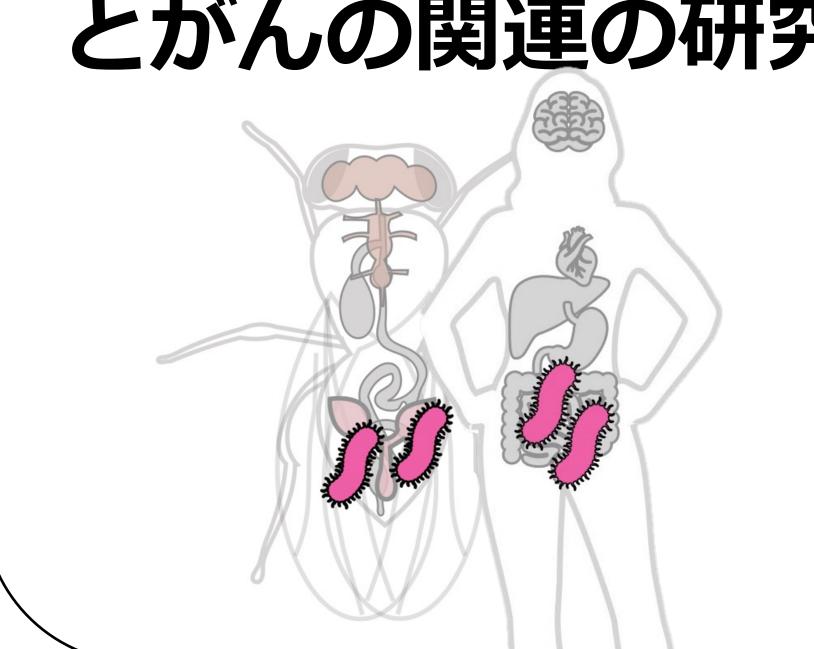
【令和6年度構成員:計22名】 教授1名、准教授1名、助教4名、 研究員1名、秘書1名、技術補佐員1名、 博士後期課程5名(内、学振採択者3名、 JST-SPRING2名)、

修士課程3名、学類生5名

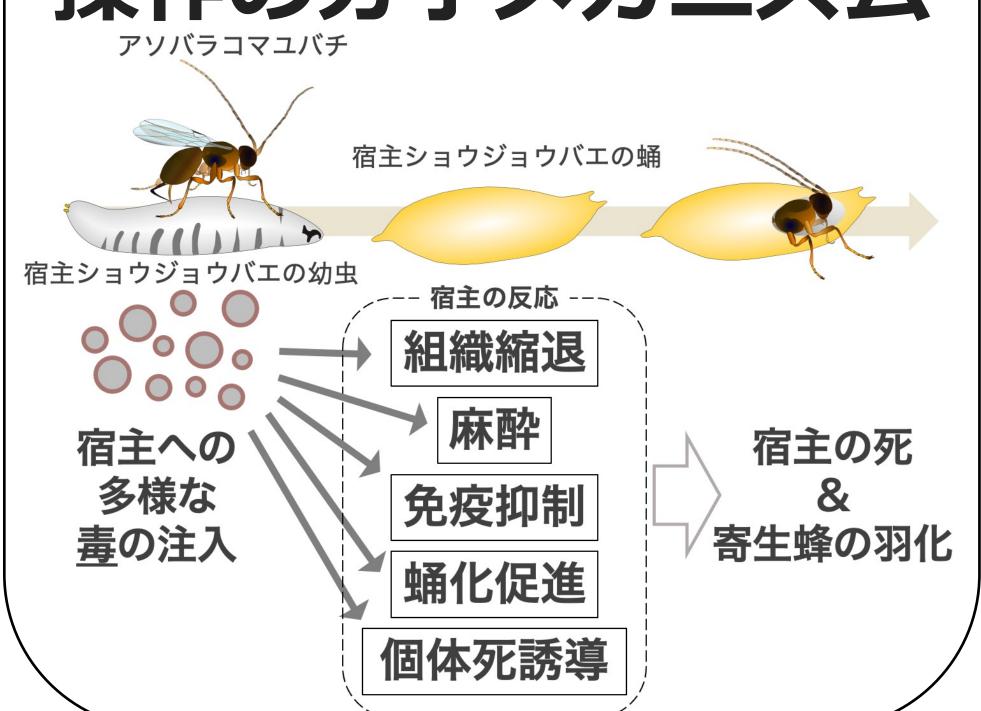




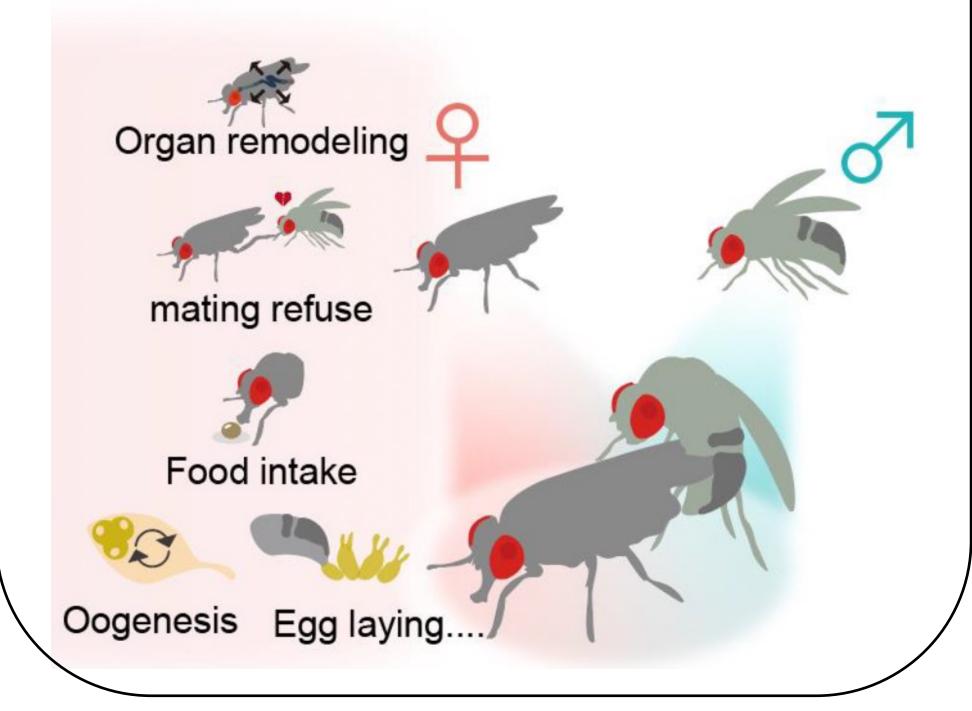
### ショウジョウバエを モデルとした腸内細菌 とがんの関連の研究



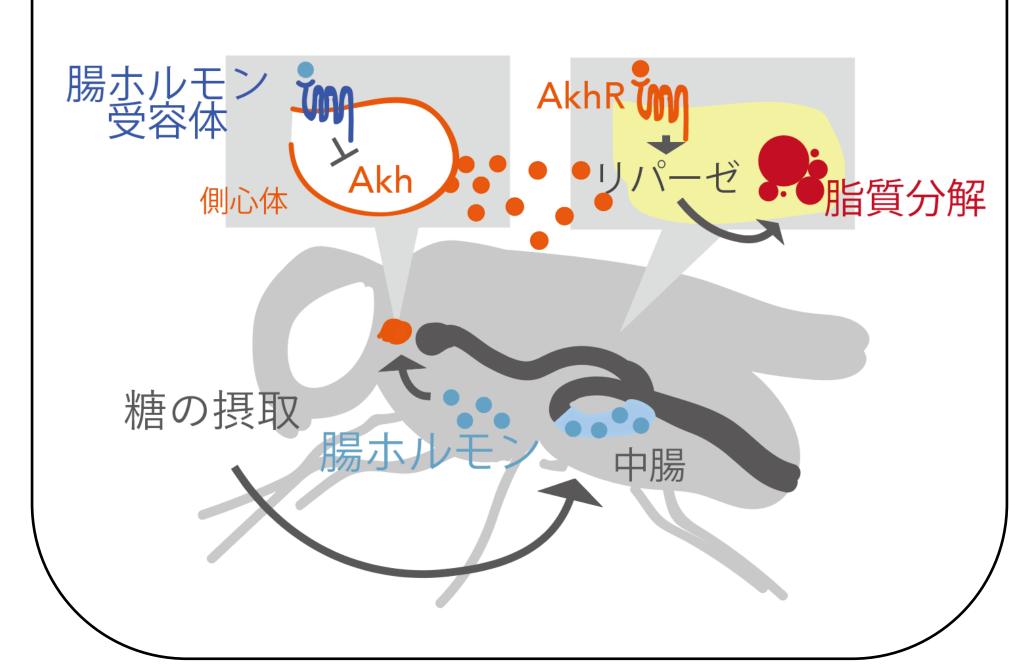
### 寄生蜂毒による宿主 操作の分子メカニズム



# 交尾に伴う個体の変化のメカニズム

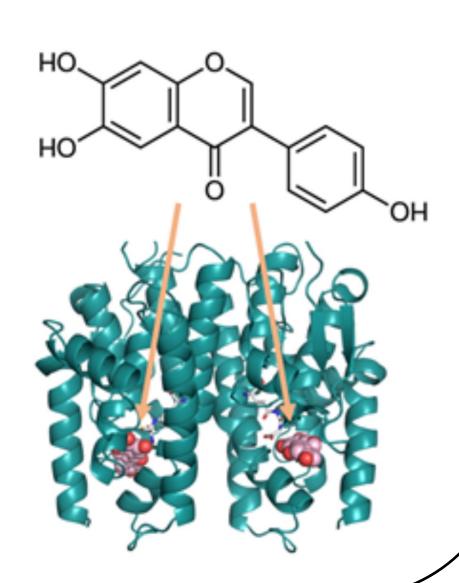


### 栄養とエネルギーの 代謝調節システム



### 昆虫生理学の 基礎的知見を 活かした創農薬科学





#### 【2020年以降の所属学生を筆頭とする主要原著論文】

J. Biol. Chem. 2020



Curr. Biol. 2020

Current Biology
The Corazonin-PTTH Neuronal Axis Controls Systemic Body Growth by Regulating Basal Ecdysteroid Biosynthesis in Drosophila melanogaster

Graphical Abstract

Authors

Eisuke Imura, 'Vuko Shimada-Niwa, Takashi Nishimura, ..., Albert Cardona, Michael J. Pankratz, Ryusuke Niwa

Corespondence shimada.yuko.gn@u.tsukuba.ac.jp
In Brief
The insect steroid hormone, ecdysteroid, coordinates growth and maturation. Imura et al. identify that the Crz-PTTH neuronal axis controls growth by regulating basal ecdysteroid production in response to octopamine neurons. Crz/Crz is homologous to GnRH/GnRHR, which is required for puberty, implying an analogous role in growth and maturation.

PTTH neurons respond to Crz neurons during the mid-L3 stage with CrzR expression

Octopamine neurons contact with Crz neurons in the SEZ, regulating systemic growth

Imura et al. 2020. Current Biology 20, 1-10
June 6, 2020 © 2020 The Author(e). Published by Elsevier Inc. https://doi.org/10.1016/j.cub.2020.033050

eLife 2020

Neuronal octopamine signaling regulates mating-induced germline stem cell increase in female Drosophila melanogaster

Yet Oshinari , Tomotsune Ameku'', Shu Kondo', Hiromu Tanimoto', Takayuki Kuraishi. ", Yuko Shimada-Niwa', Ryusuke Niwa''s

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Nature Commun. 2021

ARTICLE

Migrat/Mol. org/L00.1031/4/14647-021-25146\*

OPEN

The sugar-responsive enteroendocrine neuropeptide F regulates lipid metabolism through glucagon-like and insulin-like hormones in Drosophila melanogaster

Yuto Yoshinaril<sup>2</sup>, Hina Kosakamoto <sup>3,4</sup>, Takumi Kamiyama<sup>2</sup>, Ryo Hoshino<sup>2</sup>, Rena Matsuoka<sup>2</sup>, Shu Kondo<sup>5</sup>, Hiromu Tanimoto<sup>6</sup>, Akira Nakamura <sup>3,7,8</sup>, Fumiaki Obata <sup>13,4,9,10</sup> & Ryusuke Niwa <sup>1,10</sup> Ulife The enteroendocrine cell (EEC)-derived incretins play a pivotal role in regulating the secretion of glucagon and insulins in mammals. Although glucagon-like and insulin-like hormones have been found across animal phyla, incretin-like EEC-derived hormones have not yet been characterised in invertebrates. Here, we show that the miglid-derived hormones have not yet been characterised in invertebrates. Here, we show that the miglid-derived hormones have not yet been characterised in invertebrates. Here, we show that the miglid-derived hormones have not yet been characterised in invertebrates. Here, we show that the miglid-derived hormones have not yet been characterised in invertebrates. Here, we show that the miglid-derived hormones have not yet been characterised in invertebrates. Here, we show that the miglid-derived hormone producing cells. NPF-NPFR signalling resulted in the suppression of the glucagon-like hormones or cardiaca and in insulin-producing cells. NPF-NPFR signalling resulted in the suppression of the glucagon-like hormones producing and the enhancement of the insulin-like peoply depression. Similar to the loss of incretin function in mammals, loss of midgut NPF led to significant metabolic drysfunction, accompanied by liquody-trophy, hyperphagia, and hypoglycamia. These results suggest that enteroendocrine hormones regulate sugar-dependent metabolism through glucagon-like and insulin-like hormones not only in mammals but also in insacts.

\*\*Ille Science Center for Sunival Dynamica, Takuba Advanced Research Alliance (TASA), University of Takuba, Takuba, Ispan, Pognative of Generice

BMC Biol. 2022

RESEARCH ARTICLE

Open Access

Molecular action of larvicidal flavonoids
on ecdysteroidogenic glutathione S-transferase
Noppera-bo in Aedes aegypti

Kazue Inaba¹², Kana Ebihara²³, Miki Senda², Ryunosuke Yoshino⁴ō, Chisako Sakuma⁴, Kotaro Koiwa¹²,
Daisuke Takaya², Chiduru Watanabe², Akira Watanabe², Vusuke Kawashina³, Kaori Fukuzawa³, Ryo Imamura²,
Hirotatsu Kojima³, Takayaoni Chabe², Nacoru Imema¹a³, Shinikasia Kanuka⁵, Takashi Nishimura¹¹,
Kodai Watanabe², Hideshi Inoue²², Yutufa Fujikawa¹², Teruki Honma², Takatsugu Hirokawa⁴⁵₅¹³,
Toshiya Senda²¹⁴₅¹³ and Ryusuke Niwa²¹²⁵ ⊚

Abstract

Background: Mosquito control is a crucial global issue for protecting the human community from mosquito-borne
diseases. There is an urgent need for the development of selective and safe reagents for mosquito control. Flavonoids,
a group of chemical substances with variable phenolic structures, such as daidzein, have been suggested as potential
mosquito lavicides with less risk to the environment. However, the mode of mosquito lavicidal action of flavonoids
has not been elucidated.

Results: Here, we report that several flavonoids, including daidzein, inhibit the activity of glutathione-Stransferase
Noppera-bo (Nobo), an enzyme used for the biosynthesis of the insect steroid hormone ecdysone, in the yellow
fever mosquito and its molecular dynamics simulation revealed that Glu 113 forms a hydrogen bond with the flavonoids
and its molecular dynamics simulation revealed that Glu 113 forms a hydrogen bond with the flavonoid
inhibitors. Consistent with his observation, substitution of Glu 113 with Ala darastical produced the inhibitory activity
of the flavonoids against AeNobo. Among the identified flavonoid-ype inhibitors, activity of the flavonoids activity as desmethylglyciten suppressed Ae aegypti Produced the inhibitory activity
of the flavonoids against AeNobo. Among the identified flavonoid on the Ae aegypti Nobo protein at the atomic,
enzymatic, and organismal levels.

Keywords: Aedes aegypti flavona-1-1-1 revosal flavona-1 fla

Development 2023

RESEARCH ARTICLE

Female reproductive dormancy in Drosophila is regulated by DH31-producing neurons projecting into the corpus allatum

Yoshitomo Kuroqii, Eisuke Imura<sup>2,3,4</sup>, Yosuke Mizuno<sup>3</sup>, Ryo Hoshino<sup>3</sup>, Marcela Nouzova<sup>4,6</sup>, Shigeru Matsuyama<sup>6</sup>, Akira Mizoquchi<sup>7</sup>, Shu Kondo<sup>5,3</sup>, Hiromu Tanimoto<sup>10</sup>, Fernando G. Noriega<sup>4,11</sup> and Ryusuke Niwa<sup>3,2</sup>

ABSTRACT

Female insects can enter reproductive diapause, a state of suspended egg development, to conserve energy under adverse environments. In many insects, including the full 8, Drosophila melanogaster, reproductive diapause, also frequenty called reproductive domanor, bi dudout order low-temperature and short-day conditions by the downegulation of juvenile hormone (Phy Diosynthesis in the corpus allatum (CA). In this study, we demonstrate that neuropaptice Direct hormone 31 (DH31) produced by brain neurons that project into the CA plays an essential role in regulating reproductive domancy, bin special proproductive domancy by suppressing JH biosynthesis in adult D. melanogaster, The CA expresses the gene encoding the DH31 receptor, which is required for DH31-friagened elevation of intracelular cAMP in the CA-Krocking down DH31 in these CA-projecting neurons or DH31 receptor in the CA suppresses the decrease of JH titer, normally observed under domancy-inducing conditions, leading to ahnormal yold accumulation in the ovaries. Our findings provide the first molecular genetic evidence demonstrating has the absorbance of the conditions, leading to a proproductive domancy by suppressing JH biosynthesis.

Degree Programs in Life and Earth Sciences, Gindustis School of Science and Technology, University of Taskota, Ternoduction, Careb Republic. Acres Republic. Sciences and Technology, University of Taskota, Ternoduction, Careb Republic. Acres Republic. Sciences and Technology, University of Taskota, Ternoduction, Careb Republic. Acres Republic. Sciences and Technology, University of Taskota, Ternoduction, Careb Republic. Acres Republic. Sciences and Technology

Handling Editor: Irene Miguel-Aliaga Received 3 August 2022; Accepted 12 April 2023 Science Adv. 2023



ウェブページURL https://sites.google.com/view/niwa-lab-tsukuba/

