Juvenile Hormones: Guiding the Lives of Insects

LXL XLM WR

20241226

Outline

Part I Overview: Past and Present Insights into the Function of Juvenile Hormones

--LXL

Part II Juvenile Hormones: Key Regulators of Development

--XLM

Part III Juvenile Hormones: Shaping Innate Behavioral Patterns

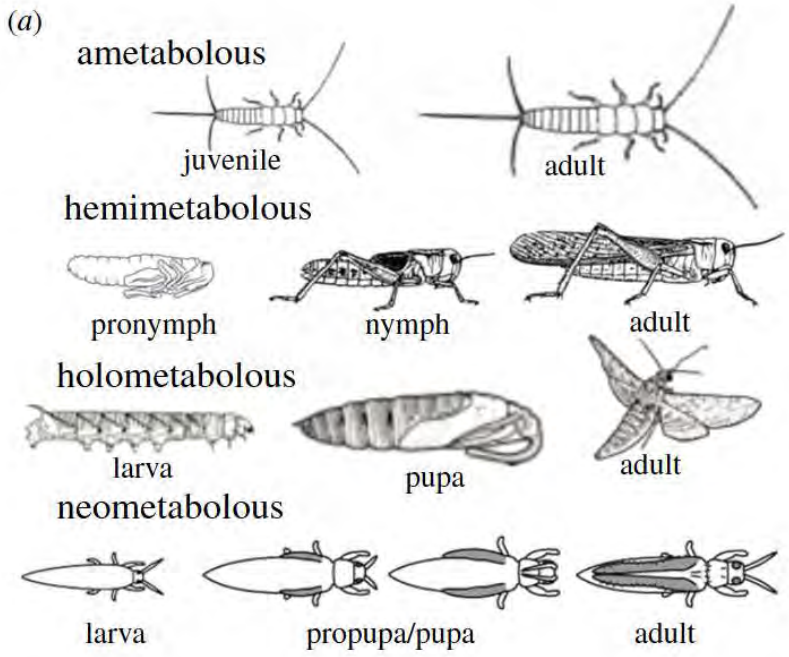
--WR

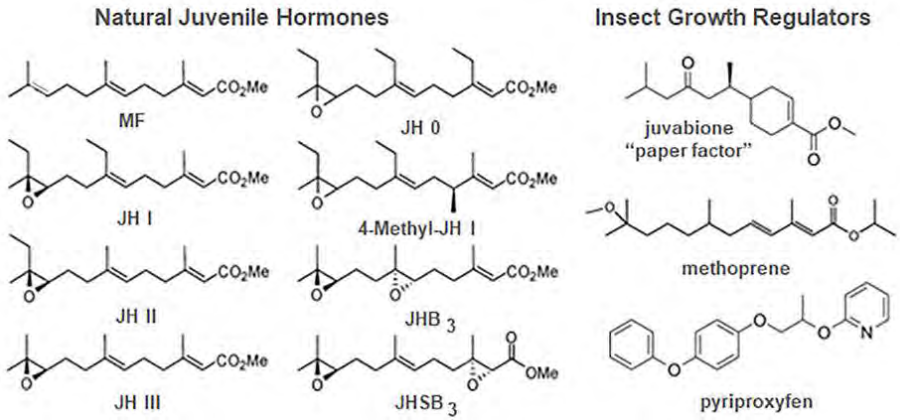
Part I Overview: Past and Present Insights into the Function of Juvenile Hormones

LXL

Juvenile Hormones

- Juvenile hormone (JH) is a unique sesquiterpenoid hormone(倍半萜类激素)which regulates both insect metamorphosis and insect reproduction





Truman JW et al. , *Philos Trans R Soc Lond B Biol Sci,2019*

Riddiford LM. , *Front Cell Dev Biol, 2020*

Questions

- How was Juvenile hormone discovered ?
- What is the receptor and downstream of juvenile hormone?
- What regulates juvenile hormone?

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Sir Vincent Wigglesworth

Vincent Wigglesworth

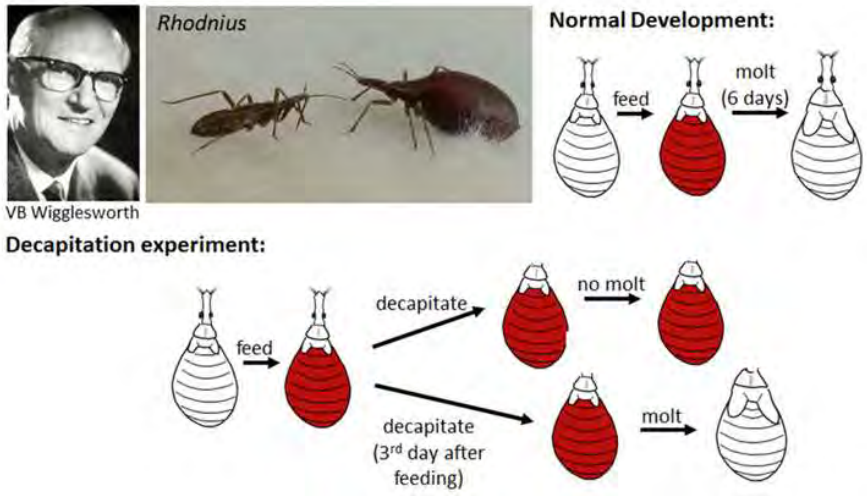
Born	17 April 1899 Wesham, Lancashire
Died	11 February 1994 (aged 94)
Nationality	British
Known for	Metamorphosis hormones
Awards	Royal Medal (1955) Fellow of the Royal Society
Scientific career	
Fields	Entomologist
Institutions	University of Cambridge
Doctoral students	Peter Lawrence

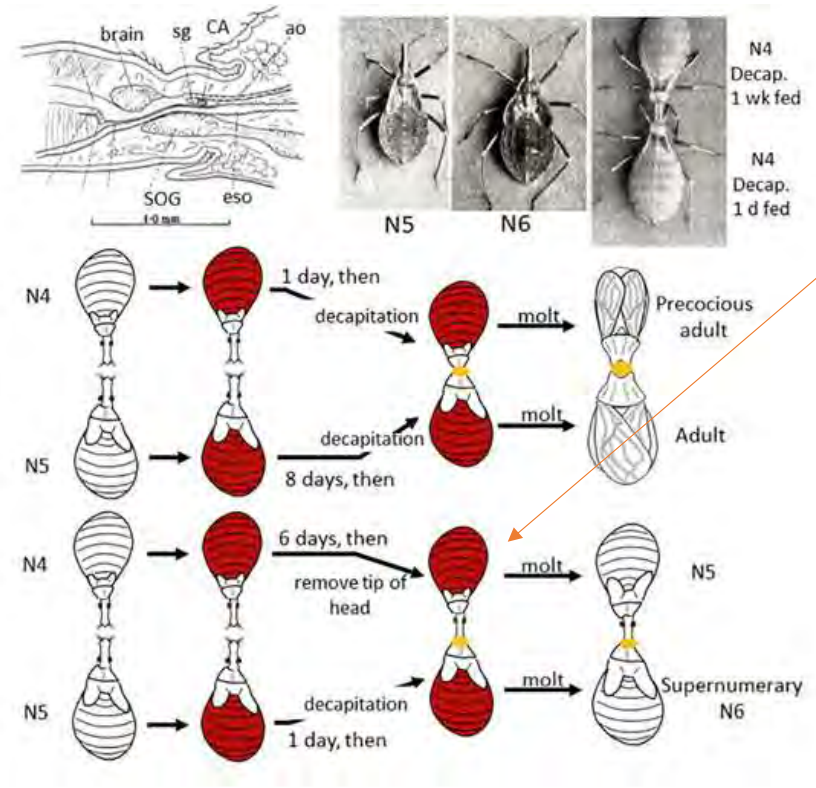
study

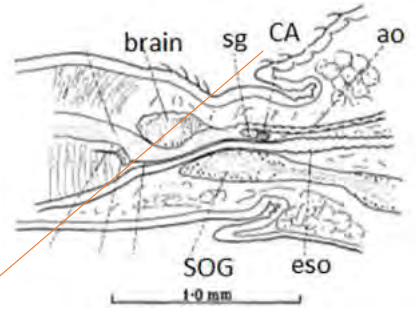
- Discovery that neurosecretory cells secrete a crucial hormone that triggers the prothoracic gland to release prothoracicotropic hormone (PTTH), which regulates the process of metamorphosis.

- Discover the juvenile hormone, which prevented the development of adult characteristics in *R. prolixus* until the insect had reached the appropriate larval stage.

Juvenile hormone (JH) of the corpus allatum inhibits metamorphosis







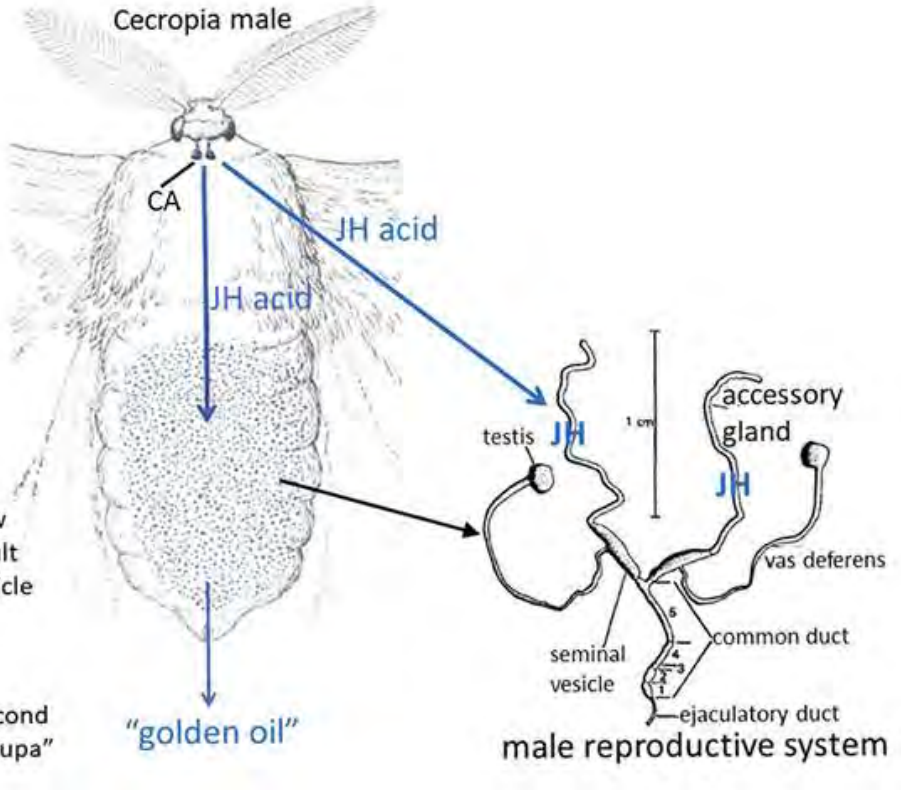
1940

Wigglesworth, V. B. , *Quart. J. Microsc. Sci, 1934*

Riddiford LM. , *Front Cell Dev Biol, 2020*

Purification of juvenile hormone (JH)

C. M. Williams

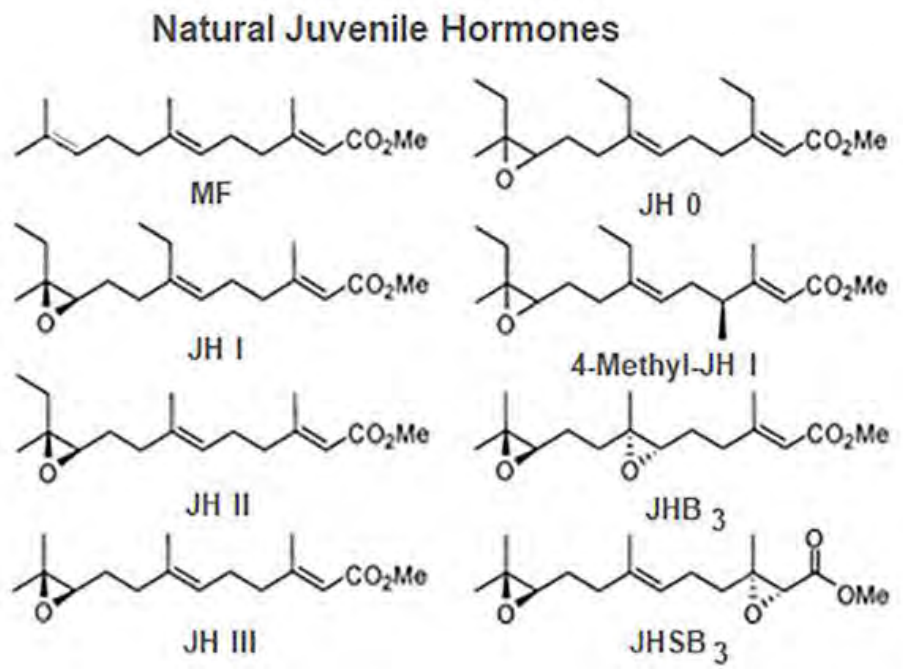


Williams, *1956*

Riddiford LM. , *Front Cell Dev Biol, 2020*

Classification of the natural juvenile hormones

JH I 和 II 从Polyphemus pupae中提取出来，仅存在于鳞翅目中



JHB3在果蝇中发现

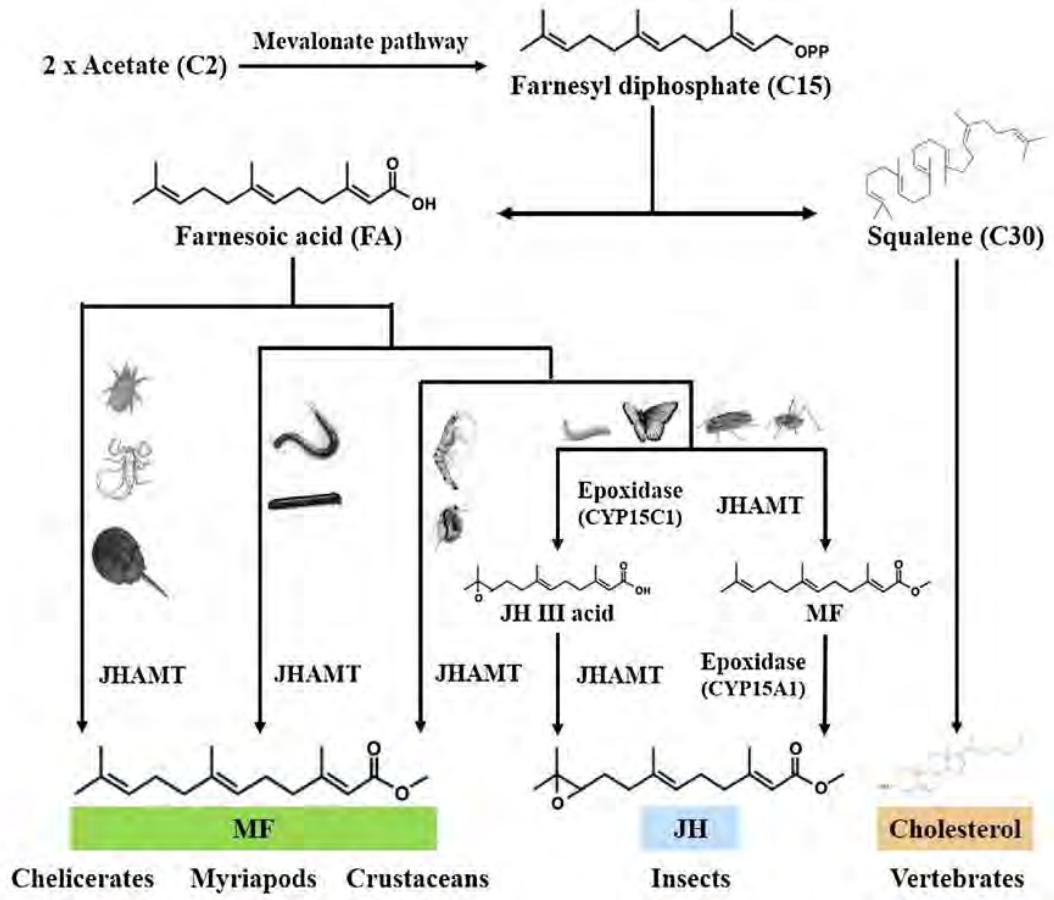
JHSB3在臭虫*Plautia stali*中发现

JH III、JH 0 和4-甲基-JH I 从鳞翅目烟草天蛾*M. sexta*中提取出来

甲基法尼酯 (MF)是甲壳动物的保幼激素

Riddiford LM.， *Front Cell Dev Biol, 2020*

The biosynthetic pathway of sesquiterpenoid hormones



Qu Z ., *J Steroid Biochem Mol Biol, 2018*

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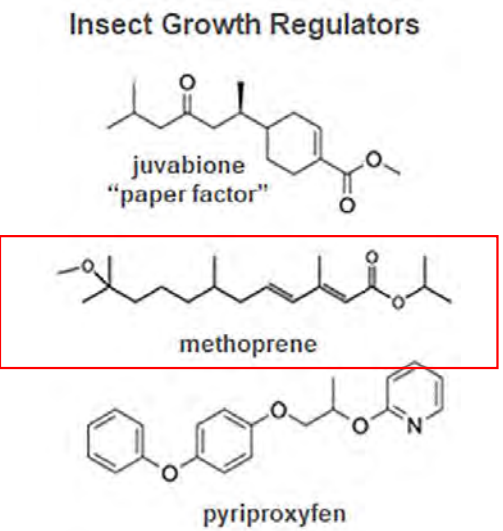
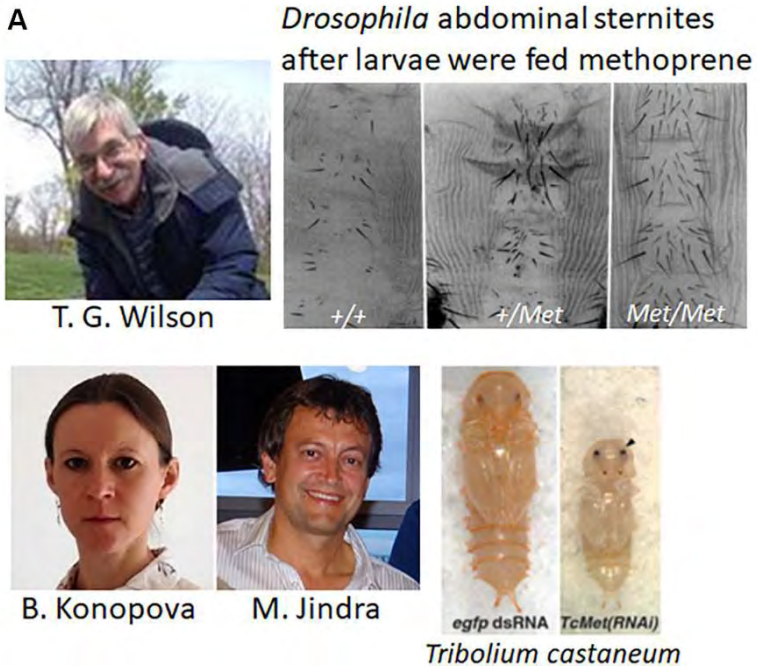
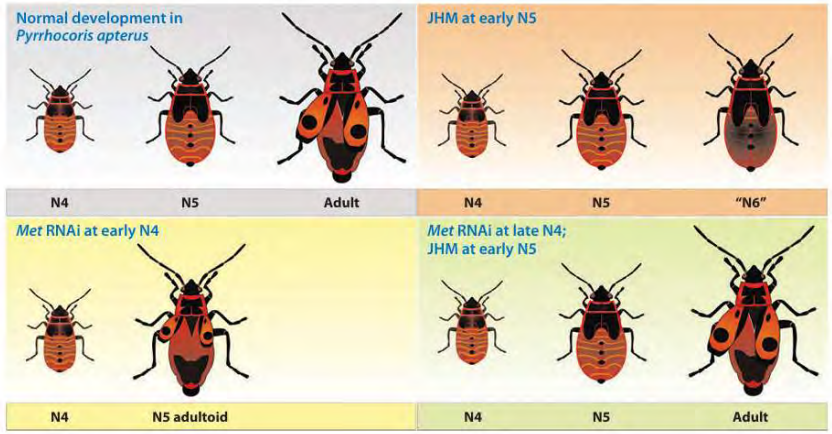
Juvenile hormone receptor :Met





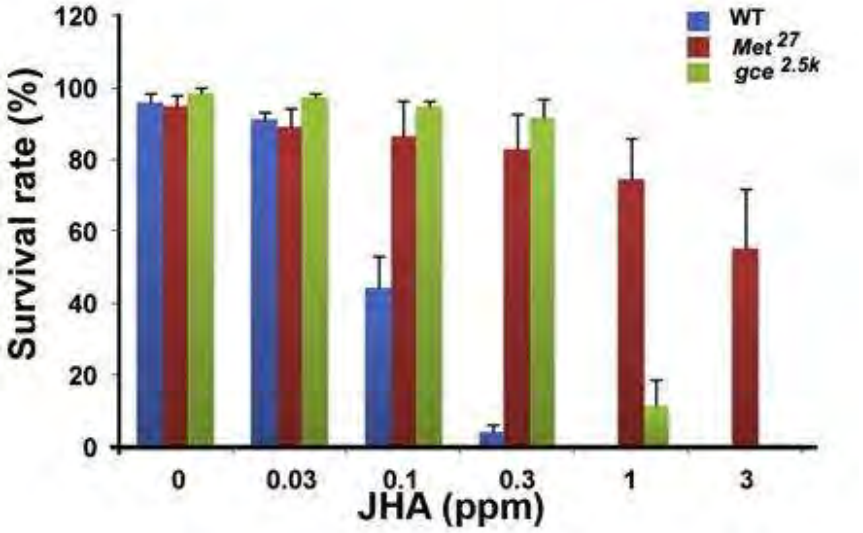


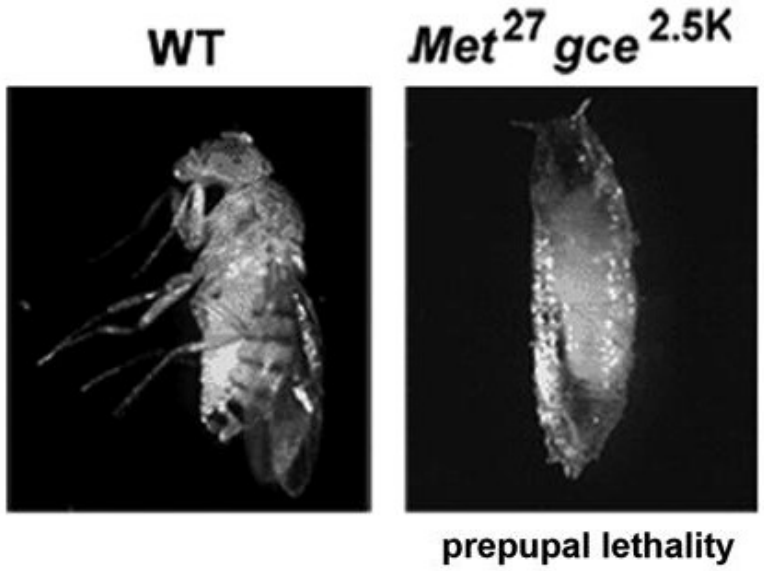
Riddiford LM. , *Front Cell Dev Biol, 2020*

Tom Wilson, *1986*

Marek Jindra. , *Annu Rev Entomol, 2012*

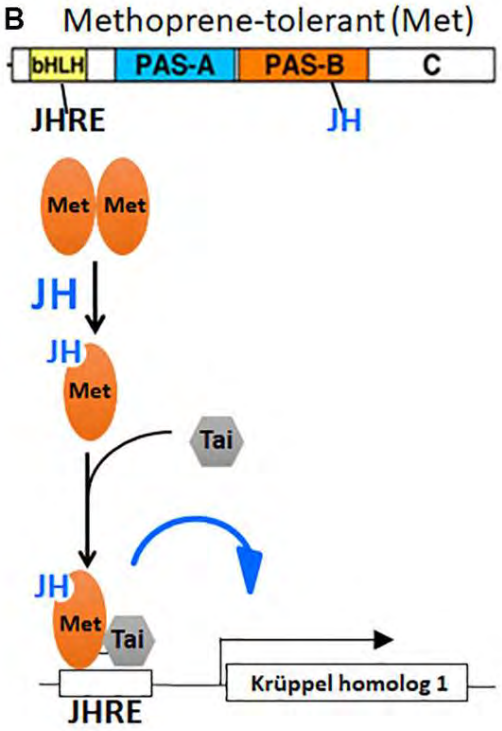
Juvenile hormone another receptor :Gce

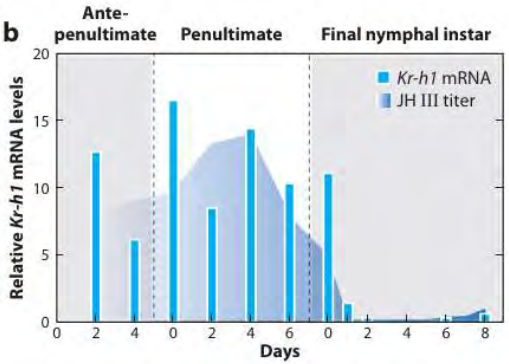


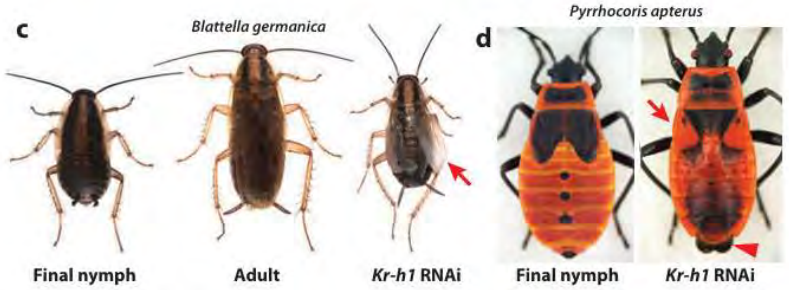


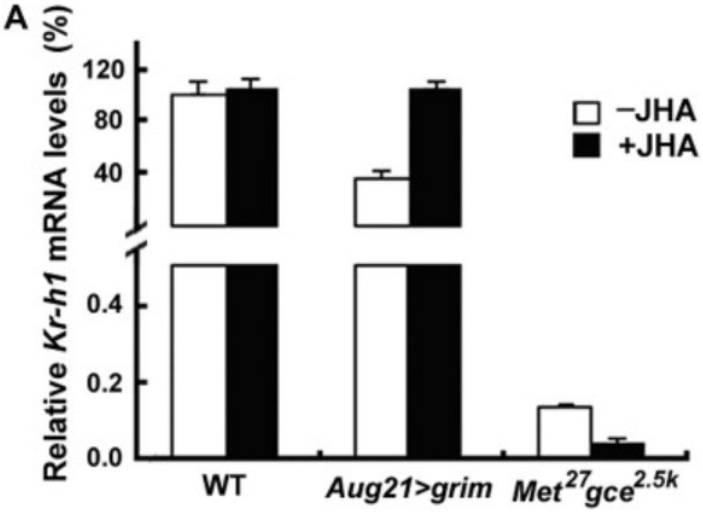
Abdou MA et al. , *Insect Biochem Mol Biol, 2011*

Kr-h1 is a universal repressor of insect metamorphosis







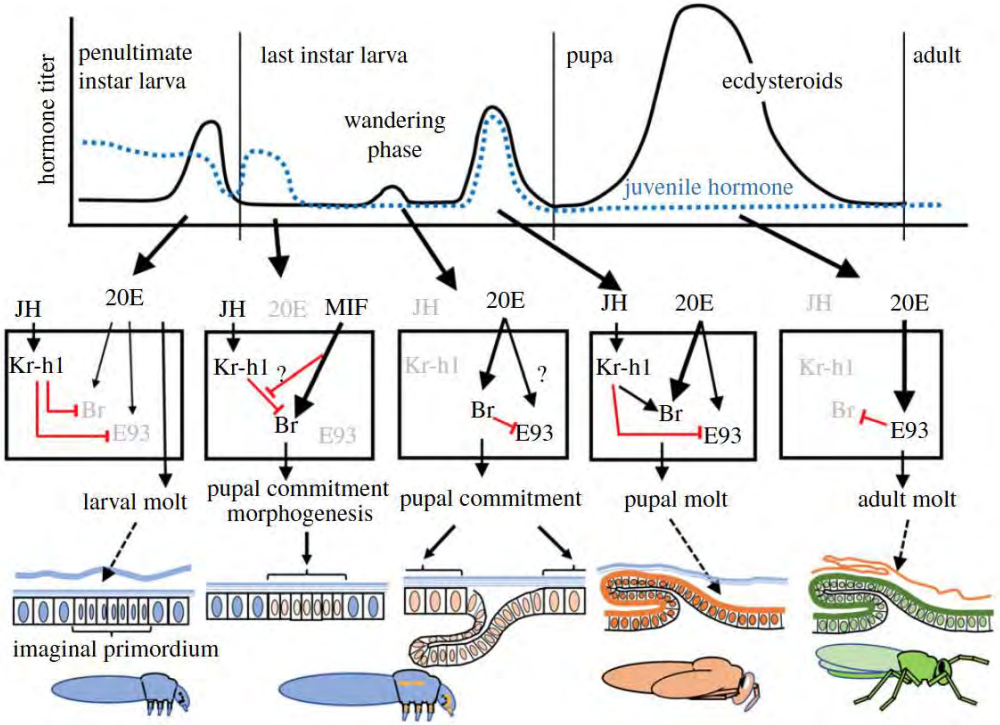


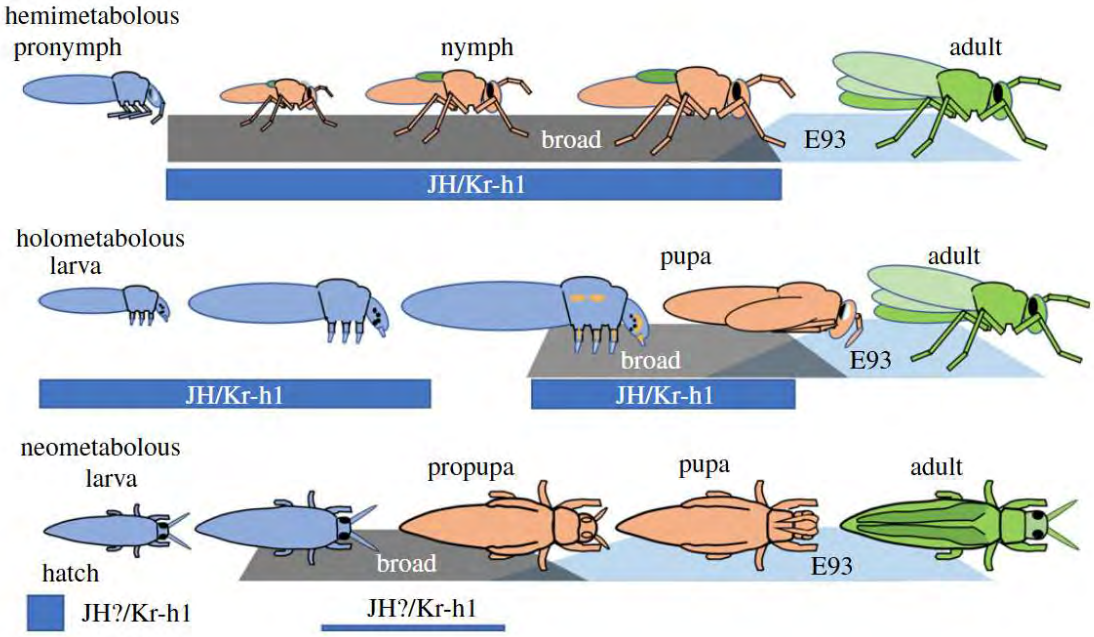
Riddiford LM. , *Front Cell Dev Biol, 2020*

Marek Jindra. , *Annu Rev Entomol, 2012*

Abdou MA et al. , *Insect Biochem Mol Biol, 2011*

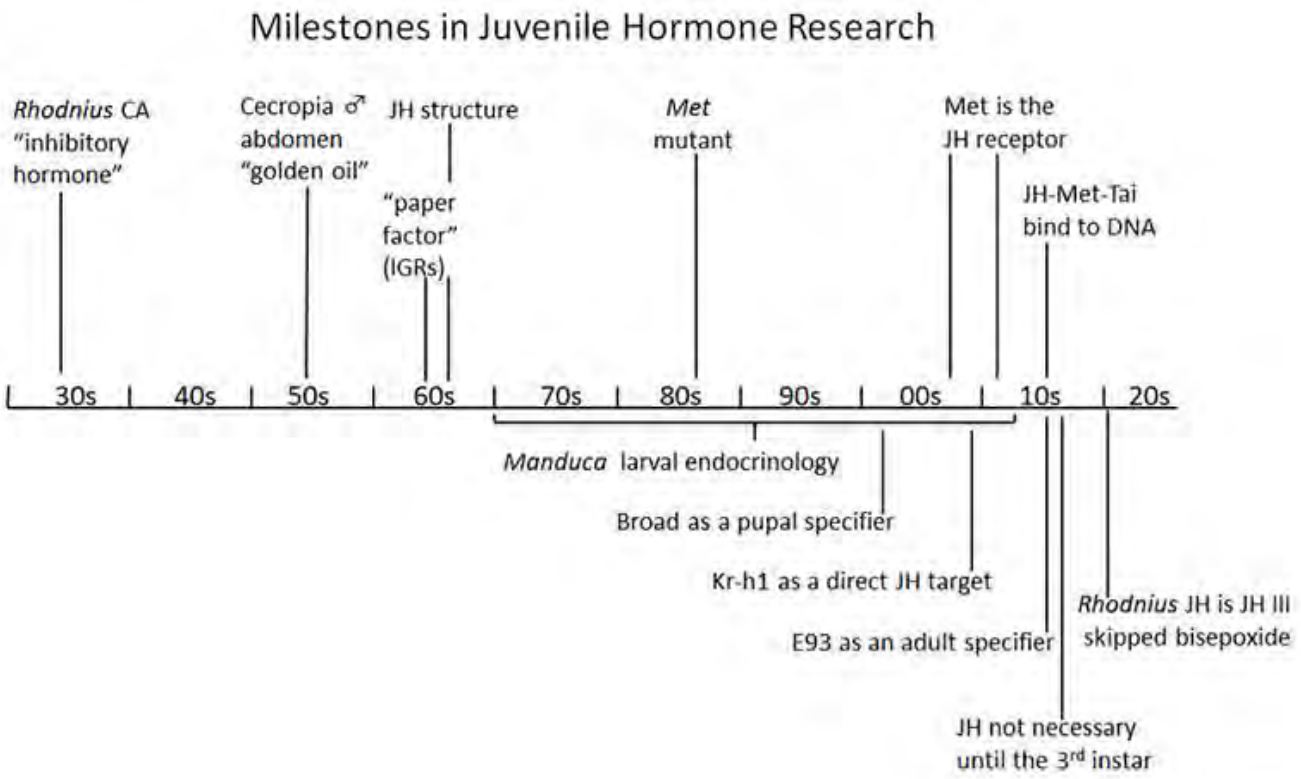
Juvenile hormone and 20E regulate insect metamorphosis





Truman JW et al. , *Philos Trans R Soc Lond B Biol Sci,2019*

Research history of juvenile hormone



Riddiford LM. , *Front Cell Dev Biol, 2020*

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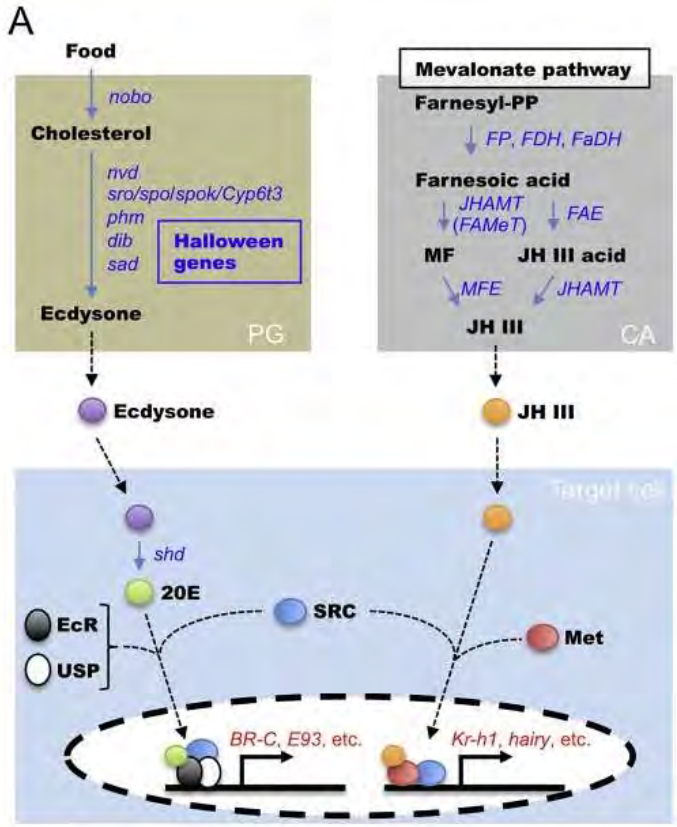
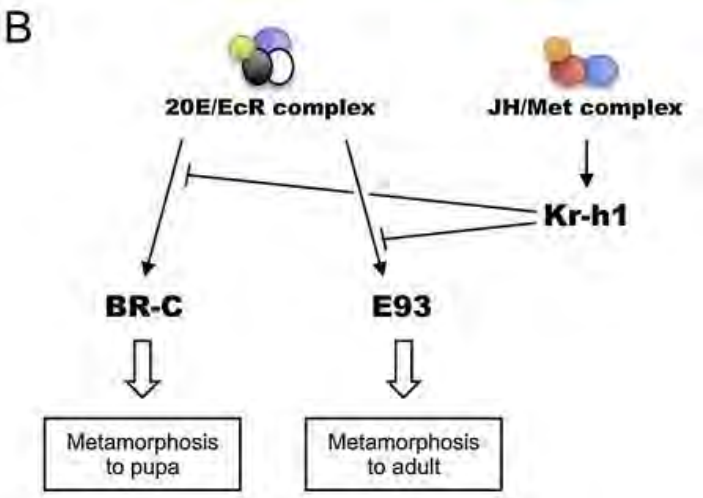
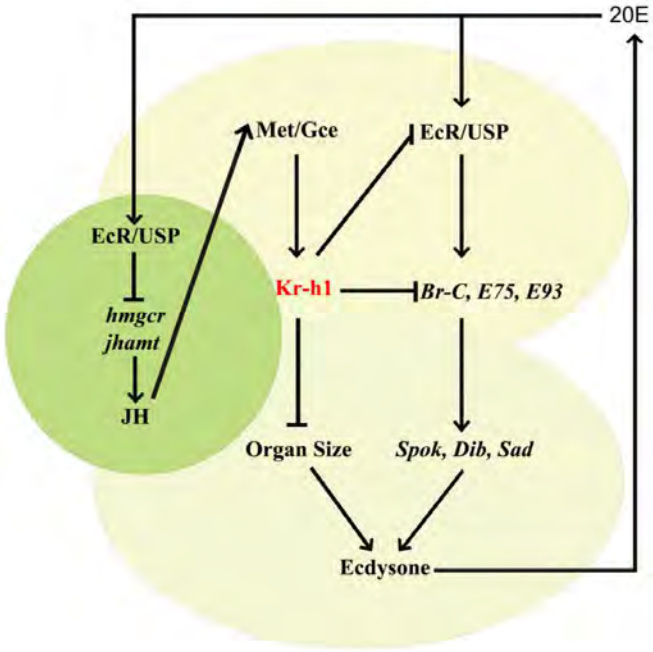
A schematic view of the ecdysteroid and juvenile hormone (JH) signaling pathways in insects



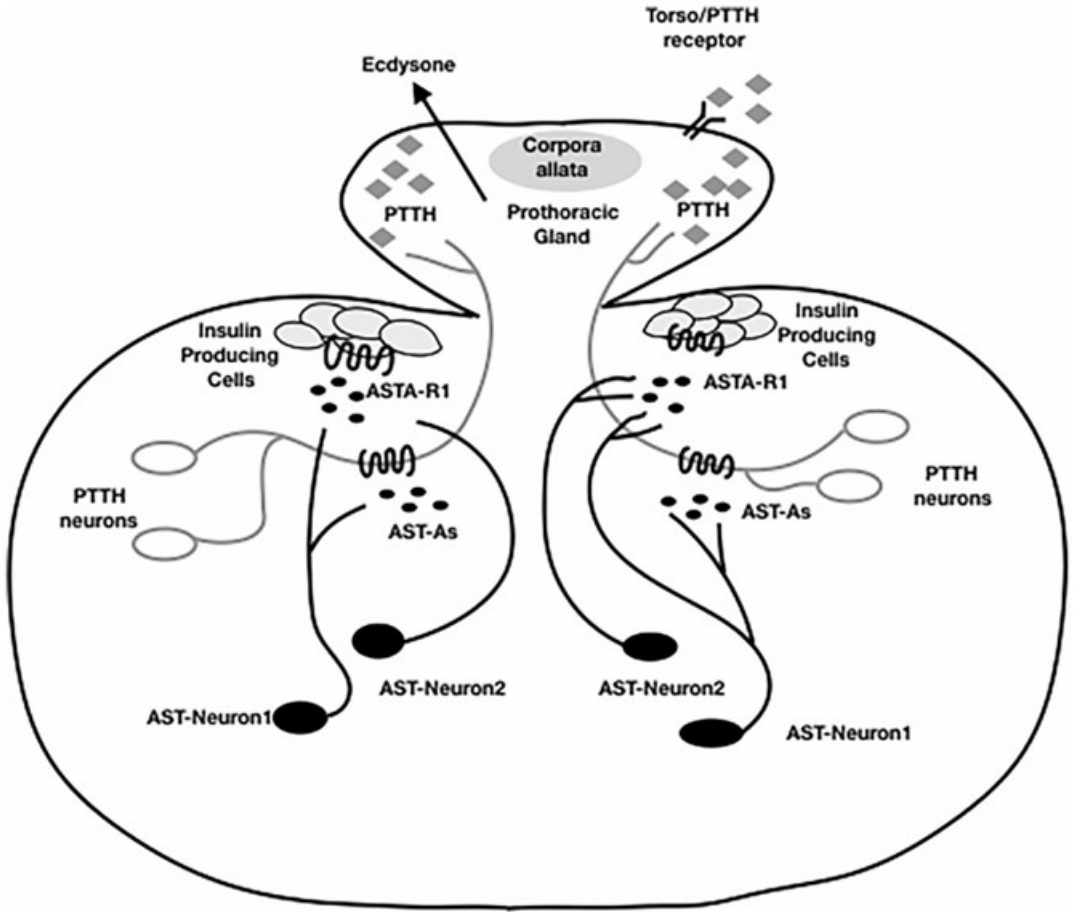




Miyakawa H et al., *J Steroid Biochem Mol Biol, 2018*

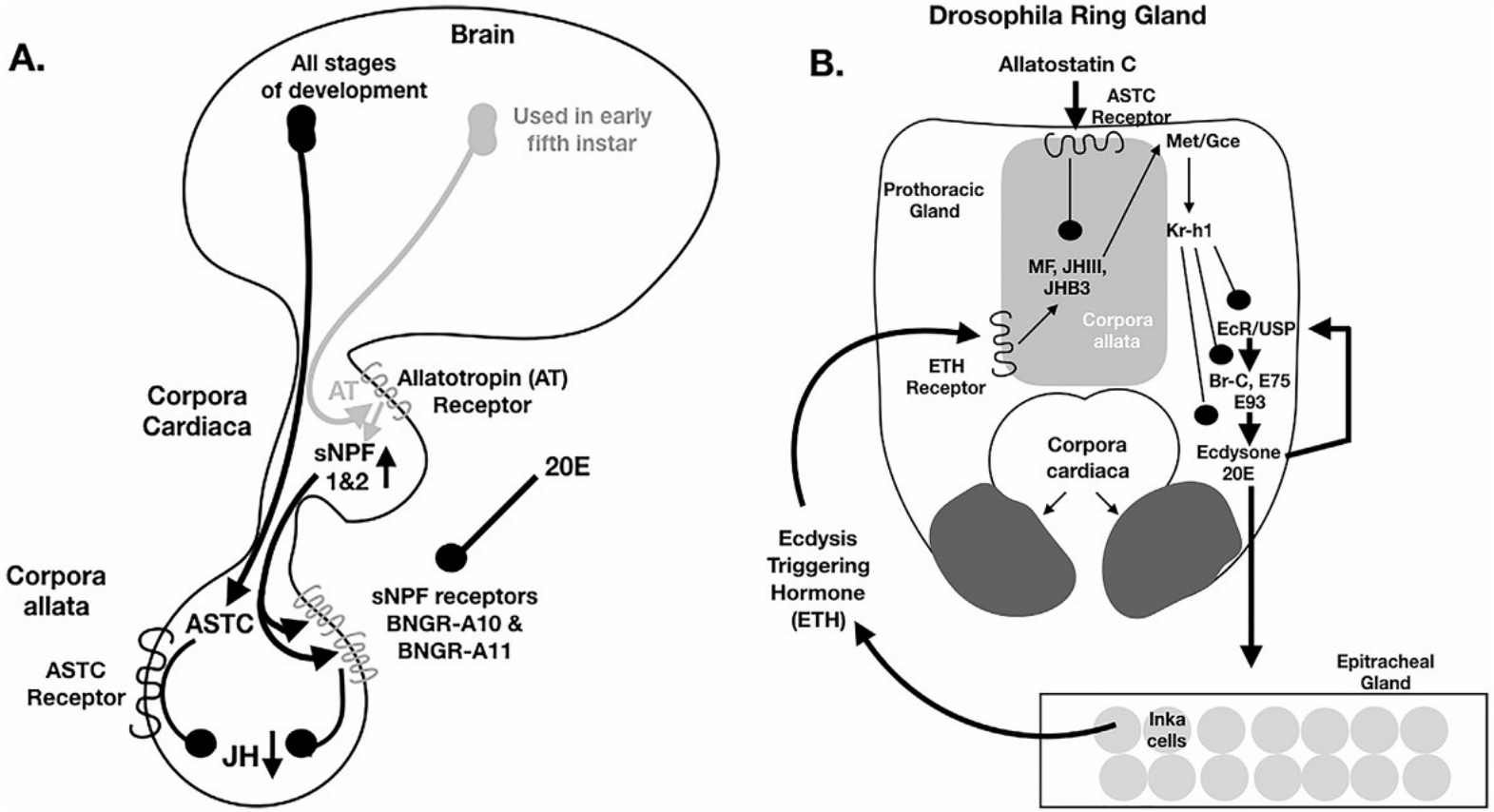
Liu S et al., *PNAS*, 2018

AST neurons deliver AST-As to AST-AR1 localized on PTTH dendrites and insulin-producing cells



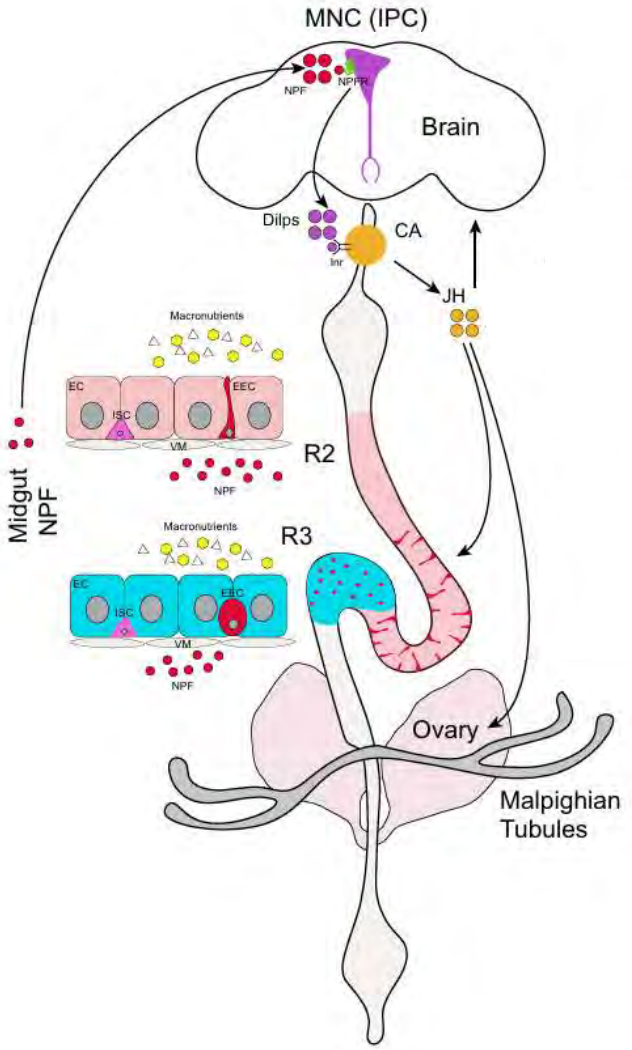
Bendena WG et al., *Gen Comp Endocrinol, 2020*

Diverse signaling pathways regulate juvenile hormone biosynthesis in the moth Bombyx mori and the fruit fly drosophila melanogaster



Bendena WG et al., *Gen Comp Endocrinol, 2020*

Model of interorgan communication between gut–brain–corpora allata in *D. melanogaster*



Chen J et al., *PNAS, 2024*

Summary

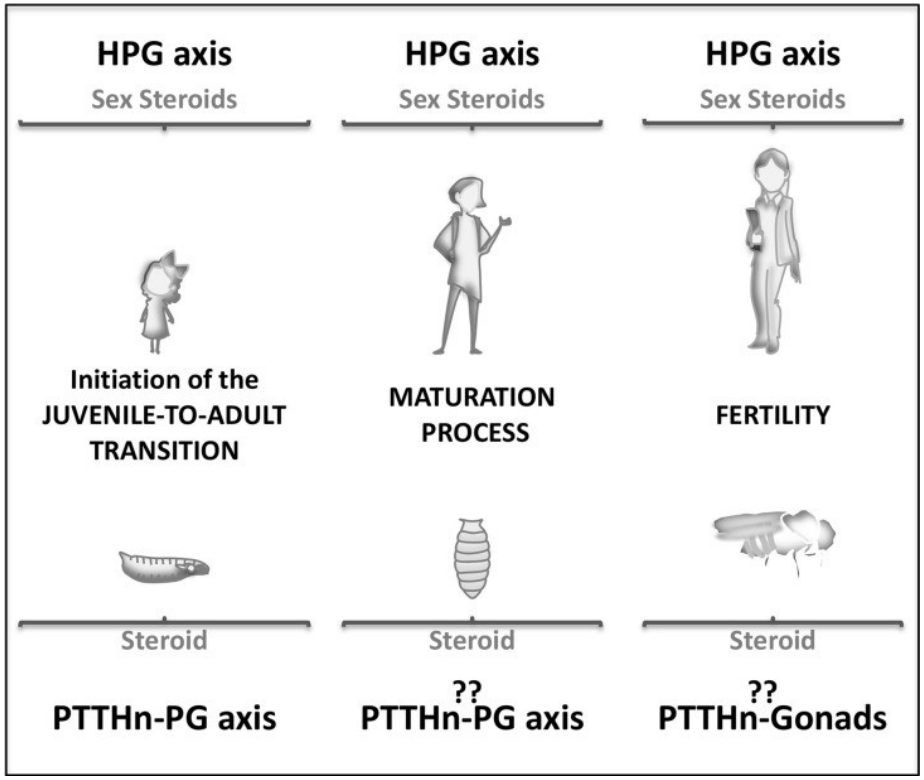
- There are different types of juvenile hormone in different insects
- Juvenile hormone receptor and downstream: Met/Gce, kr-h1
- Juvenile hormone and ecdysone antagonize each other and jointly regulate insect development

PART II

Juvenile Hormone: Key Regulator of Development

XLM

Neurohormonal axes triggering Juvenile-Adult (J/A) transition in mammals and insects

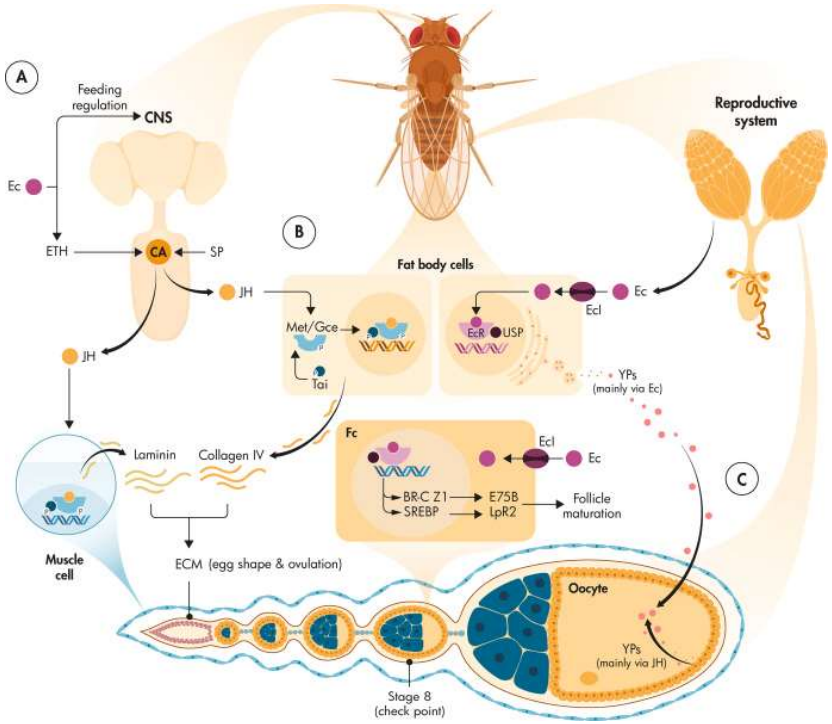


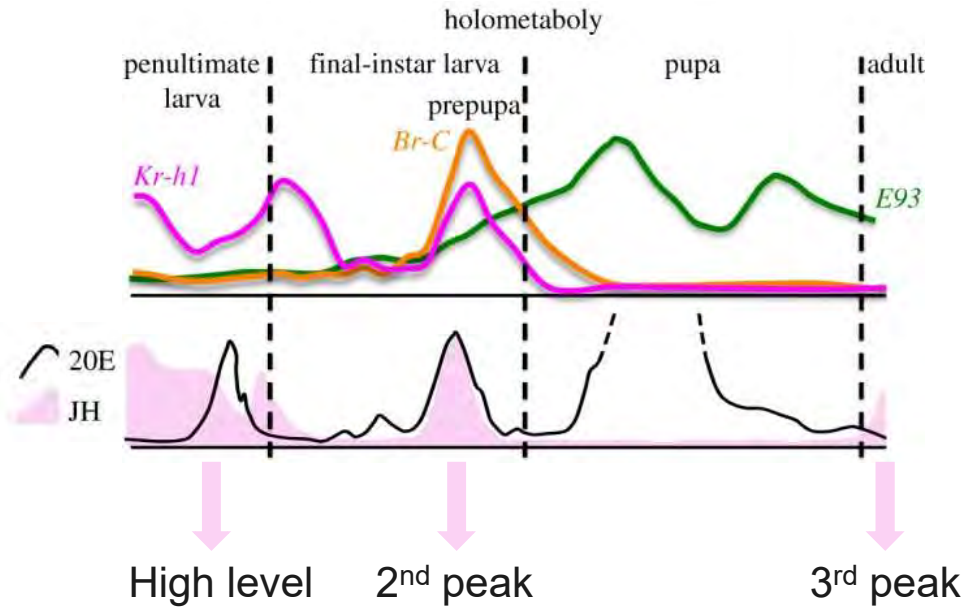
下丘脑-垂体-性腺轴

促胸腺激素-前胸腺轴

Barredo CG, *et al. Front Endocrinol (Lausanne).* 2021

Juvenile hormone plays an important role in insect development

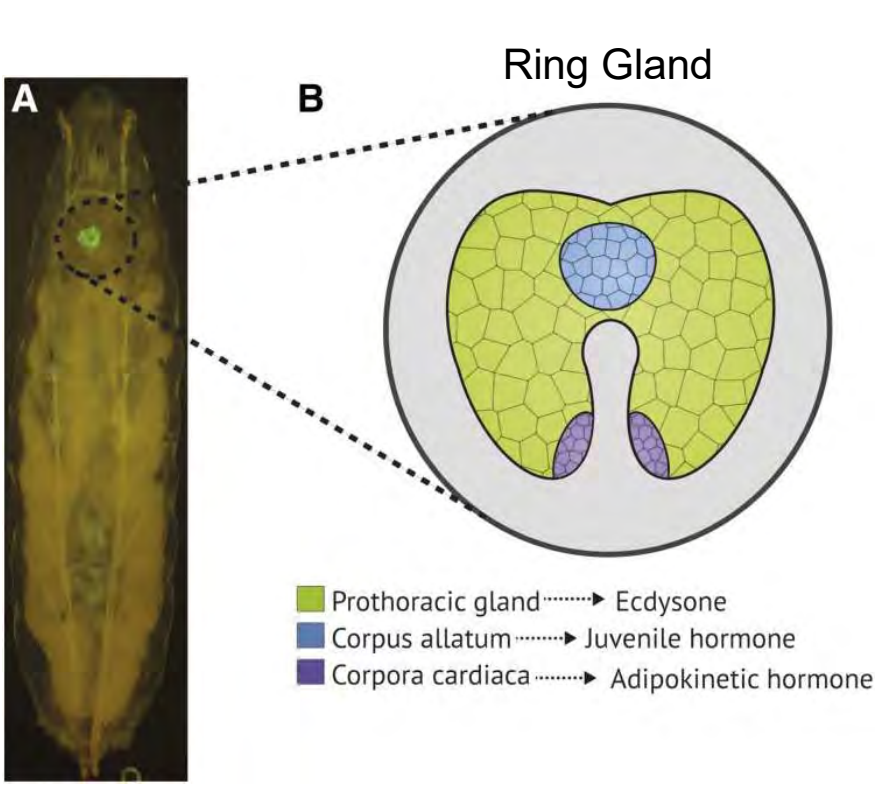


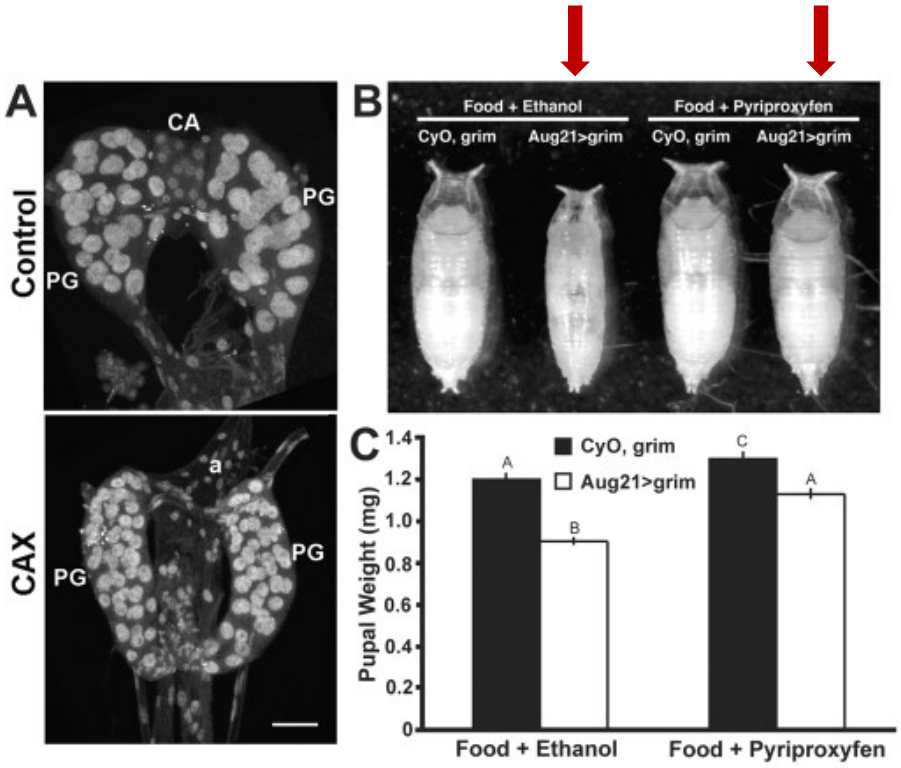


What are the biological functions of Juvenile Hormone in different stage?

Jimena Leyria. *Molecular and Cellular Endocrinology*. 2024
Jindra M. *Philos Trans R Soc Lond B Biol Sci*. 2019

JH participates in the prepupal development in *D. Melanogaster*





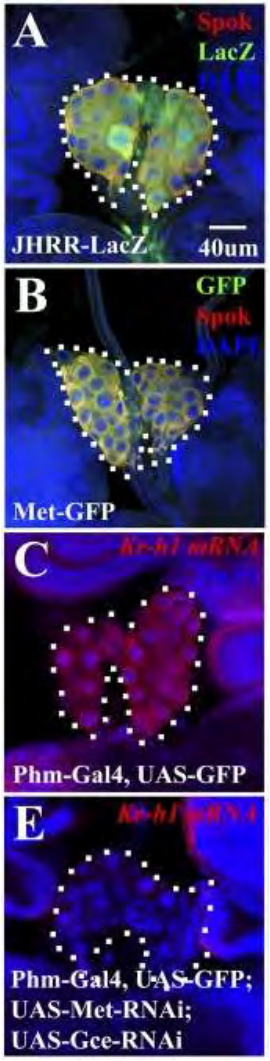
Christesen D, *et al. G3 (Bethesda)*. 2017

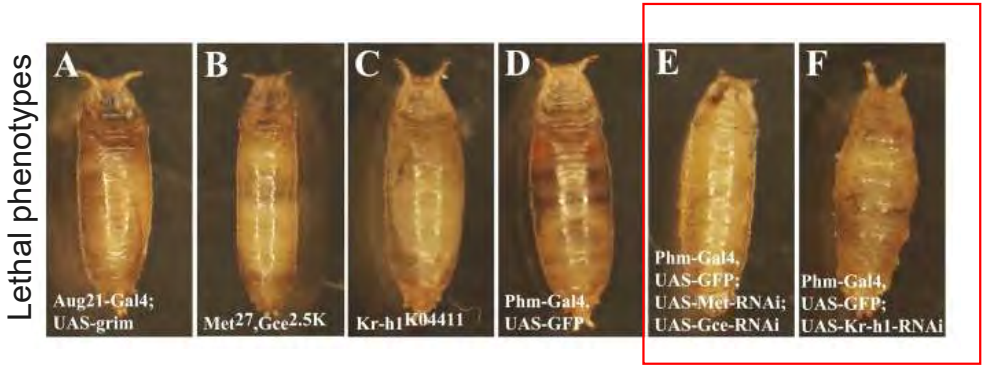
Riddiford LM, *et al. Development*. 2010

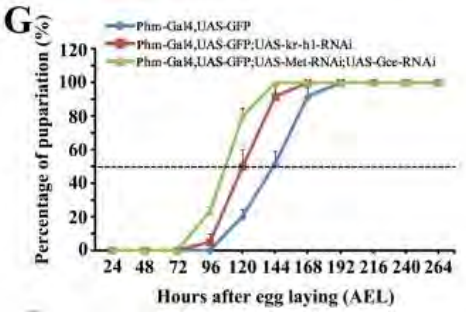
How does JH affect larval development?

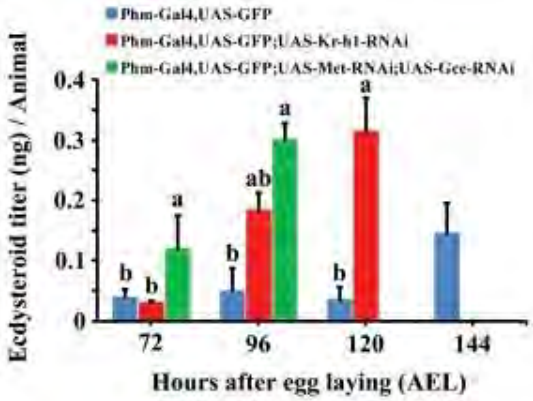
JH represses ecdysone biosynthesis in the PG to prevent premature pupariation

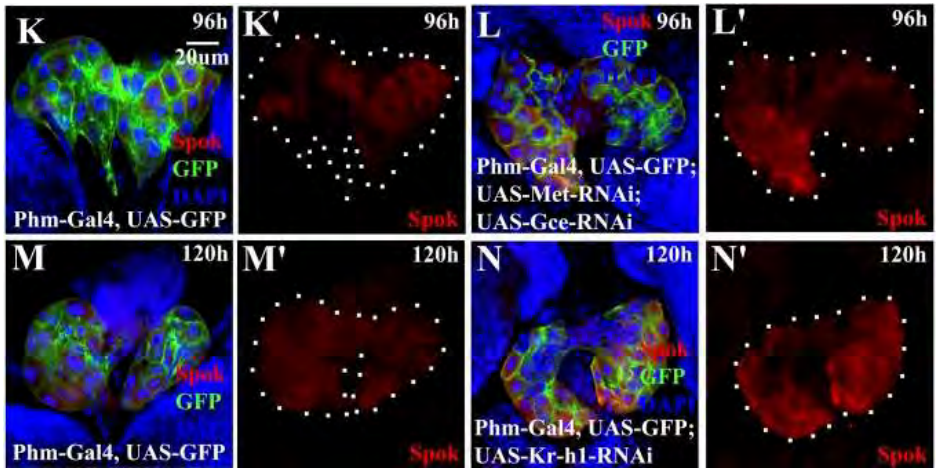
prothoracic gland (PG)





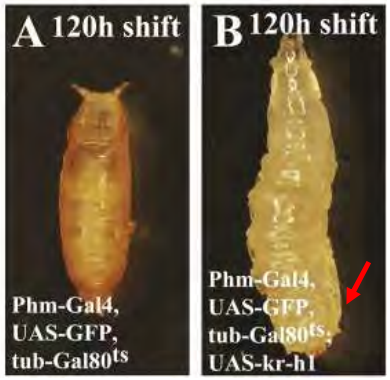


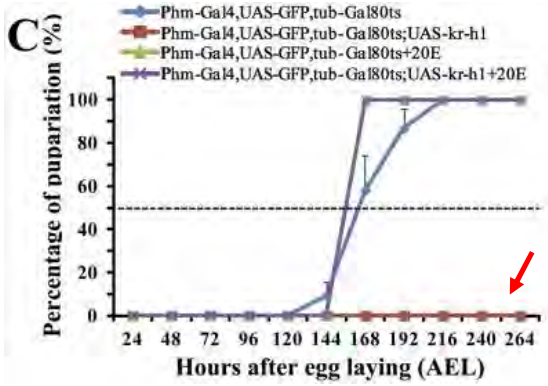


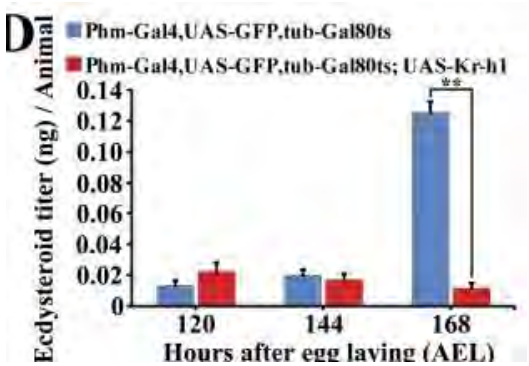


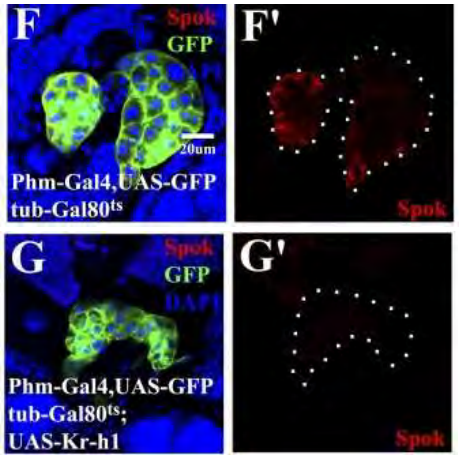
Liu S, *et al. PNAS*. 2018

Kr-h1 in the PG inhibits ecdysone biosynthesis and blocks metamorphosis





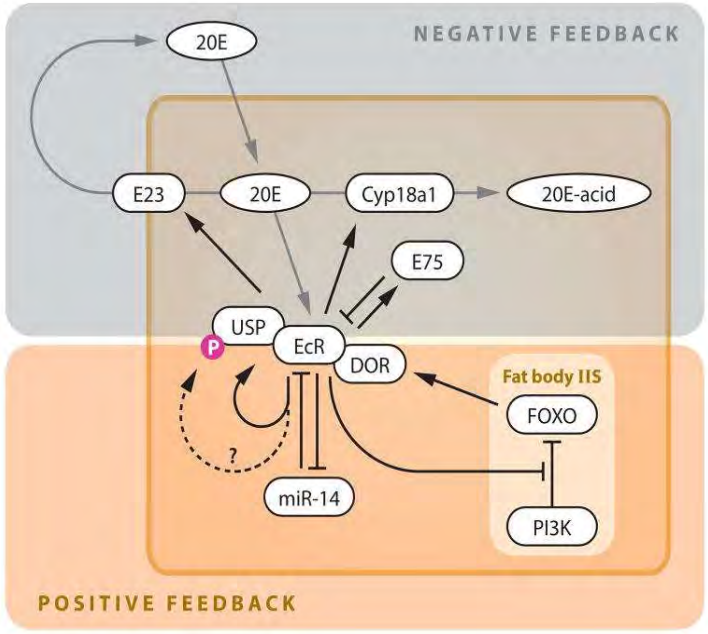




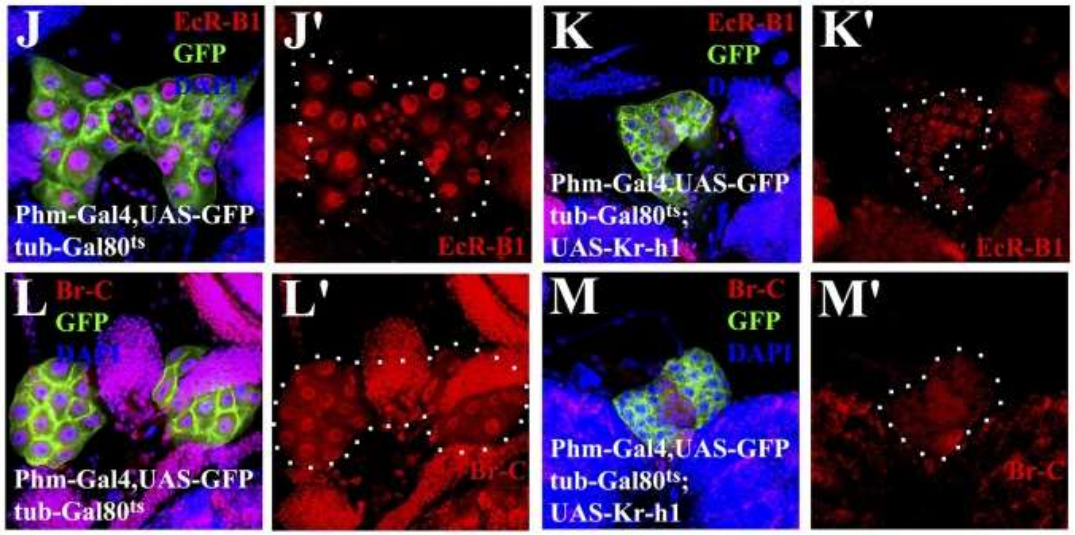
Liu S, *et al. PNAS*. 2018

What are the mechanisms by which JH signaling inhibits ecdysone biosynthesis?

JH suppresses ecdysone biosynthesis by reducing both steroidogenesis autoregulation and PG size



steroidogenesis autoregulation
(类固醇合成的自主调控)

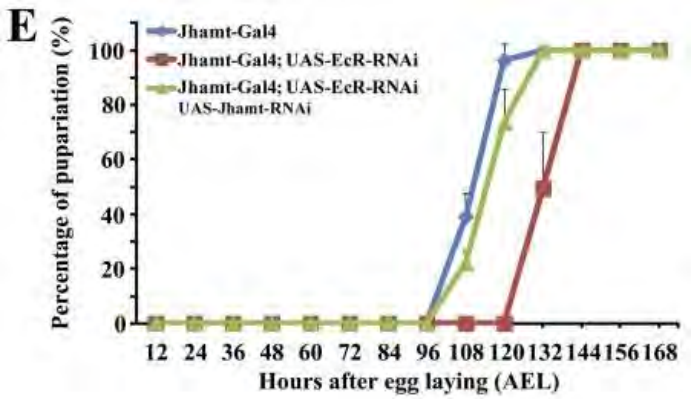


Yamanaka N, *et al. Annu Rev Entomol*. 2013

Liu S, *et al. PNAS*. 2018

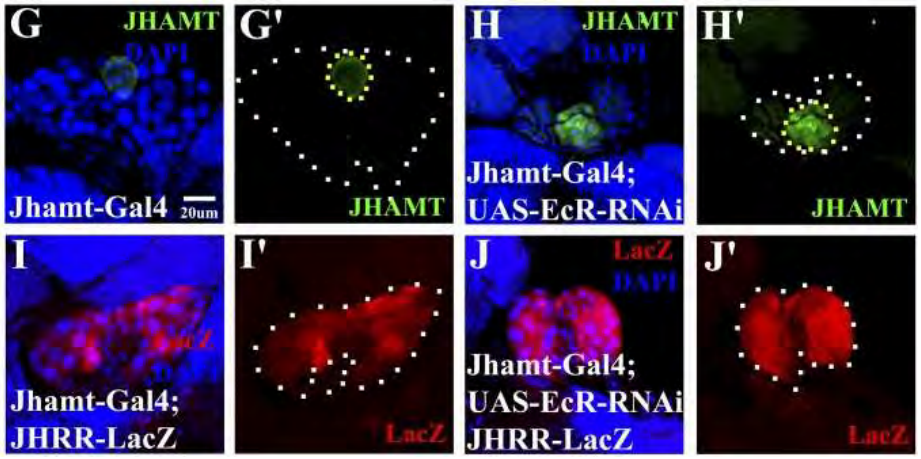
JH biosynthesis in the CA is prevented by 20E to permit metamorphosis

lethal



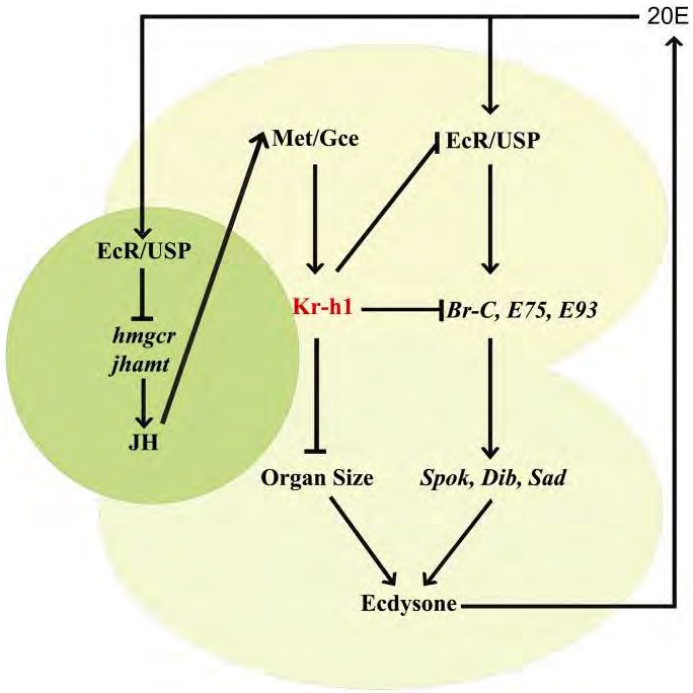
CA

PG

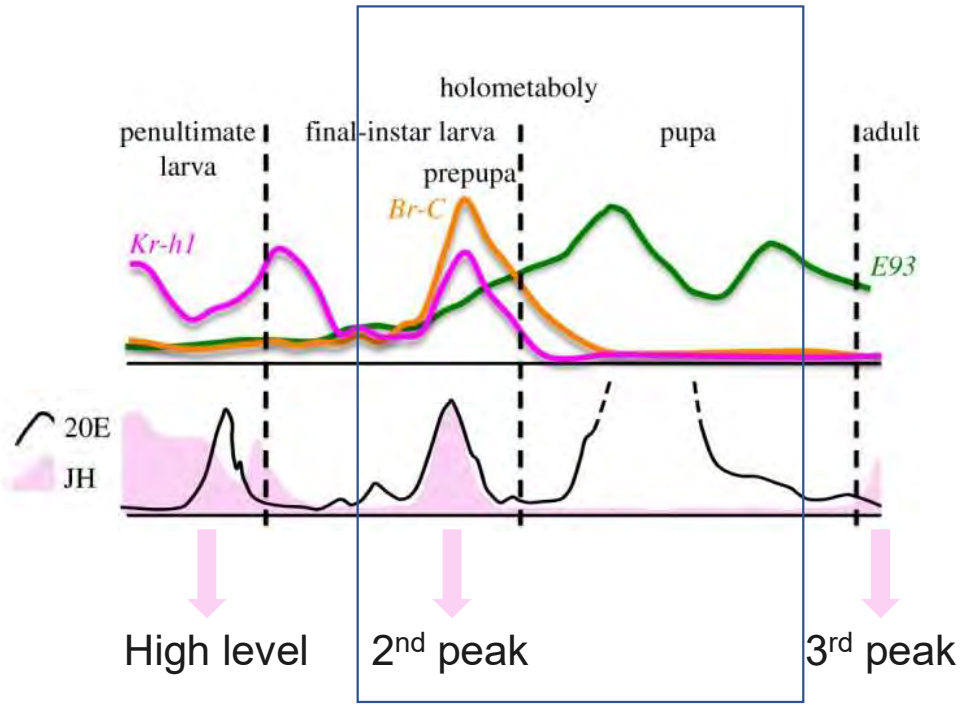


JH ↑

PG↓
Kr-h1 ↑



Liu S, *et al. PNAS*. 2018



The important biological significance of pupal stage for holometabolous insects :

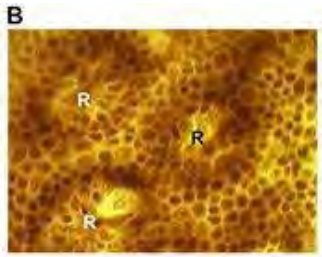
- Metamorphosis process
- Protective effect
- Organizational reorganization
- …

What is the relationship between JH and pupal stage progression?

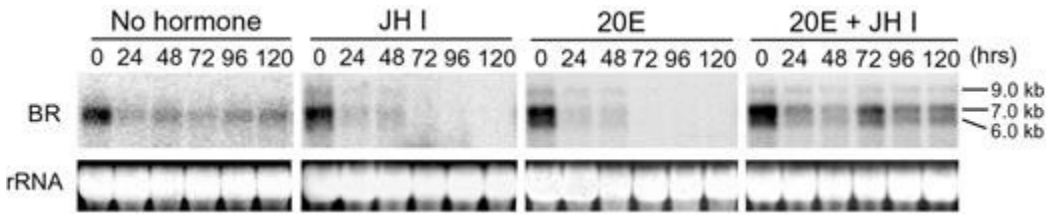
JH regulates pupal development and pupal-adult transformation by regulating BR expression

BR: a 'pupal specifier'

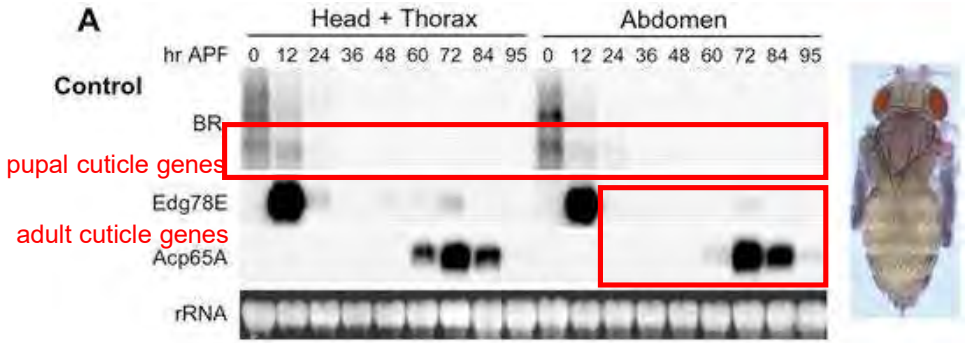
In *Drosophila melanogaster* the ecdysone-induced Broad (BR; previously called the Broad-Complex or BR-C) transcription factors are essential for the onset of metamorphosis since the amorphic *broad* (*br*) mutant *npr* can develop normally to the final larval instar but cannot undergo metamorphosis (Kiss et al., 1976; Kiss et al., 1988). The BR

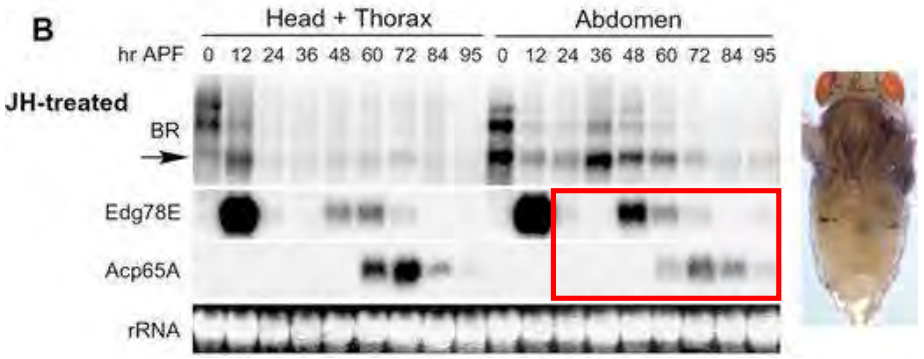


Manduca



JH/ 20E: inhibits BR JH+20E: promote BR





Zhou X, Riddiford LM. *Development.* 2002

The transcription factor E93 is the key determinant that promotes adult metamorphosis in hemimetabolous insects

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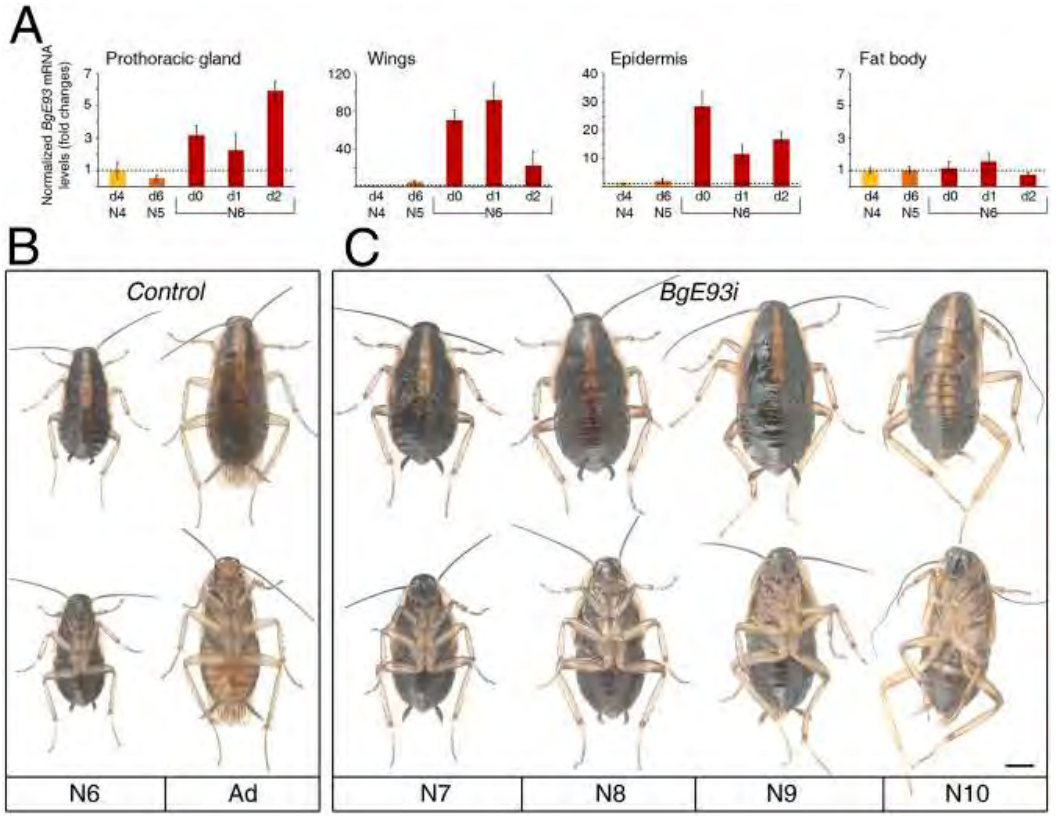
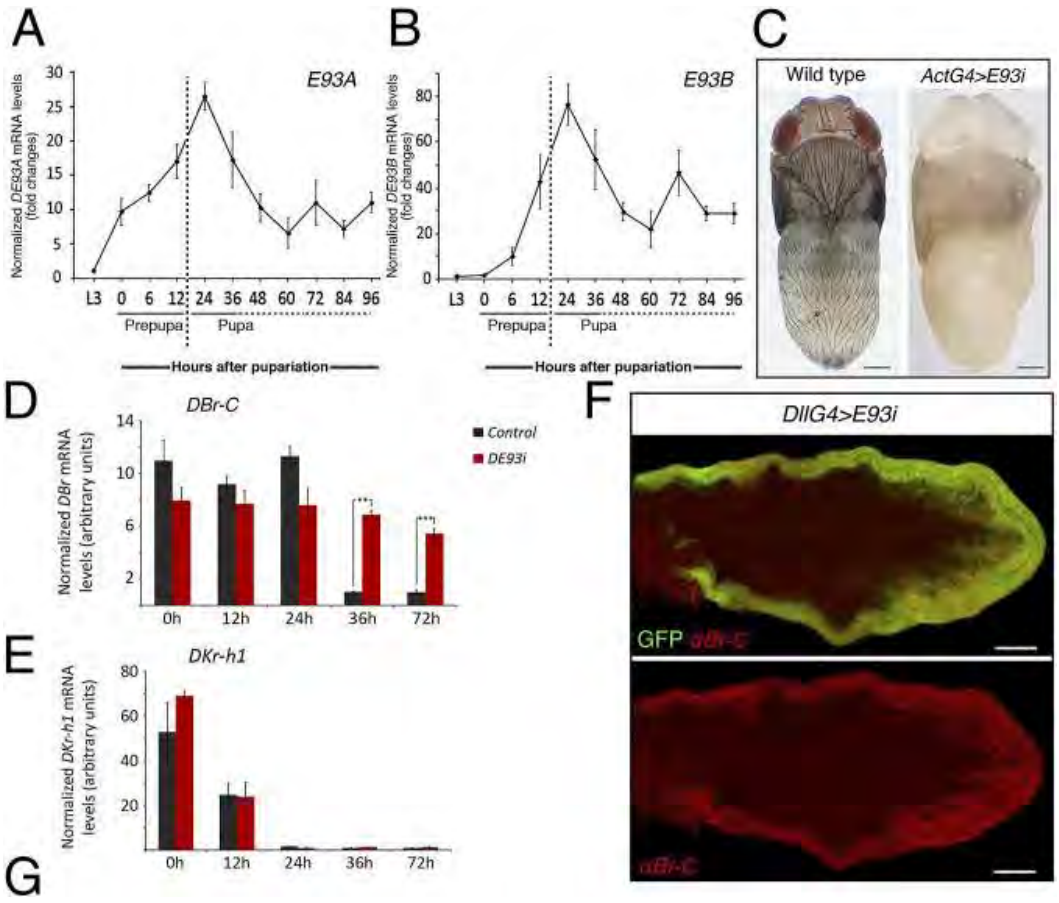
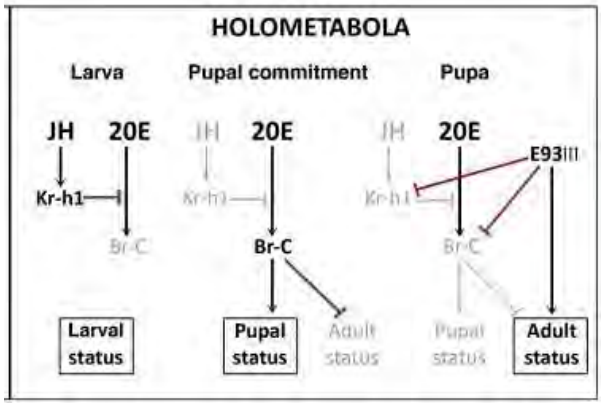


Ureña E, *et al. PNAS.* 2014

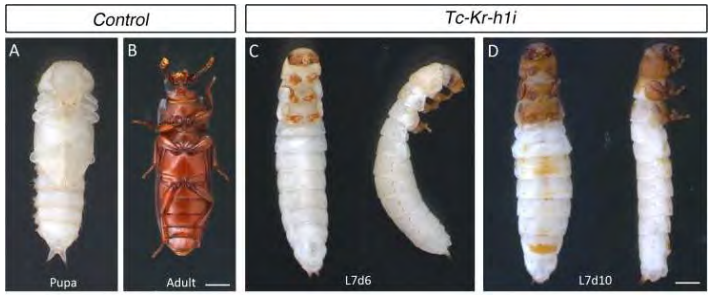
E93 Is also Required for Adult Differentiation in the Holometabolous *D. melanogaster*.

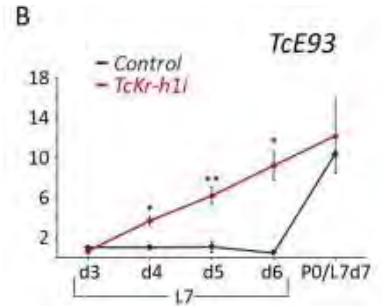


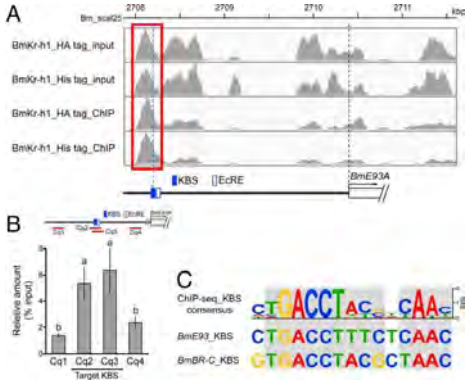


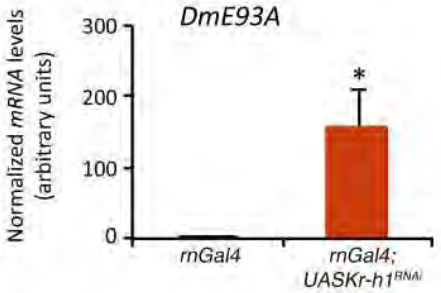
Ureña E, *et al. PNAS.* 2014

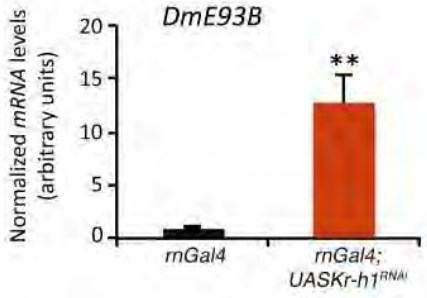
JH prevents precocious larval–adult metamorphosis via direct *Kr-h1*–dependent *E93* gene repression

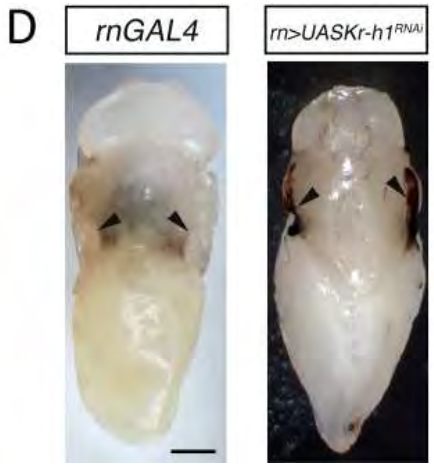


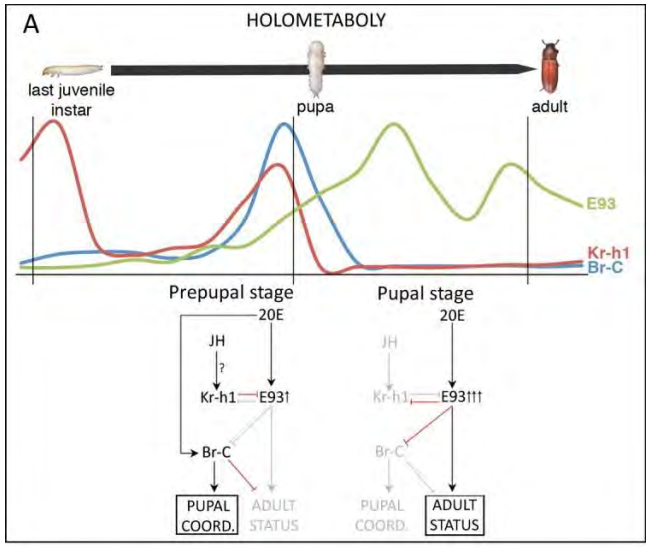




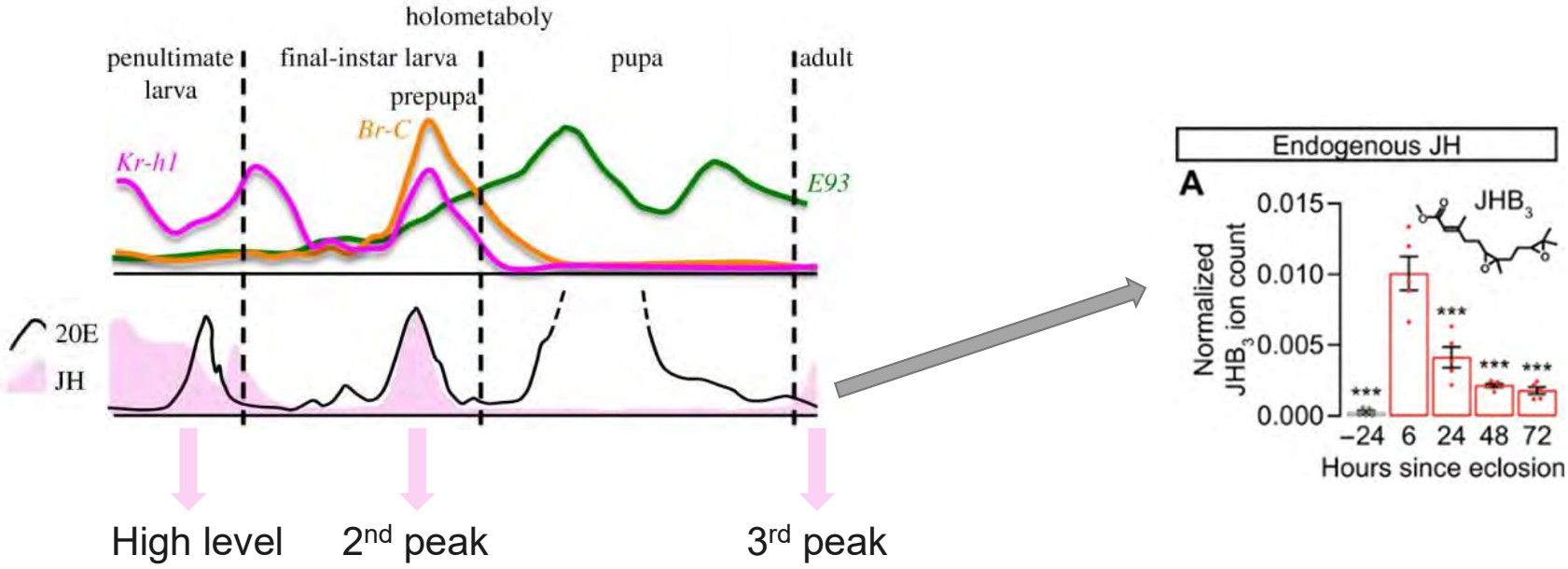






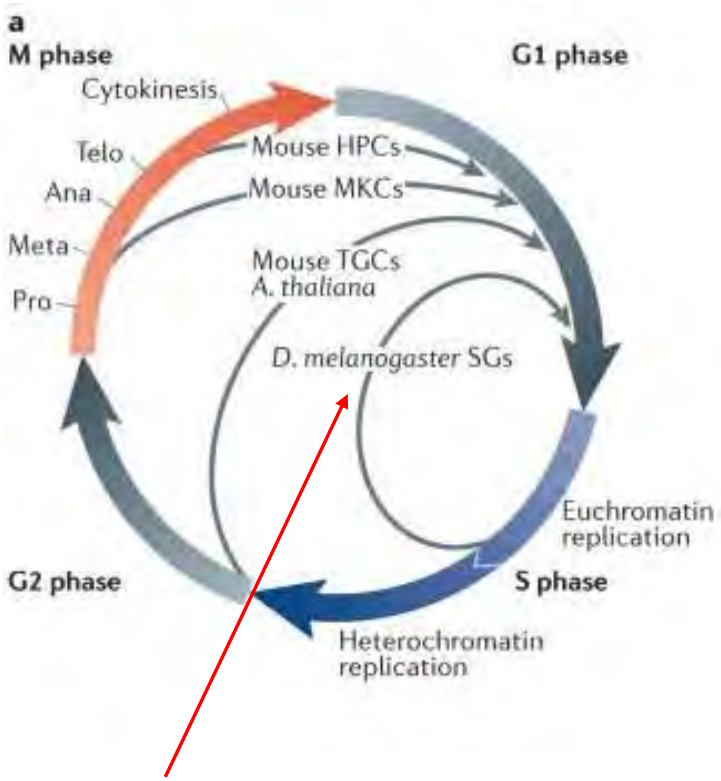


Ureña E, *et al. PLoS Genet*. 2016
Kayukawa T.*et al. PNAS*. 2017



What is the function of JH in adult development?

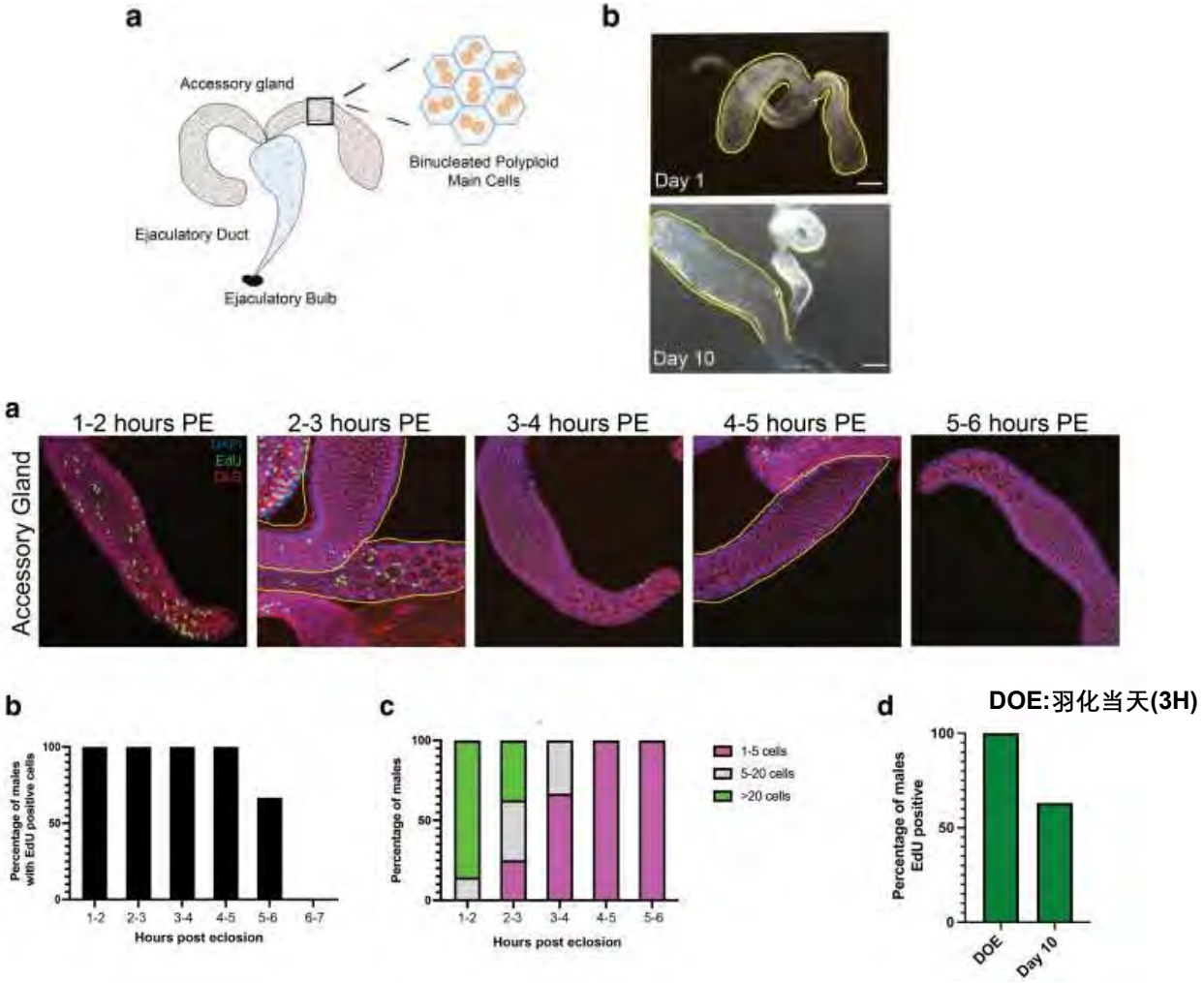
The male accessory gland cells (AGs) undergo endocycling, starting immediately post-eclosion



In endoreplication cell cycles

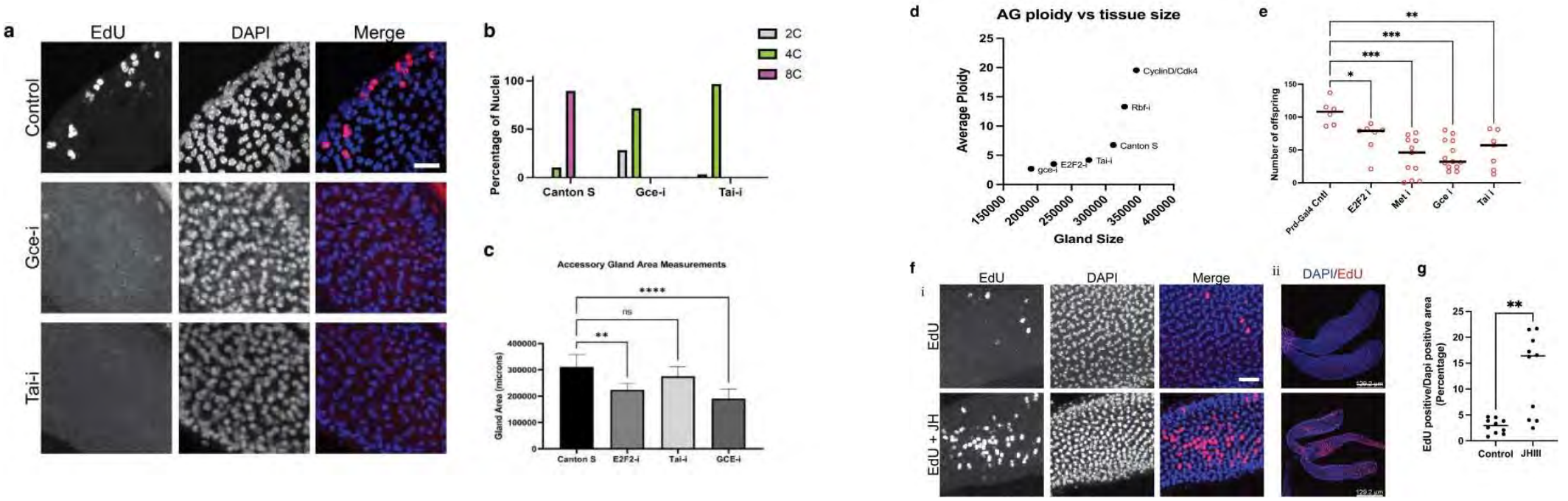
e.g. D. melanogaster salivary gland cells (SGs)

一种特殊的细胞周期：核内周期



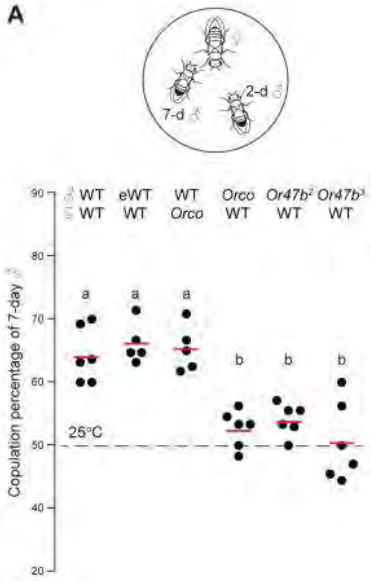
Box AM, *et al*. *G3*. 2024

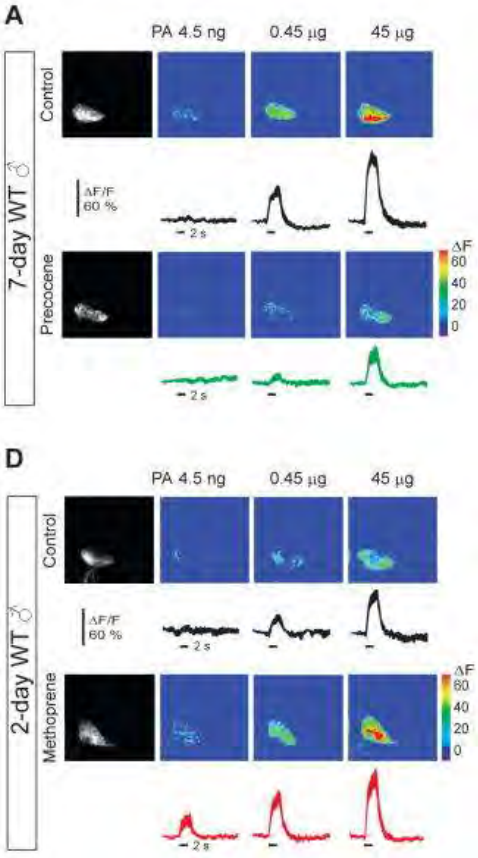
JH regulates endocycling on the DOE in AG main cells

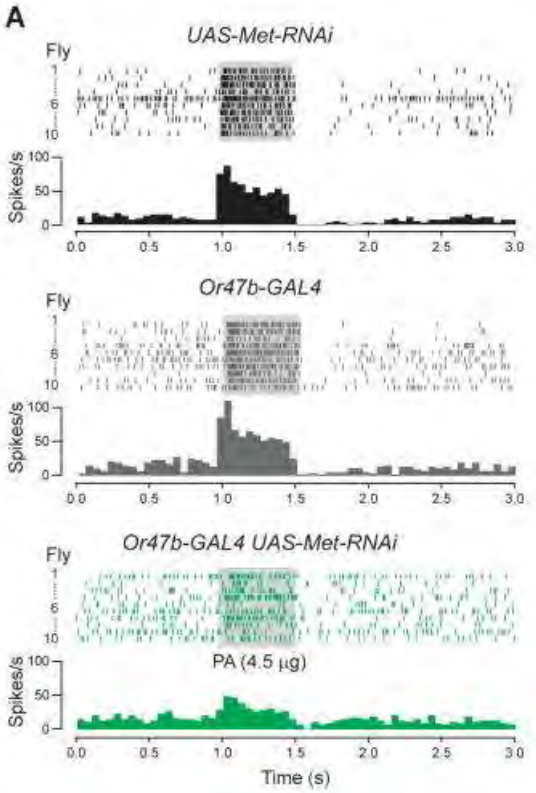


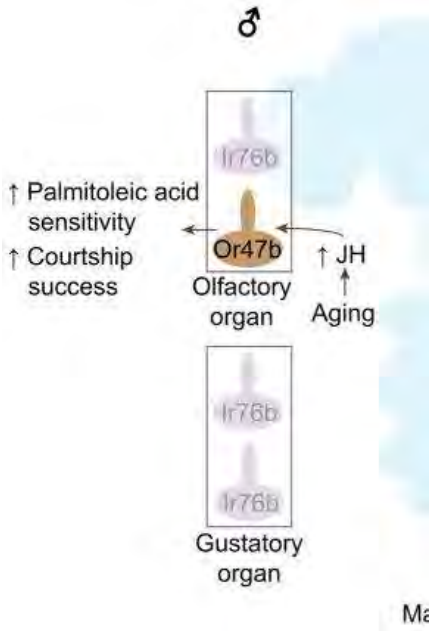
Box AM, *et al. G3.* 2024

JH increase in sensitivity of Or47b, which mediates age-dependent courtship enhancement behavior



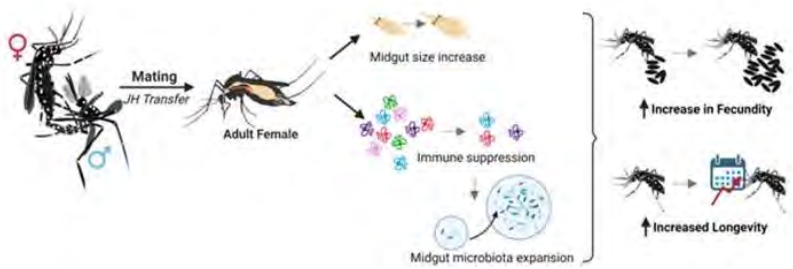


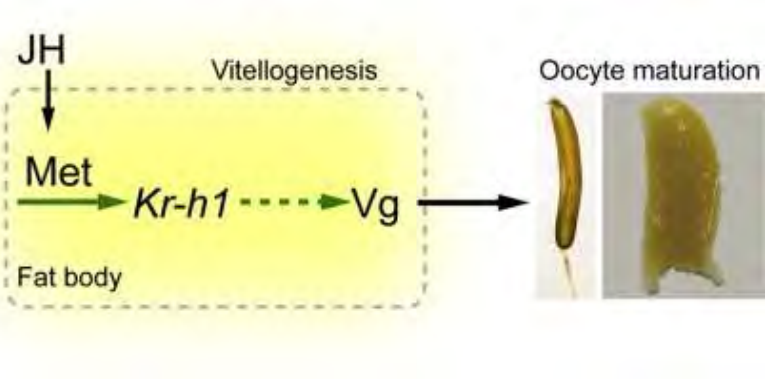


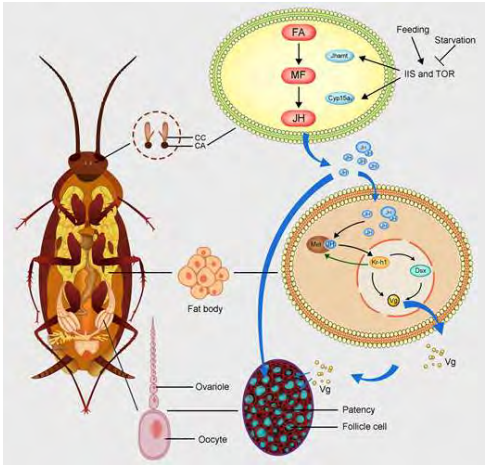


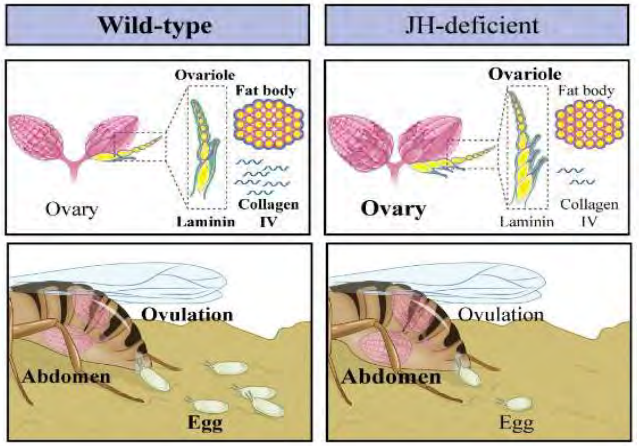
Lin HH. *et al.Neuron*.2016

JH extensively promotes vitellogenesis and egg laying in the insects



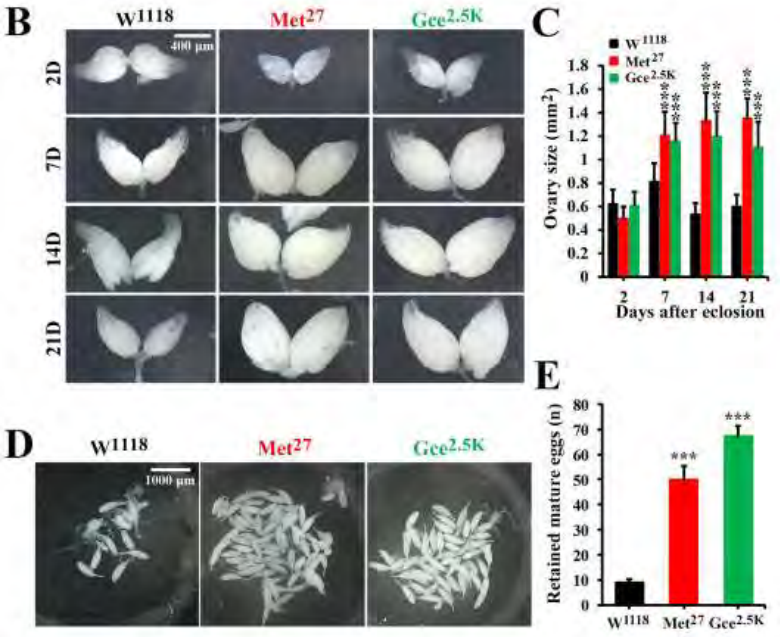


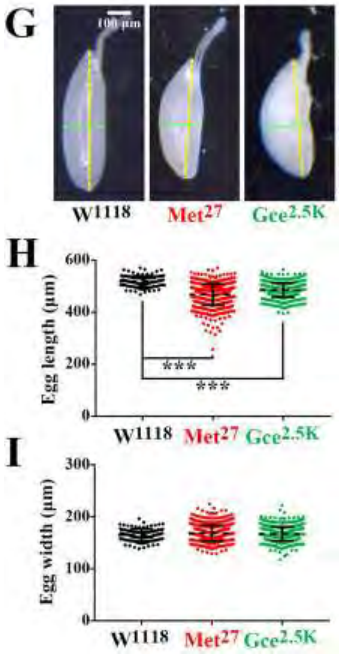


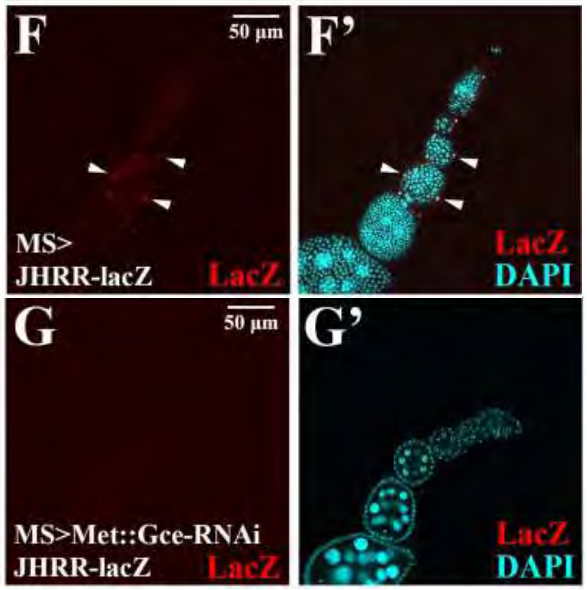


Song J, *et al. Insect Biochem Mol Biol*. 2014
Taracena-Agarwal ML, *et al. Commun Biol*. 2024
Zhu S, *et al. Development*. 2020
W. Luo, *et al. PNAS*. 2021

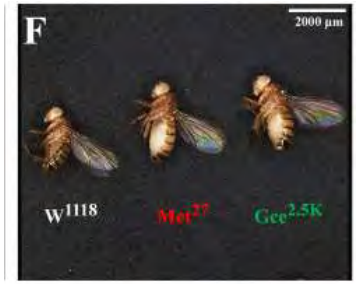
Reduction of JH signaling causes ovulation deficiency and abnormal egg shape





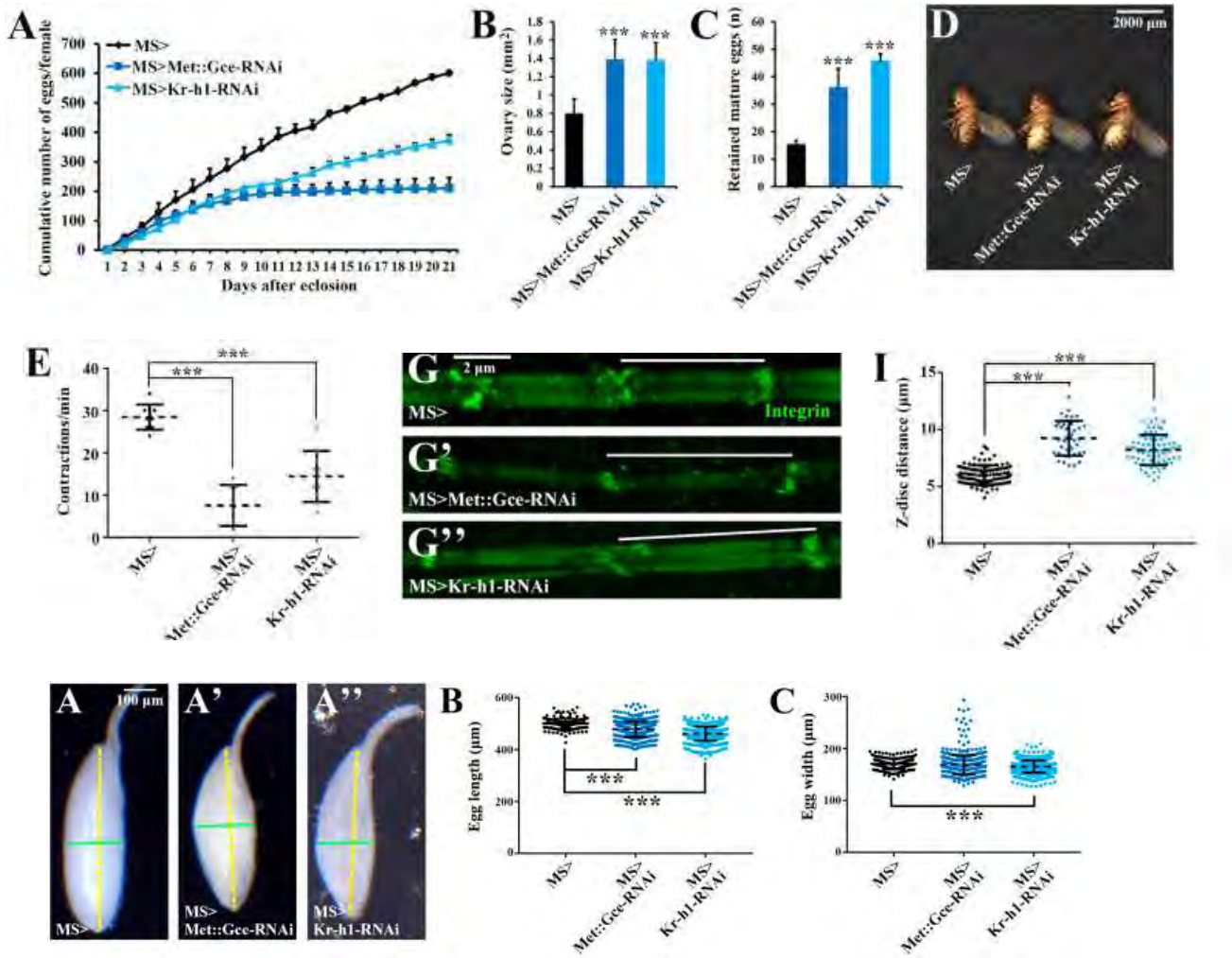


JH signaling is exclusively activated in ovarian muscle cells.



Luo W, *et al. PNAS*. 2021

JH signaling in ovarian muscles promotes ovulation and maintains egg shape by affecting ovarian muscle contraction



Luo W, *et al. PNAS*. 2021

Caste transitions occur in a socially flexible ant (*Harpegnathos saltator*跳蚁)

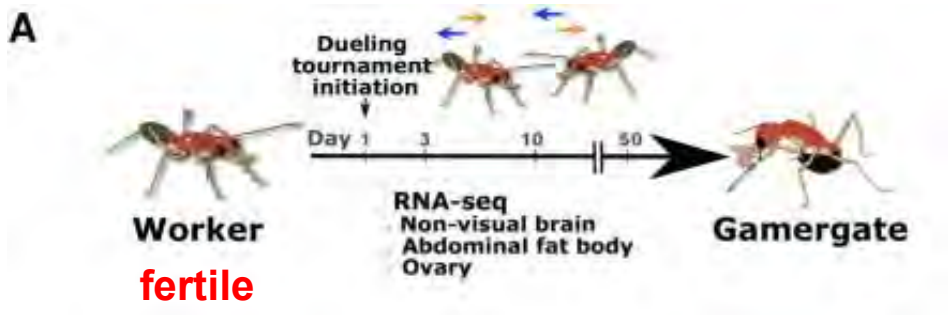
Danny F. Reinberg, M.S., Ph.D.

Department: The Dr. John T. Macdonald Foundation Department of Human Genetics

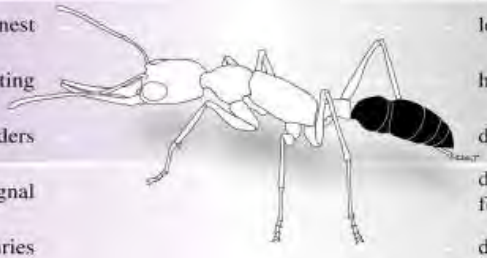
Roles

Distinguished Professor, John T. MacDonald Department of Human Genetics Miller School of Medicine and Sylvester Comprehensive Cancer Center

Associate Director for Faculty Training and Recruitment University of Miami Miller School of Medicine

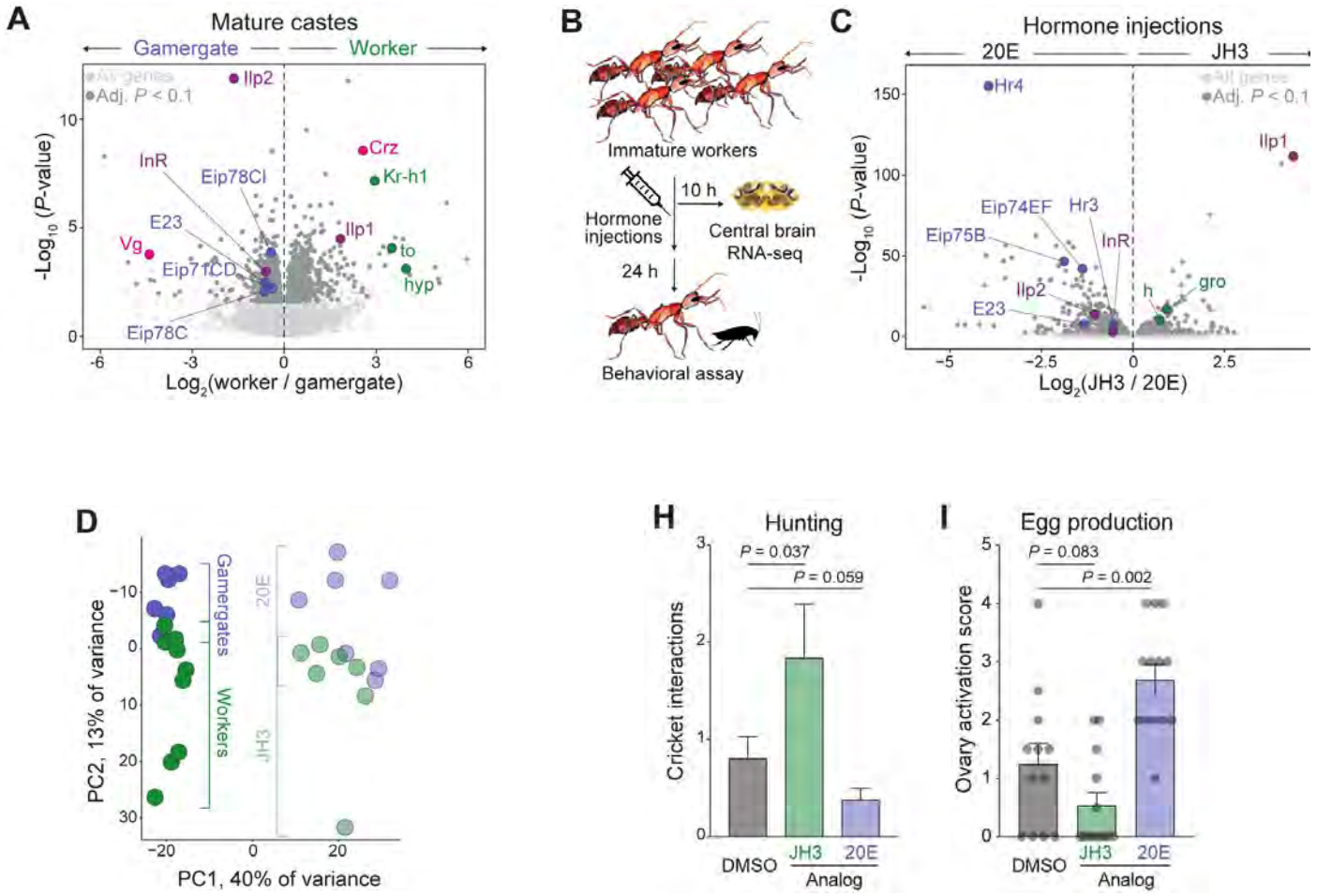


	gamergate	forager
brain	decreased brain volume	increased brain volume
	decreased optic lobe volume	increased optic lobe volume
behaviour	remains inside nest	leaves nest
	avoids hunting	hunts prey
	hides from intruders	defends against intruders
physiology	displays CHC fertility signal	does not display CHC fertility signal
	activated ovaries	deactivated ovaries
	decreased venom production	increased venom production
	increased vitellogenin (*Vg*) expression	decreased vitellogenin (*Vg*) expression
	increased elongase (*ELOV*) expression	decreased elongase (*ELOV*) expression



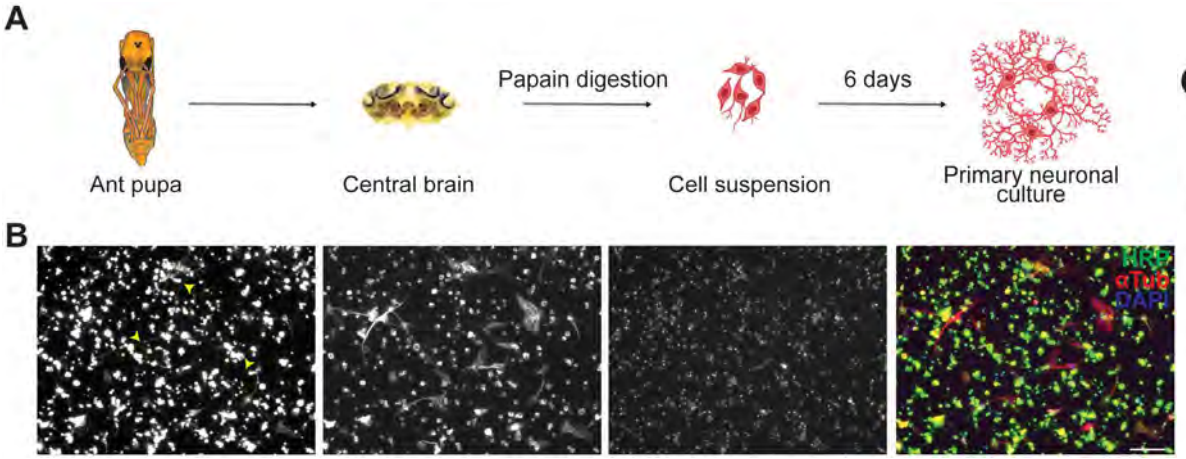
Opachaloemphan C. *et al. Genes Dev*. 2021

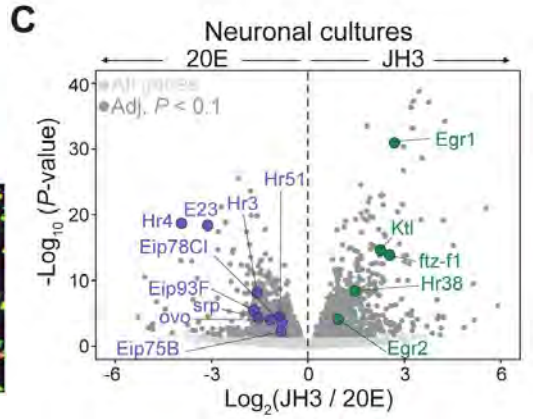
JH3 and 20E drive caste-specific gene expression and behavior



Gospocic J, *et al. Cell*. 2021

Kr-h1 can be induced by JH3 and 20E

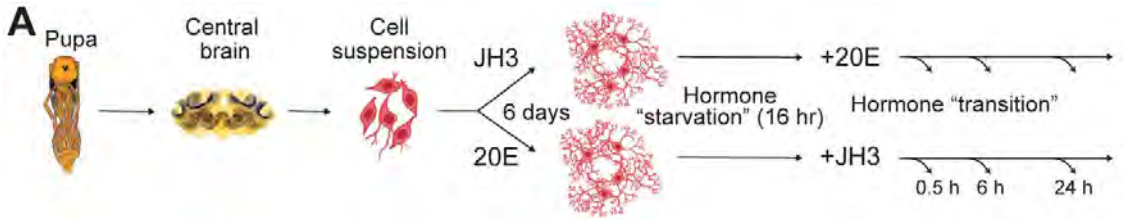


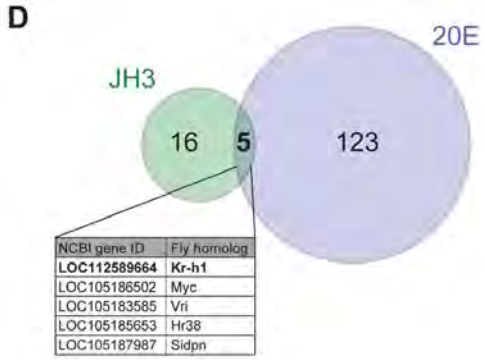


ecdysone-responsive genes (*Eip75B*, *Eip78Cl*, *Eip93F*, *E23*, *Hr3*, *Hr4*, *Hr51*) ,
reproduction (*srp*, *ovo*)

foraging behavior (*Egr1*, *Egr2*, *Hr38*),
neuronal remodeling (*ftz-f1*),
aggression (*Ktl*)

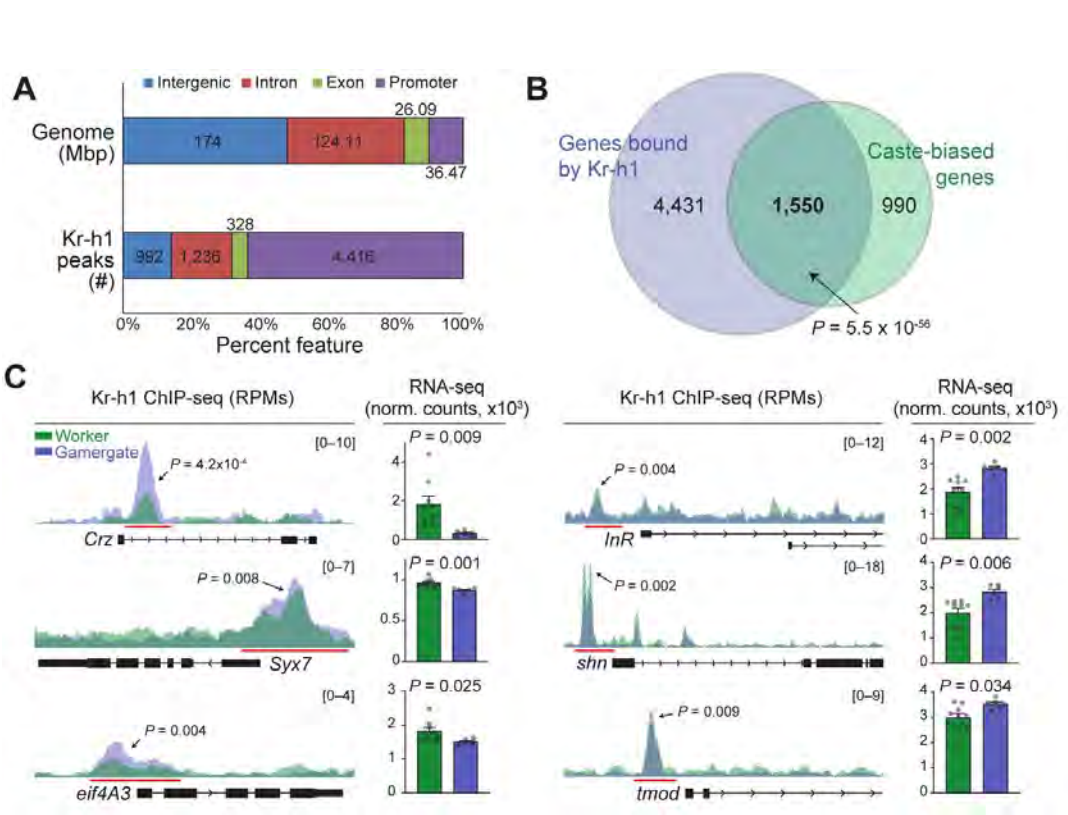
To define the plastic response of the neuronal transcriptome to socially regulated hormonal changes:

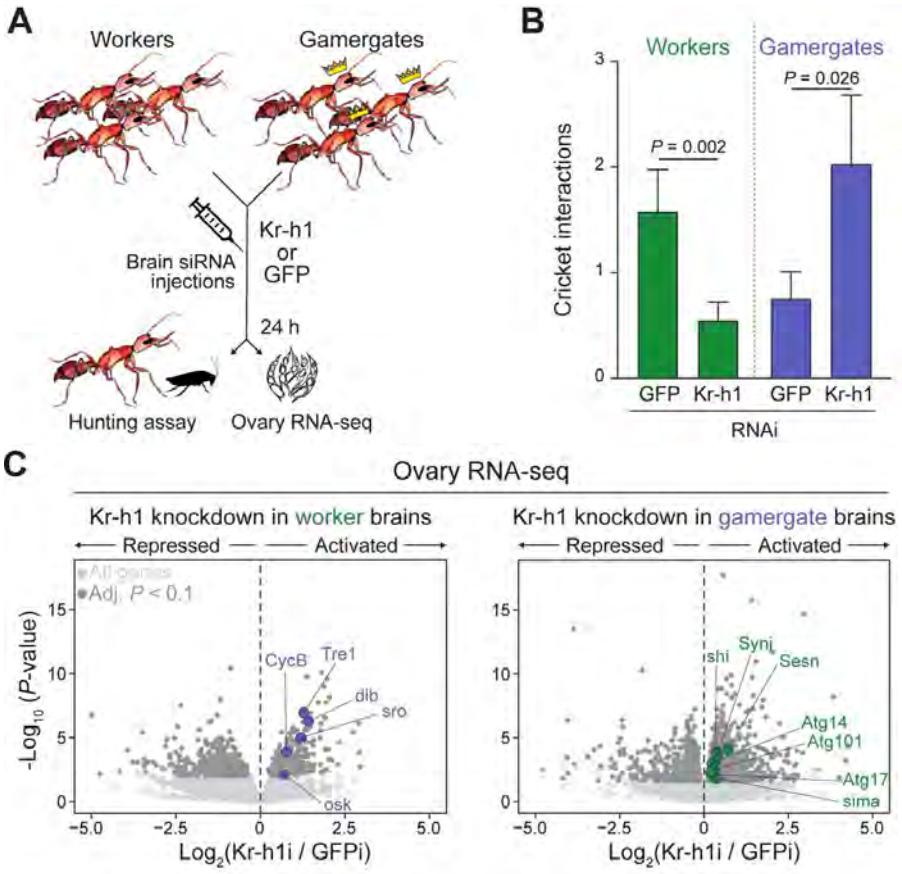




NCBI gene ID	Fly homolog
LOC112589664	**Kr-h1**
LOC105186502	Myc
LOC105183585	Vri
LOC105185653	Hr38
LOC105187987	Sidpn

Kr-h1 binds to caste-biased genes, and represses caste-inappropriate genes





Conclusions

- JH and 20E inhibit each other and regulate larval development and pupal stage formation
- JH regulates pupal development and pupal-adult transformation by regulating BR expression
- E93 interacts with JH to regulate larval–adult metamorphosis
- In adult stage, JH functions on development of the reproduction related system in both male and female

THANKS

Juvenile Hormone：Shaping innate behavioral patterns

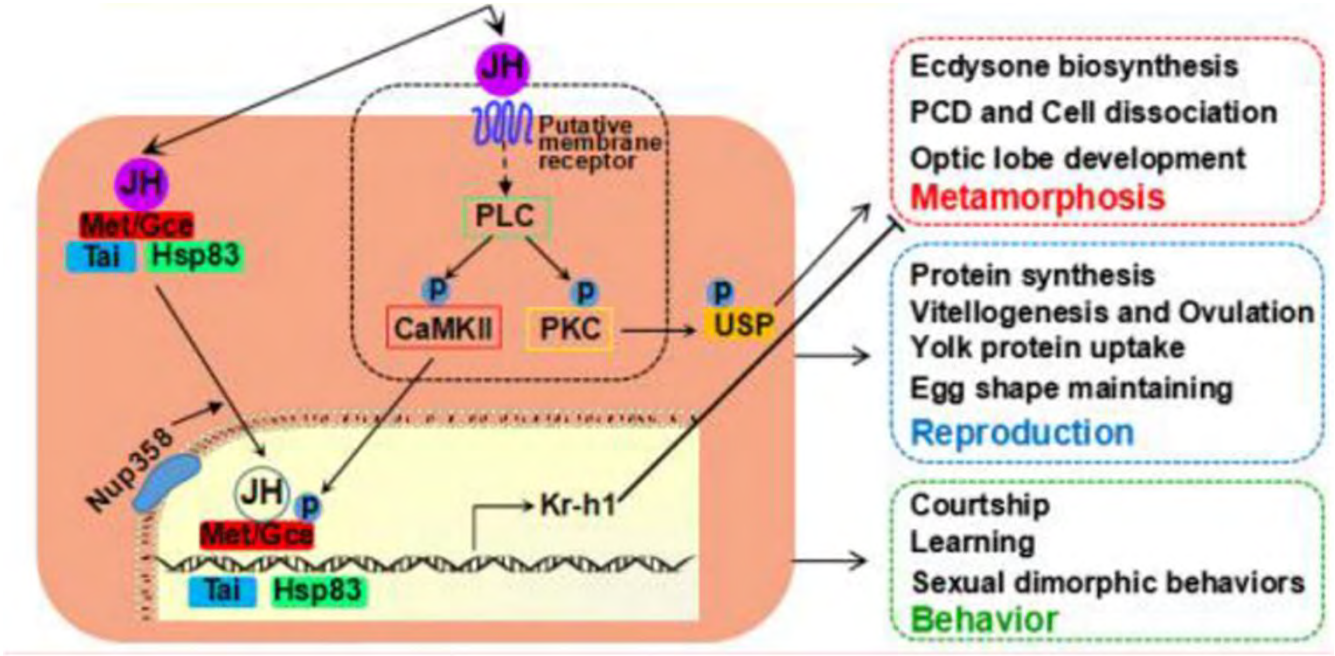
- What are the **effects** of JH on animal **behaviors**?
- How does JH regulate behaviors in **Drosophila**?
- How does JH regulate behaviors in **other insects**?

2024.12.26

WR

What are the effects of JH on animal behaviors ?

JH is known to play roles in the behaviors of Drosophila



(Xiaoshuai Zhang et.al.*Frontiers* .2020)

RESEARCH ARTICLE

Sexual dimorphism of sleep regulated by juvenile hormone signaling in *Drosophila*

Article

Neuron

Juvenile hormone drives the maturation of spontaneous mushroom body neural activity and learned behavior

Regulation of onset of female mating and sex pheromone production by juvenile hormone in *Drosophila melanogaster*

Social modulation of oogenesis and egg-laying in *Drosophila melanogaster*

Neuron

Hormonal Modulation of Pheromone Detection nhances Male Courtship Success

Article

Current Biology

Hormonal Signaling Cascade during an Early-Adult Critical Period Required for Courtship Memory Retention in *Drosophila*

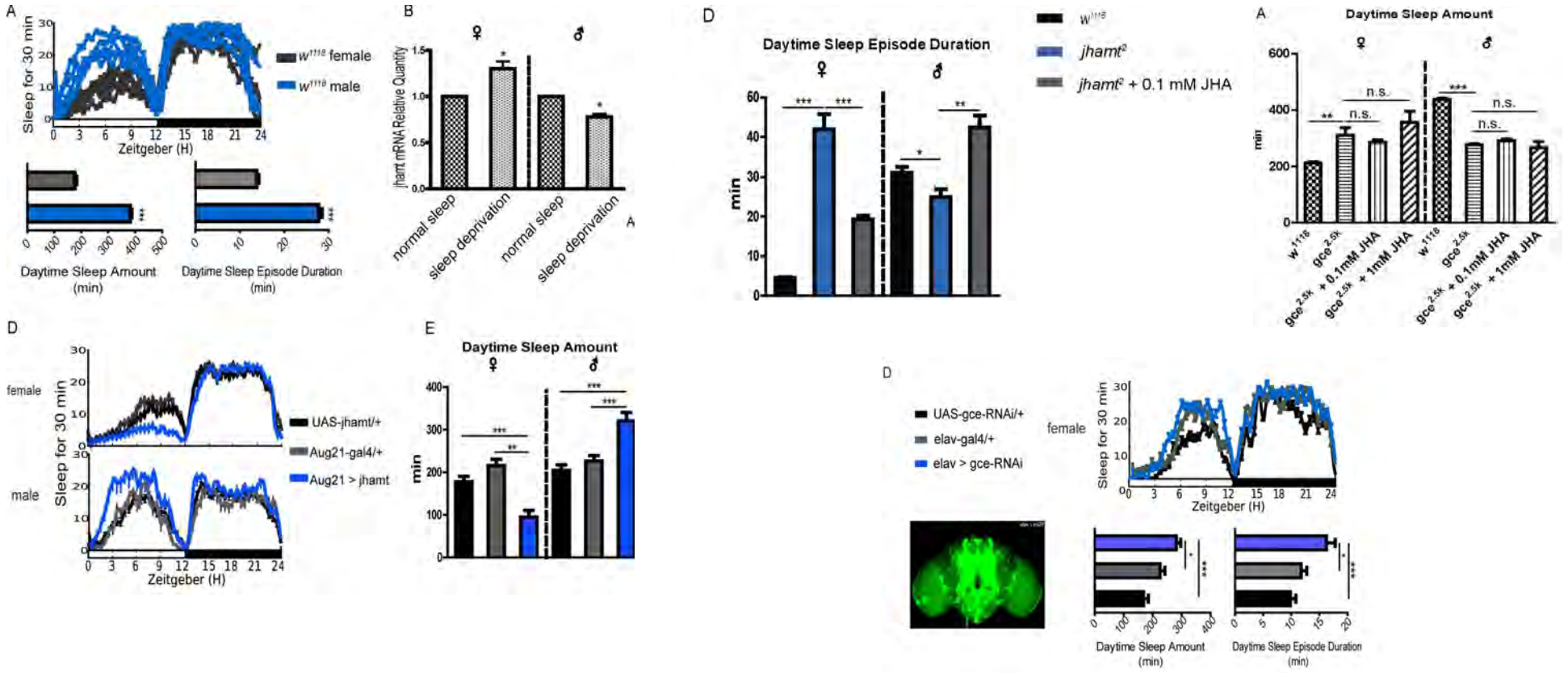
PLOS ONE

RESEARCH ARTICLE

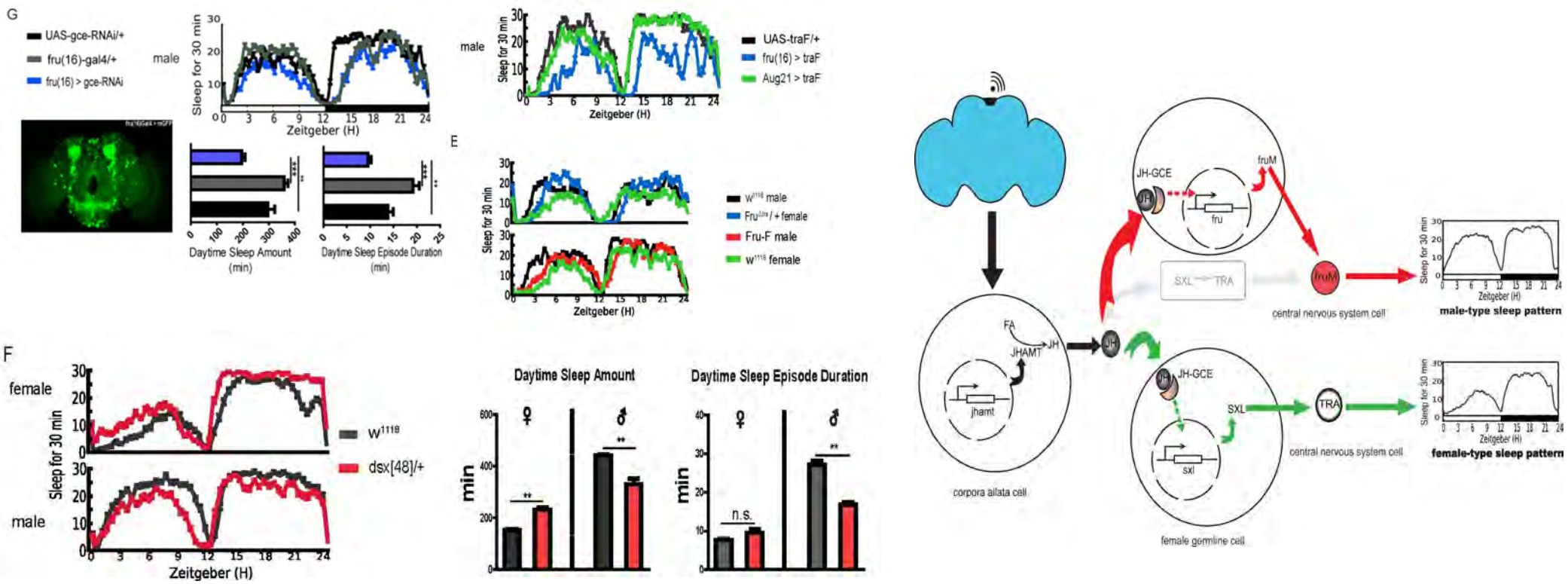
Juvenile Hormone Is Required in Adult Males for *Drosophila* Courtship

How does JH regulate behaviors in Drosophila?

Sexual dimorphism of sleep regulated by juvenile hormone signaling in *Drosophila*

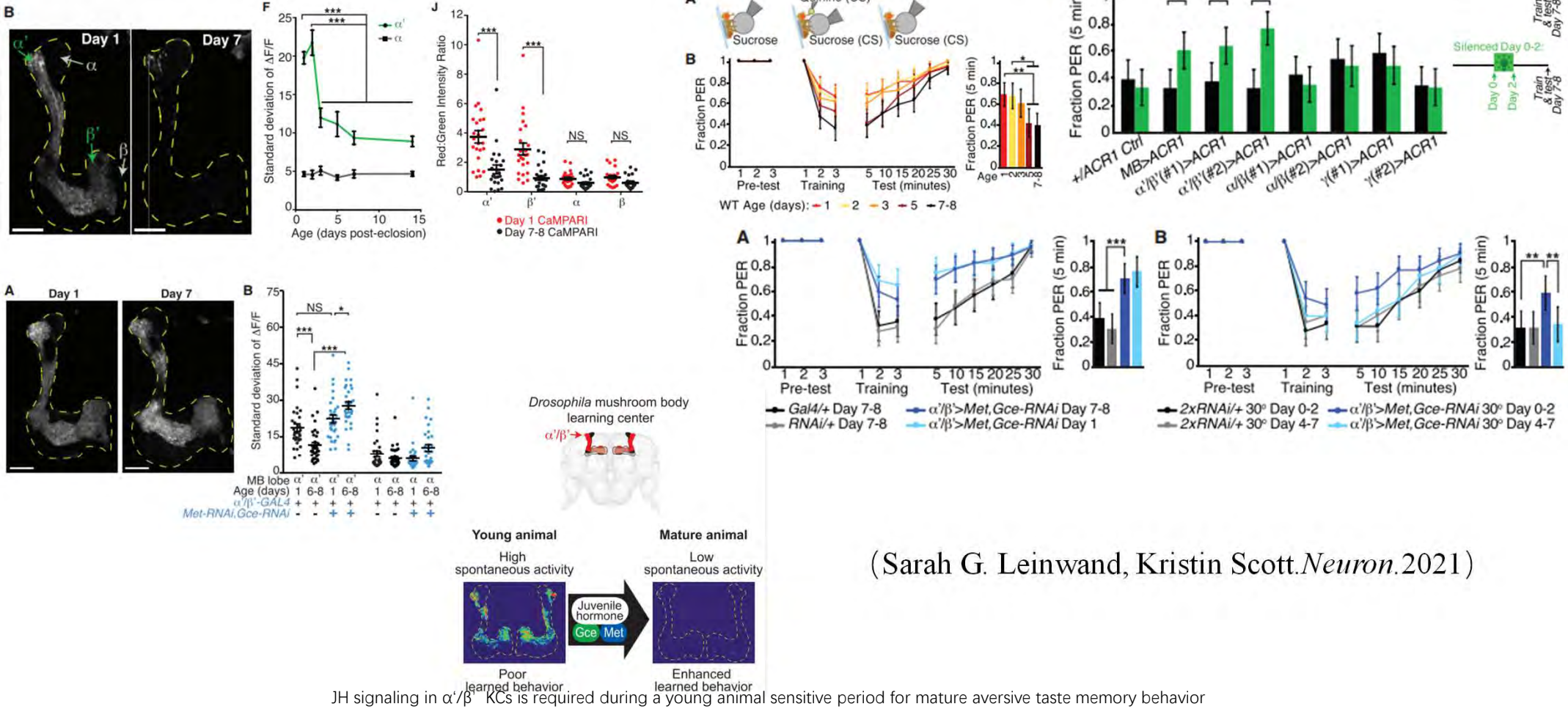


(Binbin Wu et.al.*PLOS Genetics*.2018)



JH signals from Drosophila brain target sex differentiation-related genes and sustain male and female sleep types

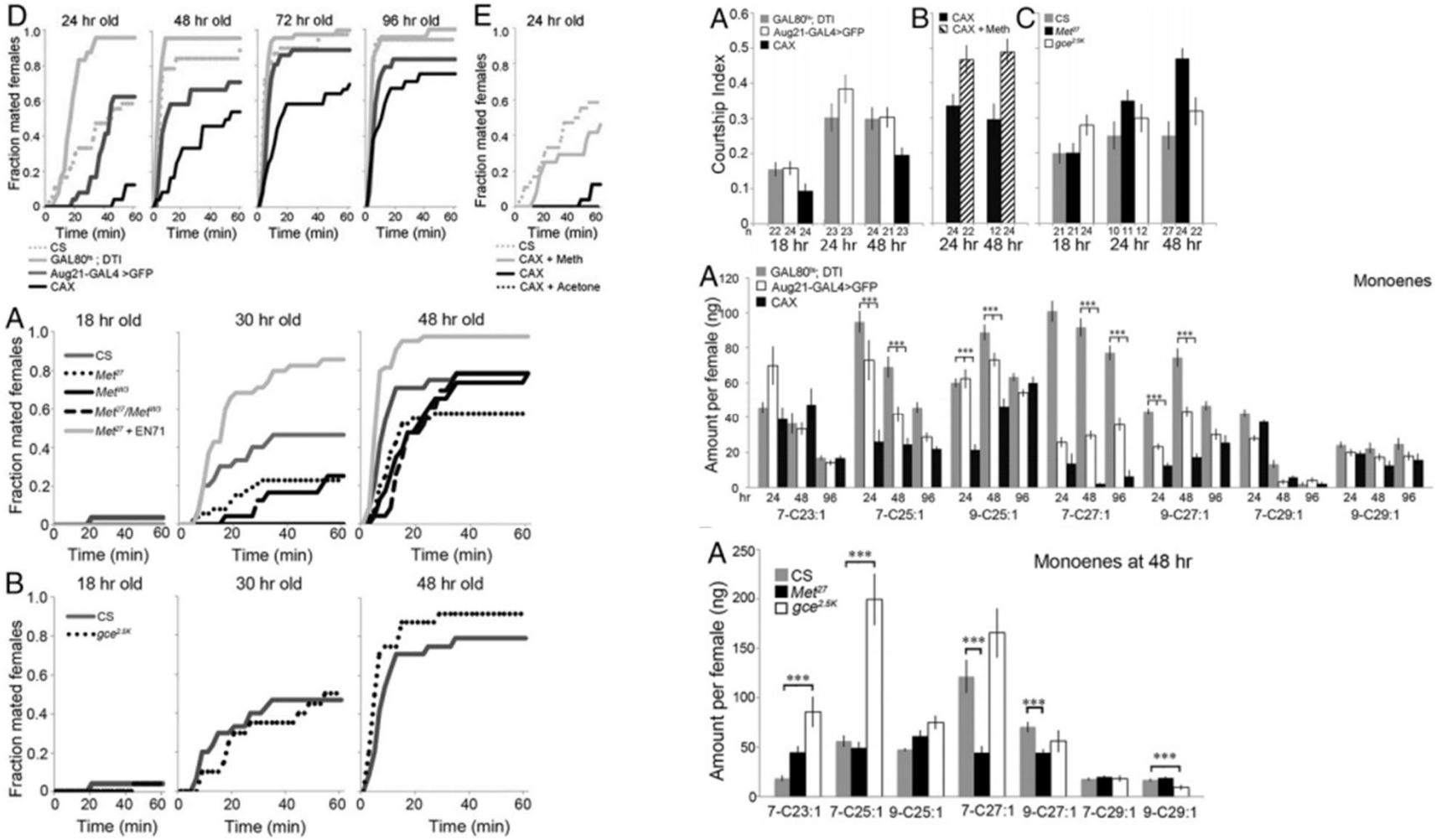
Juvenile hormone drives the maturation of spontaneous mushroom body neural activity and learned behavior



(Sarah G. Leinwand, Kristin Scott.*Neuron*.2021)

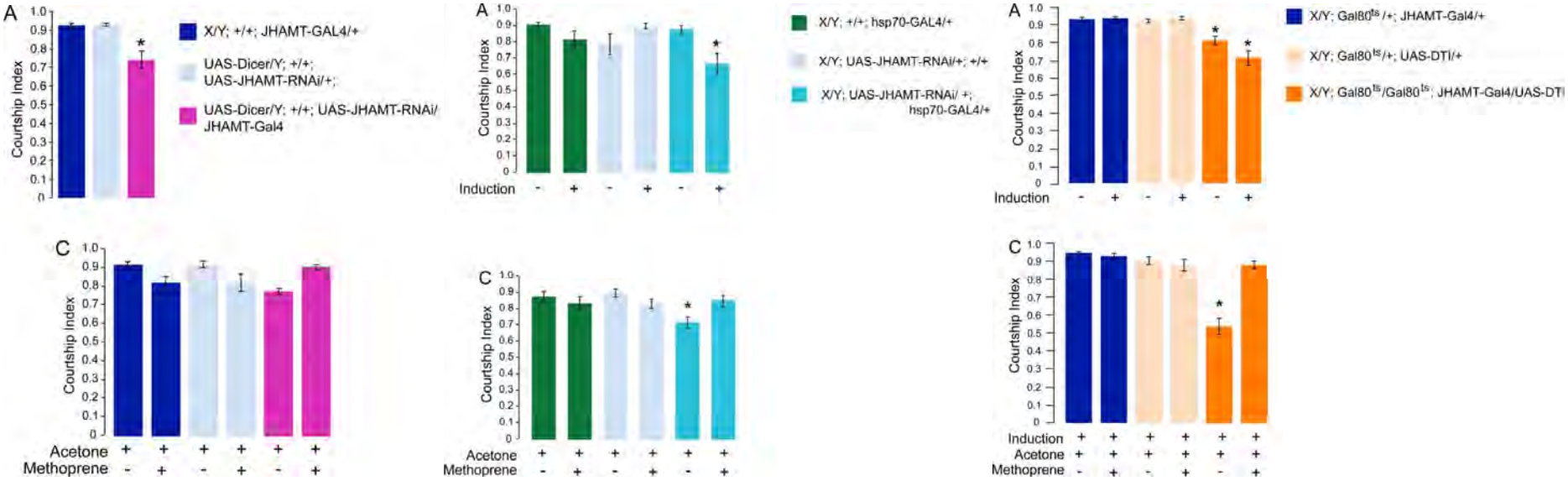
JH signaling in α'/β' KCs is required during a young animal sensitive period for mature aversive taste memory behavior

Regulation of onset of female mating and sex pheromone production by juvenile hormone in Drosophila melanogaster



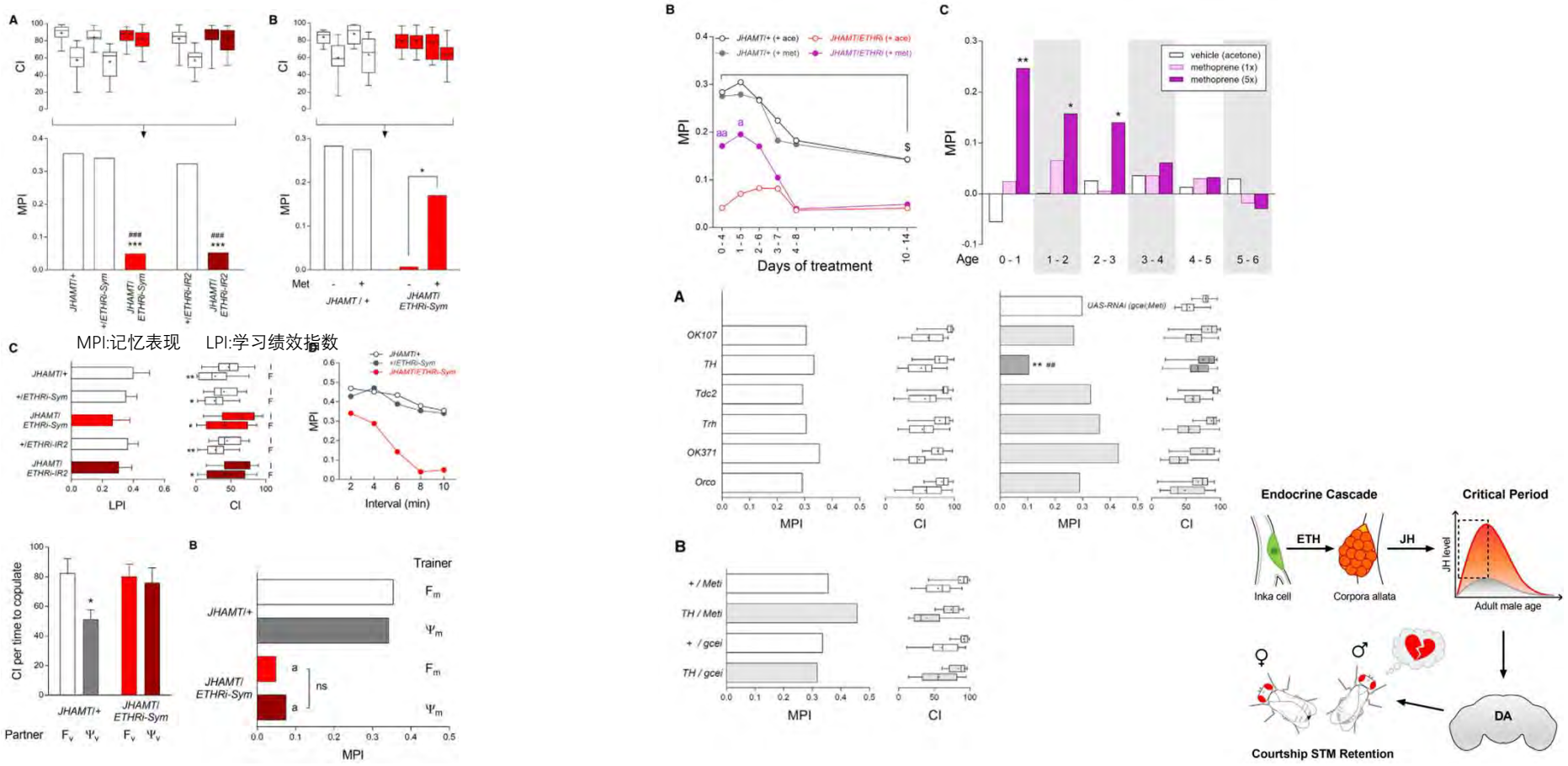
(Julide Bilen et.al.*PNAS*.2013)

Juvenile hormone is required in adult males for drosophila courtship



(Thilini P. Wijesekera et.al.*PLOS ONE*.2016)

JH regulates memory performance（STM） by targeting tyrosine hydroxylase-positive neurons

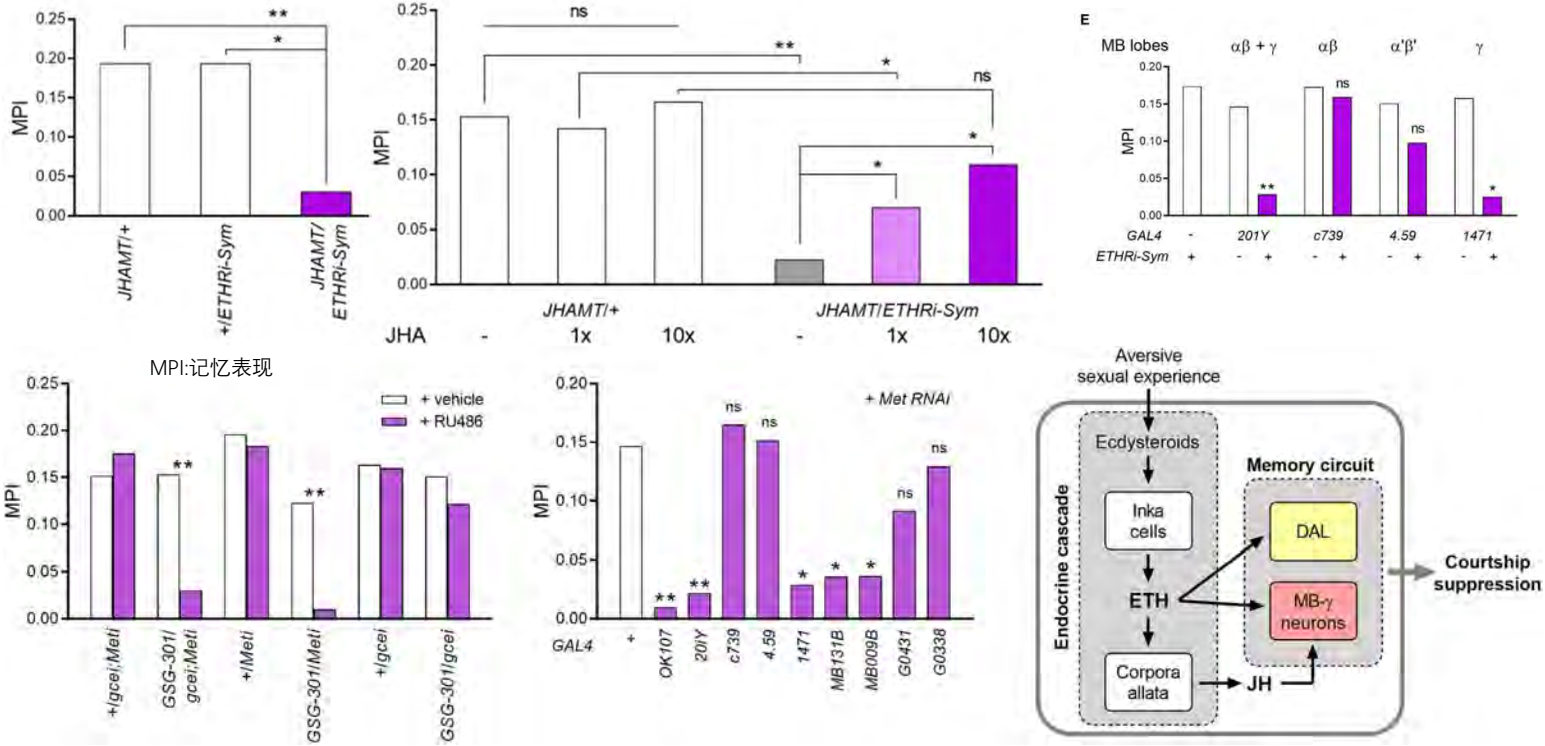


MPI:记忆表现　LPI:学习绩效指数

φv：乐意交配的伪处女；φm：不乐意交配的伪交配雌性

（Sang Soo Lee et.al.*Current Biology*.2017）

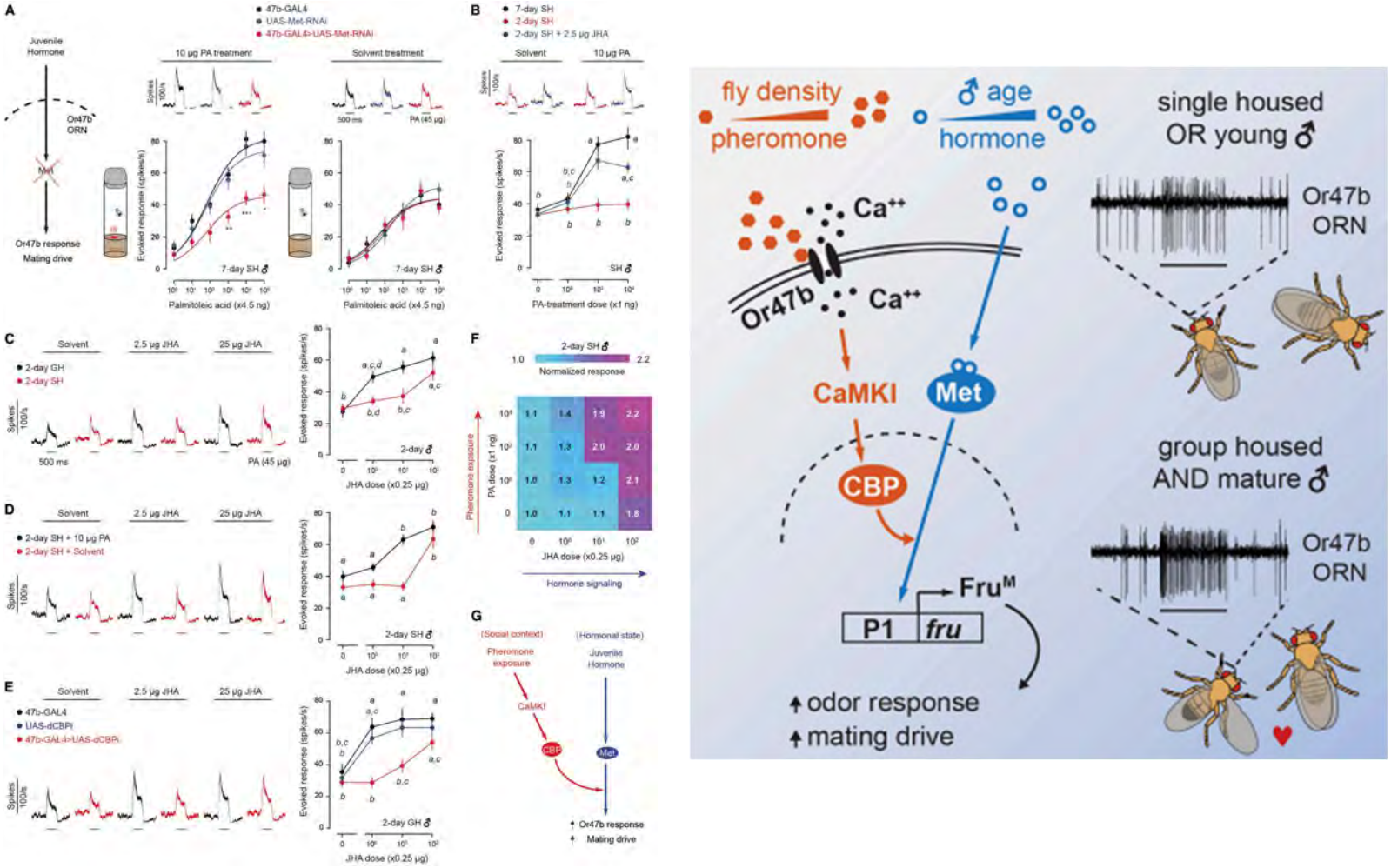
ETH-JH hormonal cascade is essential for courtship LTM



MPI:记忆表现

（Sang Soo Lee and Michael E. Adams.*Frontiers in Neuroscience*.2021）

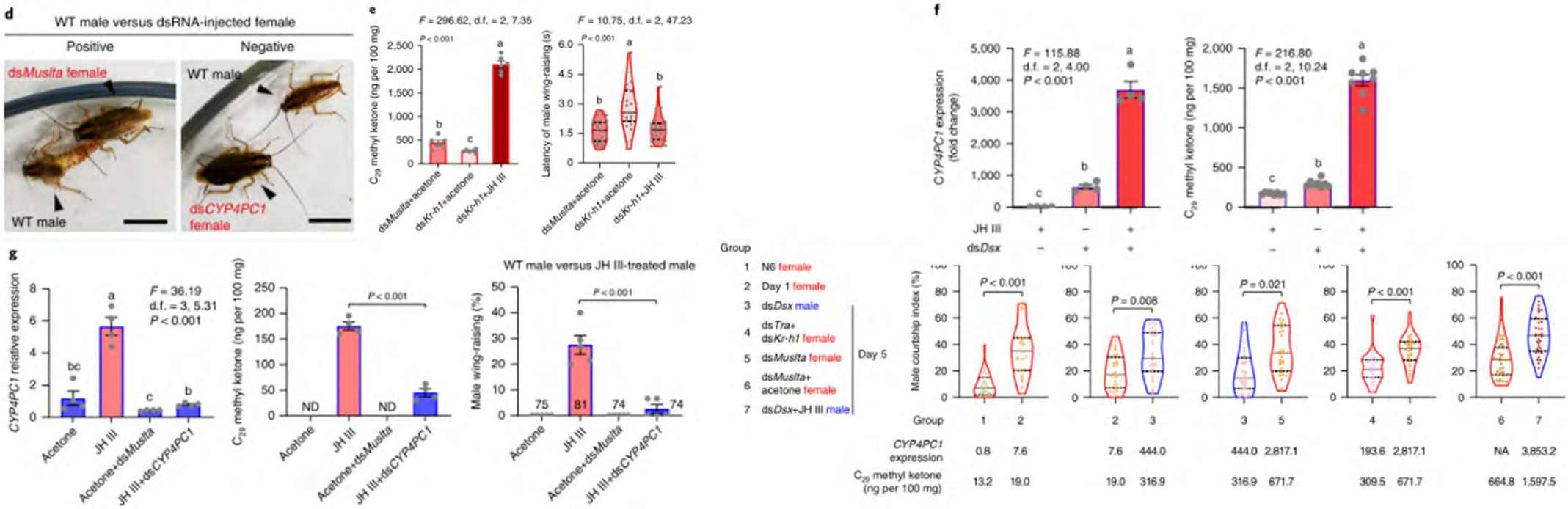
Interaction between dCBP and JH signaling underlies the integrative effect of age and social context on courtship behavior



(Sachin Sethi et.al.*Current Biology*.2019)

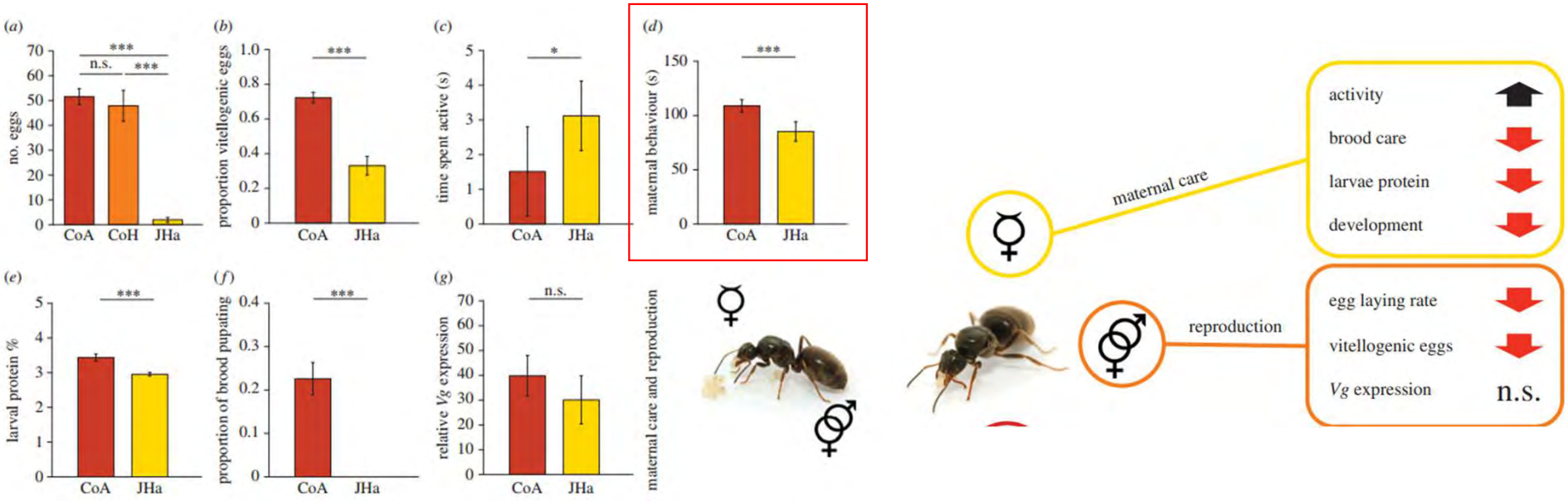
How does JH regulate behaviors in other insects?

A single gene integrates sex and hormone regulators into sexual attractiveness



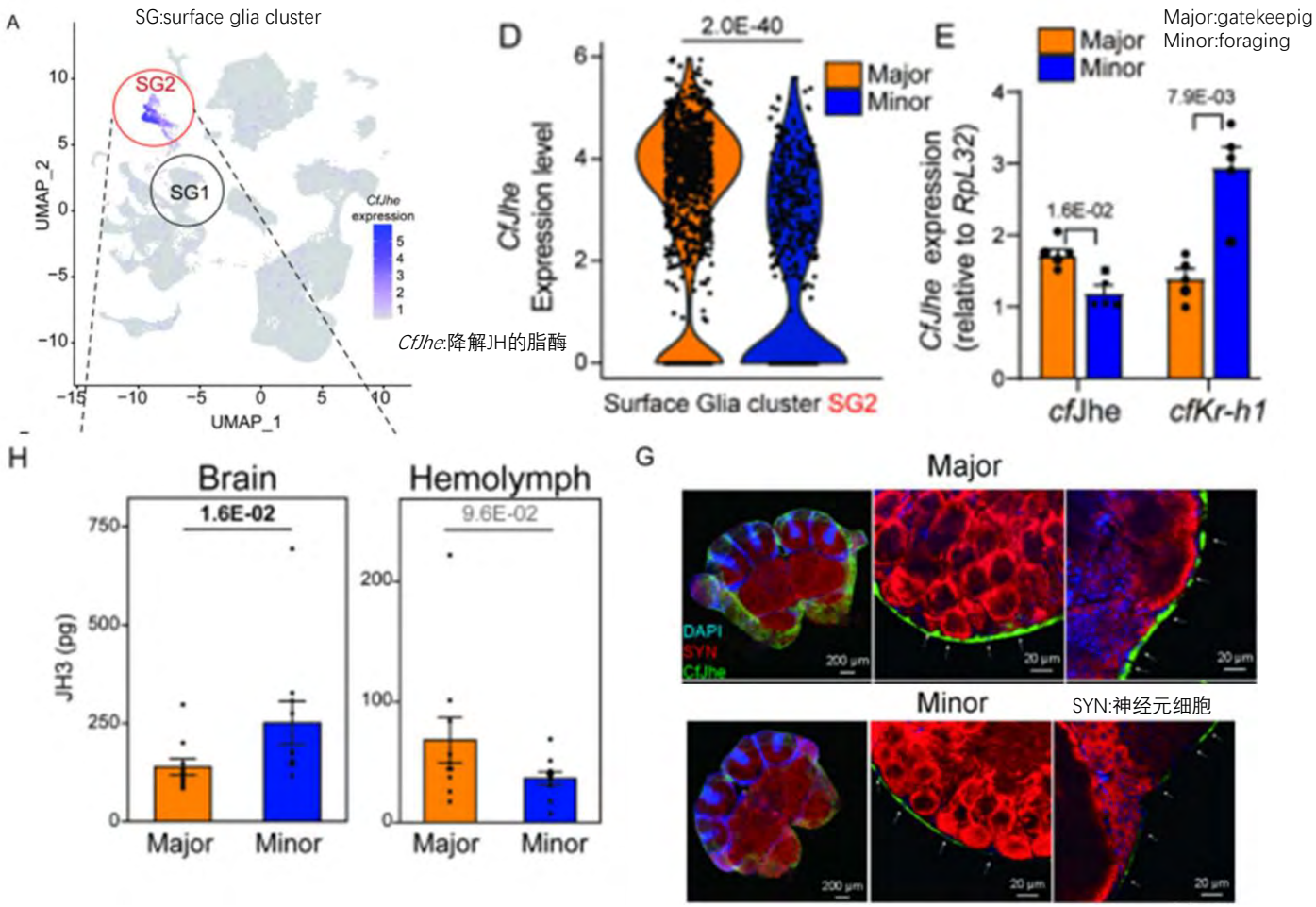
(Nan Chen et.al.*Nature ecology &evolution*.2022)

Effects of juvenile hormone on behavioural and reproductive traits of Lasius niger ant queens

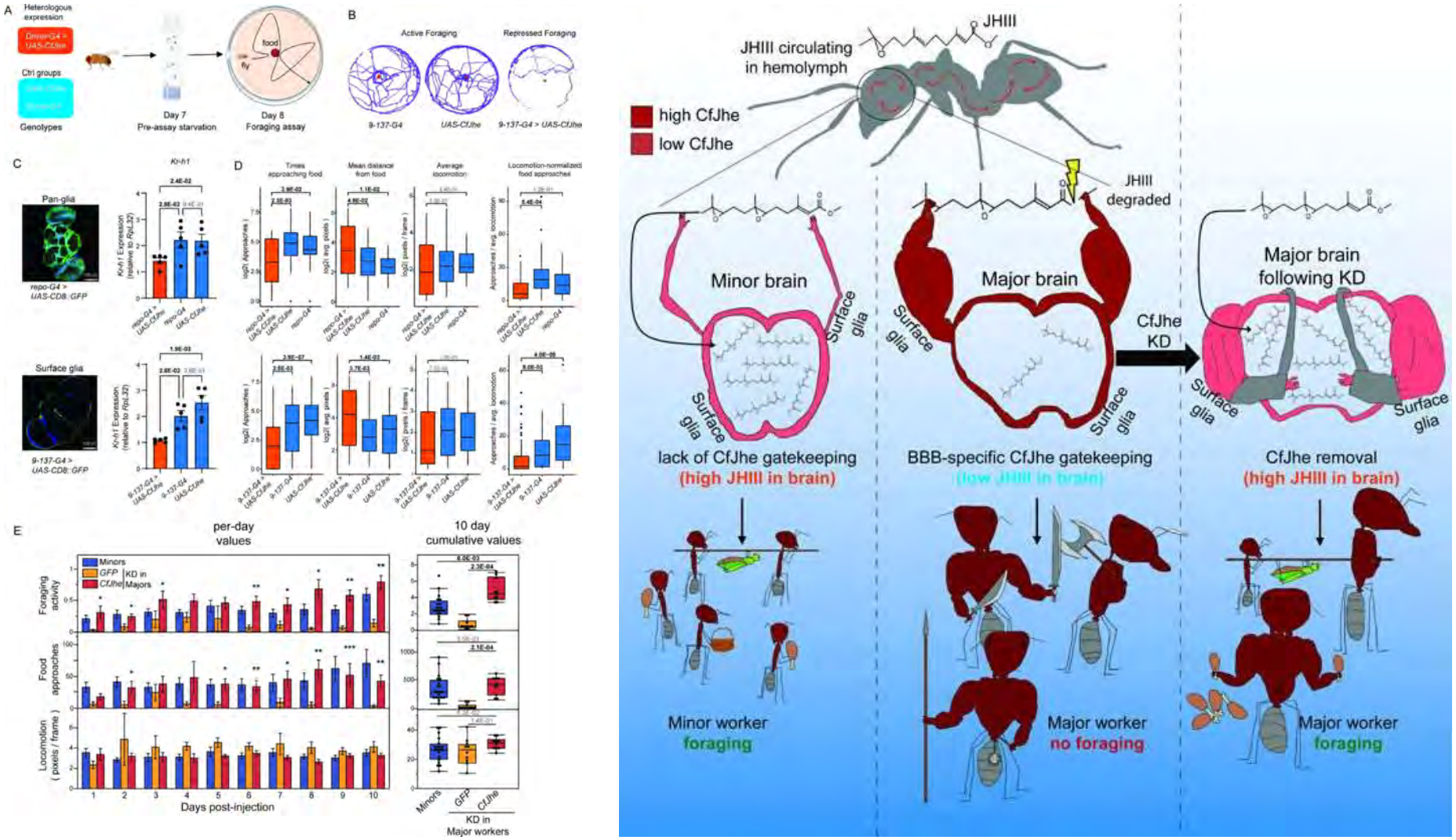


(Pamminger T et.al.*Proc. R. Soc. B*.2016)

Hormonal gatekeeping via the blood brain barrier governs caste specific behavior in ants

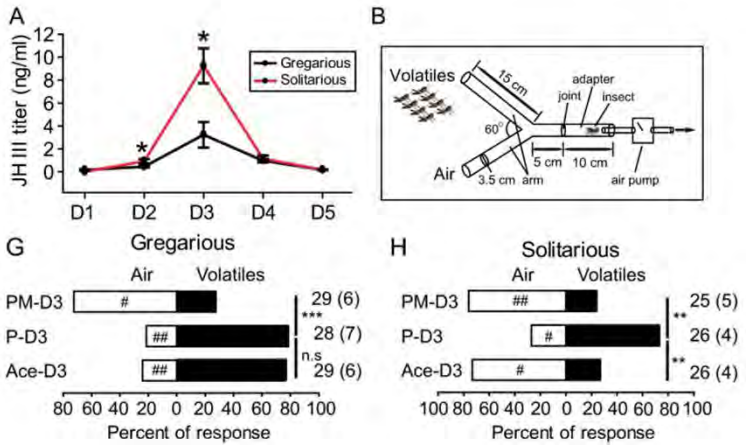


（Linyang Ju et.al.*Cell*.2023）

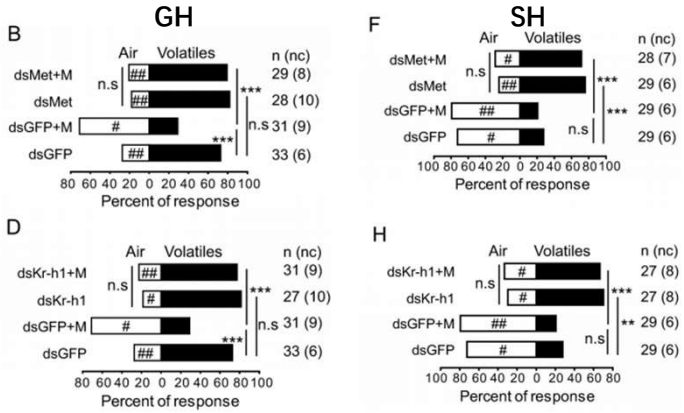

A
Heterologous expression
Ctrl groups
Genotypes
Day 7
Pre-assay starvation
Day 8
Foraging assay
food
fly
B
Active Foraging
Repressed Foraging
9-137-G4
UAS-CfJhe
9-137-G4 > UAS-CfJhe
C
Kr-h1
Pan-glia
repo-G4 > UAS-CD8::GFP
Kr-h1 Expression (relative to Rpl.32)
Surface glia
9-137-G4 > UAS-CD8::GFP
D
Times approaching food
Mean distance from food
Average locomotion
Locomotion-normalized food approaches
log2(Approaches)
log2(avg. pixels)
log2(pixels / frame)
Approaches / avg. locomotion
E
per-day values
10 day cumulative values
Minors
KD in Majors
GFP
CfJhe
Foraging activity
Food approaches
Locomotion (pixels / frame)
Days post-injection
KD in Major workers
JHIII
JHIII circulating in hemolymph
high CfJhe
low CfJhe
JHIII degraded
Minor brain
Major brain
Surface glia
CfJhe KD
Major brain following KD
lack of CfJhe gatekeeping
(high JHIII in brain)
BBB-specific CfJhe gatekeeping
(low JHIII in brain)
CfJhe removal
(high JHIII in brain)
Minor worker
foraging
Major worker
no foraging
Major worker
foraging

Juvenile hormone suppresses aggregation behavior through influencing antennal gene expression in locusts

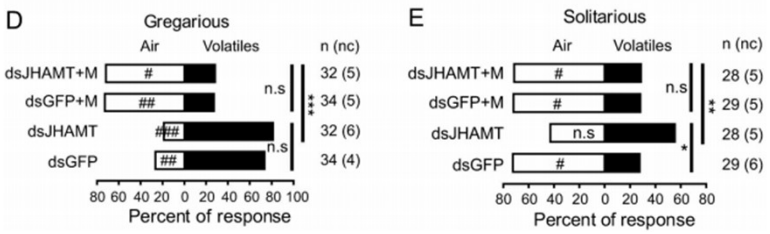
The effects of **JH analog** on attraction/repulsion behavior



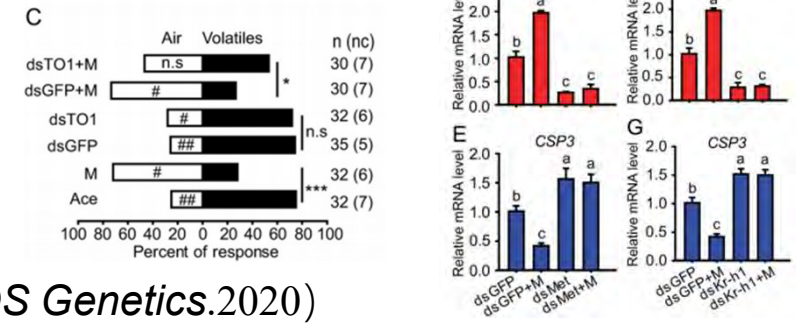
The effects of **Met and Kr-h1** knockdown on attraction/repulsion behavior



The effects of **JHAMT** knockdown on attraction/repulsion behavior



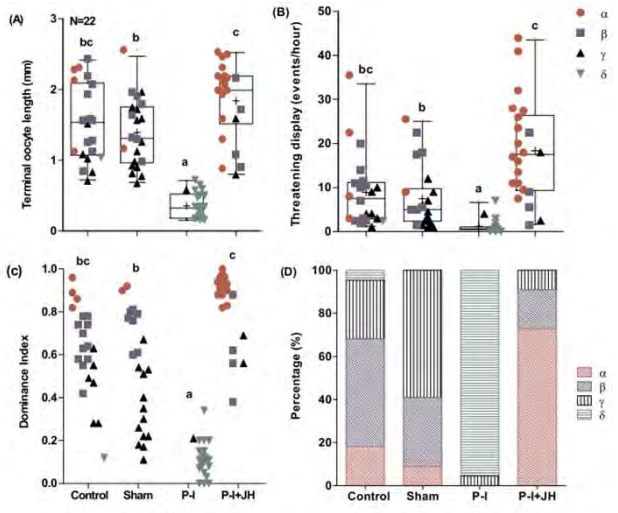
The effects of JH signaling on *TO1* and *CSP3* gene expression and choice behavior



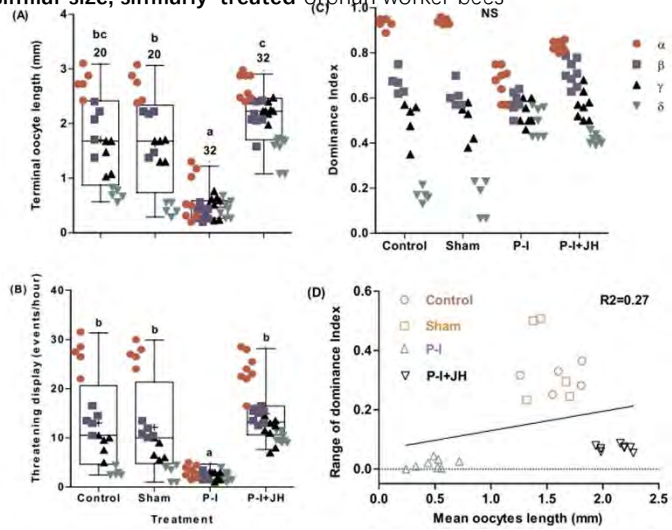
(Wei Guo et.al.*PLOS Genetics*.2020)

Juvenile hormone interacts with multiple factors to modulate aggression and dominance in groups of orphan bumble bee workers

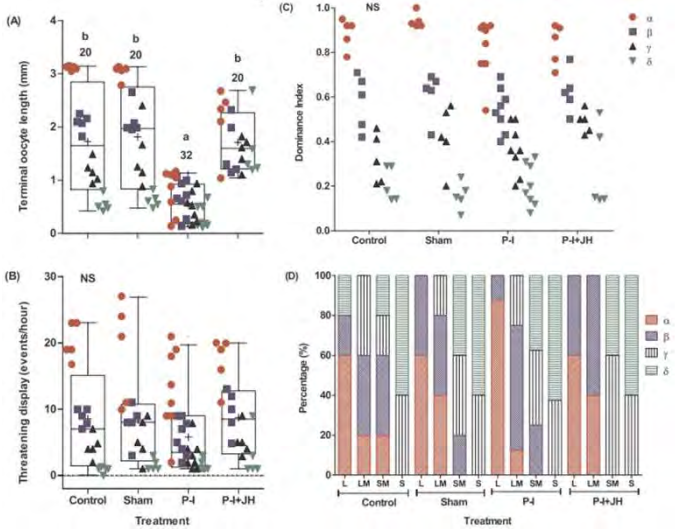
JH ——**similar size, differently-treated** queenless worker bees



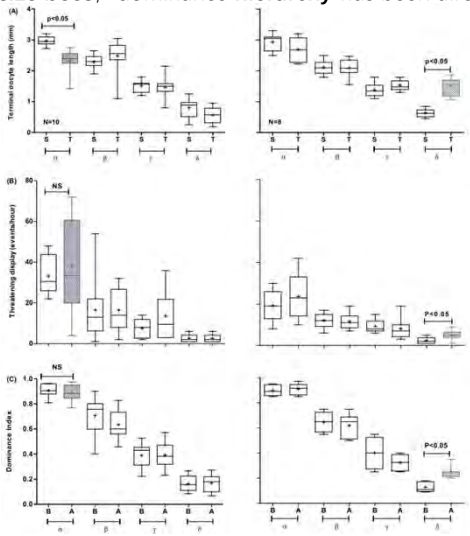
JH ——**similar size, similarly-treated** orphan worker bees



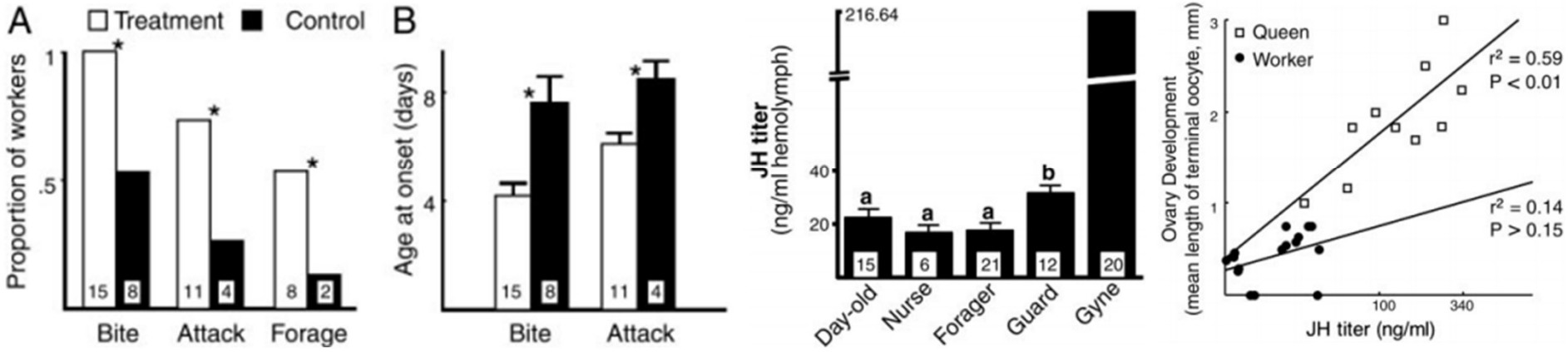
JH ——**different size, similarly-treated** queenless worker bees



JH——**same size bees**，dominance **hierarchy** has been already **established**



Juvenile hormone, reproduction, and worker behavior in the neotropical social wasp Polistes canadensis



(Tugrul Giray et.al.*PNAS*.2004)

Summary

- JH can regulate a variety of behaviors in insects;
- In Drosophila melanogaster, JH regulates memory behavior, male courtship behavior and female receptivity behavior and dimorphic sleep behavior;
- In other insects,

  JH regulates sexual behavior in cockroaches;

  In ants, JH regulates the maternal behavior of queen ants and the caste specific behavior;

  In locusts, JH regulates aggregation behavior (JH inhibits aggregation behavior);

  In bees, JH regulates social division of labor, such as aggression and foraging.

THANK YOU !