

Dietary nutrition and lifespan of Drosophila melanogaster

王蓉、张豫宁、陈江涛 2021.10.29 报告主题: **Dietary nutrition and lifespan of Drosophila** 报告内容:

Relationship between Dietary nutrition and Lifespan12:00-12:30 王蓉Protein diet and Lifespan12:30-13:00 张豫宁Carbohydrate-lipid and Lifespan13:00-13:30 陈江涛

13:30- 讨论~



>Relationship between diet and longevity in Drosophila

>Mechanisms of diet regulating longevity in Drosophila

Relationship between dietary nutrition and drosophila lifespan





(Sudhakar Krittika and Pankaj Yadav. Biogerontology. 2019)

Model organisms for nutrition and longevity—Drosophila



(Nieves Baenas and Anika E. Wagner. *Genes & nutrition*. 2019) (*Zoi Evangelakou, Maria Manola* et al. *Genes & nutrition*. 2019)

Molecular links between nutrition and longevity in Drosophila—TOR /IIS pathway



(Zoi Evangelakou, Maria Manolaet al, Genes & nutrition₈2019)

Summary:

•There are two main nutrient perception signaling pathways in drosophila——TOR pathway and IIS pathway.

•These two pathways coordinate and regulate each other and play a crucial role in influencing longevity.

How diet modifies lifespan of Drosophila

Sexual dimorphism in the nutritional requirement for adult lifespan in Drosophila



Nutritional requirements for sustaining life are much lower in males than in females

(Ting Lian, Qi Wu et al. Aging Cell. 2020)

Sex chromosome complement and mating status do not explain the sexual dimorphism of adult nutritional requirement



Female oogenesis is the key cause of the gender difference in life-sustaining nutritional requirements



Males only need a constant source of sugars and amino acids, while females have a strong additional reliance on dietary cholesterol and vitamins throughout their lives

Sex Differences in the Effect of Dietary Restriction on Life Span in Female and Male Drosophila



Transgenerational programming of longevity and reproduction by post-eclosion dietary manipulation in Drosophila

Unmated males



Unmated females

(Brian Xia and Steven de Belle. Aging. 2016)

No evidence for trade-off between longevity and reproduction



Effects of larval nutrition on larvae and young adults



(Christina M. May, Agnieszka Doroszuk et al. *Ecology and Evolution*. 2015)

Effects of larval nutrition on virgin longevity



Effects of larval nutrition and reproductive environment on mated longevity



Summary:

•Drosophila has sexual dimorphism in adult nutritional requirements and DR also showed gender differences in flies' longevity.

•The effect of diet on lifespan is Transgenerational, from F0 to F2-F3 generations by transgenerational inheritance.

•The nutritional level of the larvae also affects the fly's lifespan.

What is the mechanism by which diet regulates drosophila lifespan

Carbon Dioxide Sensing Modulates Lifespan in Drosophila



Genetic Ablation of ab1C Neurons Phenocopies the Longevity Extension of a Gr63a Loss-of-Function Mutation



Gr63a Acts through Mechanisms Distinct from DR to Modulate Lifespan



Gr63a Is Required for Live Yeast Odorants to Modulate Lifespan



Regulation of Drosophila Life Span by Olfaction and Food-Derived Odors



(Sergiy Libert, Jessica Zwiener et al. Science 2007)

whether the loss of olfactory function is sufficient to increase life span



Or83b is the cause of increased life span in these animals.

Olfactory signaling modulates life span primarily by altering the onset of demographic senescence



The interaction between the olfactory and diet pathways

Genetic background	Nutrient level (% SY)	Control longevity			Or83b longevity			Absolute		Genetic	Nutrient level	Control longevity			Or83b longevity			Absolute	0/ 1
		n	Mean	(SE)	п	Mean	(SE)	change	% Increase	background	(% SY)	n	Mean	(SE)	n	Mean	(SE)	change	% Increase
Canton-S									5	Canton-S						\frown			
	3%	319	50.1	(0.77)	311	61.6	(0.86)	11.5	23.0%		3%	322	52.1	(0.83)	317	66.8	(0.75)	14.7	28.2%
	5%	319	50.1	(0.81)	304	62.5	(0.78)	12.3	24.6%		5%	315	53.2	(0.67)	282	66.3	(0.80)	13.1	24.6%
	7.5%	324	43.9	(0.80)	315	58.9	(0.83)	15.0	34.1%		7.5%	331	52.3	(0.71)	313	68.7	(0.77)	16.4	31.3%
	10%	313	44.8	(0.82)	318	58.6	(0.92)	13.8	30.7%		10%	330	52.0	(0.76)	296	67.5	(0.82)	15.6	30.0%
	15%	314	41.6	(0.69)	329	55.6	(0.76)	14.0	33.7%		15%	325	47.2	(0.74)	301	67.1	(0.85)	19.9	42.1%
уw						0.225.0347.024				yw						<u> </u>			
	3%	249	58.0	(0.85)	234	76.1	(0.63)	18.1	31.2%		3%	257	63.6	(0.81)	238	73.8	(0.57)	10.3	16.2%
	5%	244	60.0	(0.83)	239	76.5	(0.60)	16.5	27.6%		5%	242	63.9	(0.89)	243	75.2	(0.57)	11.4	17.8%
	7.5%	254	62.0	(0.74)	236	76.0	(0.76)	14.0	22.6%		7.5%	251	64.4	(0.75)	240	74.3	(0.72)	9.9	15.4%
	10%	241	61.9	(0.74)	238	75.6	(0.81)	13.7	22.1%		10%	246	65.3	(0.92)	246	75.8	(0.67)	10.5	16.0%
	15%	242	50.5	(0.57)	246	69.4	(0.60)	18.9	37.4%		15%	244	60.1	(0.73)	222	70.3	(0.69)	10.1	16.8%
	YP*	237	42.9	(0.84)	243	65.7	(0.73)	22.8	53.1%	w ¹¹¹⁸									
W ¹¹¹⁸						4947 SEC04					3%	317	63.2	(0.80)	328	69.1	(0.72)	6.0	9.5%
	3%	315	51.9	(0.89)	318	75.6	(0.86)	23.7	45.6%		5%	314	63.9	(0.77)	322	69.5	(0.77)	5.6	8.7%
	5%	326	53.2	(0.90)	320	76.0	(0.81)	22.8	43.0%		7.5%	322	63.6	(0.80)	324	73.6	(0.74)	10.0	15.7%
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	10%	316	51.1	(0.79)	317	77.6	(0.84)	26.5	51.9%		15%	317	64.4	(0.80)	305	73.8	(0.71)	9.4	14.5%
	15%	314	49.3	(0.79)	319	72.7	(0.78)	23.4	47.3%	×71						\square			

the Or83b mutation extends longevity largely, but not exclusively, through a diet-independent pathway.

Or83b2 flies exhibited altered physiology and enhanced stress resistance.



Reduced early reproductive output is not required for extended longevity in Or83b2 mutants.

Summary:

- Drosophila perceives nutrition mainly through IIS and TOR pathways, which play an important role in regulating longevity.
- Drosophila has sexual dimorphism in adult nutritional requirements and DR also showed gender differences in flies' longevity.
- The effect of diet on longevity is transgenerational programming, from F0 generation to F2-F3 generation through intergenerational inheritance, and the nutrition level of larva also influences the longevity of drosophila.
- Olfactory regulation is one of the mechanisms affecting drosophila lifespan.

THANKS

Effects of Dietary Proteins and Amino Acids on lifespan in Drosophila

张豫宁 2021-10-29

Background





Background



Hiroshi Ooka. Mechanisms of Ageing and Development



J.A. Zimmerman et al. *Experimental Gerontology*



Whether dietary protein and amino acid affect Drosophila lifespan ?

Contribution of dietary proteins to aging Role of specific amino acids in longevity

> Contribution of dietary proteins to aging


Drosophila fed low protein and high carbohydrate lived longer.



Effects of dietary P:C ratio on lifespan (mean and maximum) and egg production in female D. melanogaster.

Changes in maternal longevity caused by nutritional factors can be passed down to offspring.



Olha Strilbytska et al. Comparative Biochemistry and Physiology.2020

Reduced protein intake appears to extend lifespan by inhibiting TOR signaling pathways .

Current Biology Volume 14, Issue 10, 25 May 2004, Pages 885-890



Report

Regulation of Lifespan in Drosophila by Modulation of Genes in the TOR Signaling Pathway

Pankaj Kapahi, Brian M Zid, Tony Harper, Daniel Koslover, Viveca Sapin, Seymour Benzer ዳ 🖾





Summary

1.P :C ratio is a major determinant of lifespan, and the mechanism may be mediated by reducing protein intake may affect lifespan through inhibition of TOR signaling pathways, and this phenotype can effect offspring lifespan.

Role of specific amino acids in longevity

Imbalance of amino acids and high levels of Met decrease lifespan and reproduction.



Byung Cheon Lee et al. Nat Commun

Sex-specific decrease of lifespan by imbalance of amino acids and high levels of Met.







Byung Cheon Lee et al. Nat Commun

Lifespan extension by Met restriction was accompanied by decreased reproduction.



Under low amino acid status, particularly methionine restriction, lifespan increases lifespan in Drosophila by down regulating TOR signaling.



The effects of NAC supplementation on 3 Drosophila species



Mikhail V. Shaposhnikov et al. AGING. 2018

Summary

1.P :C ratio is a major determinant of lifespan, and the mechanism may be mediated by reducing protein intake may affect lifespan through inhibition of TOR signaling pathways, and this phenotype can effect offspring lifespan.

2. Drosophila lifespan extension by Met restriction requires low amino acid status.



Oleh Lushchak.JPNU

Sensory modulation of lifespan

Science Regulation of *Drosophila* Life Span by Olfaction and Food-Derived Odors

SERGIY LIBERT, JESSICA ZWIENER, XIAOWEN CHU, WAYNE VANVOORHIES, GREGG ROMAN, AND , SCOTT D. PLETCHER Authors Info & Affiliations

SCIENCE • 23 Feb 2007 • Vol 315, Issue 5815 • pp. 1133-1137 • DOI: 10.1126/science.1136610

Cell Volume 157, Issue 5, 22 May 2014, Pages 1023-1036

Article

TRPV1 Pain Receptors Regulate Longevity and Metabolism by Neuropeptide Signaling

Céline E. Riera ^{1, 2, 3}, Mark O. Huising ⁴, Patricia Follett ^{2, 3}, Mathias Leblanc ³, Jonathan Halloran ¹, Roger Van Andel ¹, Carlos Daniel de Magalhaes Filho ³, Carsten Merkwirth ³, Andrew Dillin ^{1, 2, 3} A



Survival (%)

Drosophila develop a preference for protein under starvation.



Jennifer Ro et al. eLife

Serotonin signaling through receptor 2a modulates protein preference.



The perceived value of dietary protein modulates lifespan via serotonin signaling



Jennifer Ro et al. *eLife*

Summary

1.P :C ratio is a major determinant of lifespan, and the mechanism may be mediated by reducing protein intake may affect lifespan through inhibition of TOR signaling pathways, and this phenotype can effect offspring lifespan.

2. Drosophila lifespan extension by Met restriction requires low amino acid status.

3. Serotonin signaling mediates protein valuation and aging

THANKS -PROTEIN K

Effects of Dietary Proteins and Amino Acids on lifespan in Drosophila

Carbohydrate-lipid and Lifespan



--Chen Jiangtao 2021/10/29



How does lipid metabolism influence aging?

How does sugar metabolism influence aging?

How does lipid metabolism influence aging?

1.1 How do cells store and organize their fat in *Drosophila*?



Lipid droplets in fat body

1.2 How does triglyceride storage in lipid droplets affect longevity?



Snz-Tg flies are obese and have more LD stores, but are healthy, starvation resistant, and long-lived

Rupali Ugrankar et al. Developmental Cell .2019

SUMMARY

Lipid and aging:

1. *Drosophila* overexpressing Snz has higher triglycerides (TAG) in the storage of lipid droplets (LDs), which is more resistant to starvation stress and longer survival time.

过表达Snz的果蝇有更高的甘油三酯(TAG)在脂滴(LDs)的存储,因而更能抵抗饥饿应激,存活时间更长

Immunity

Macrophage-Derived upd3 Cytokine Causes Impaired Glucose Homeostasis and Reduced Lifespan in Drosophila Fed a Lipid-Rich Diet

Graphical Abstract



Authors

Katie J. Woodcock, Katrin Kierdorf, ..., Marc S. Dionne, Frédéric Geissmann

Correspondence frederic.geissmann@kcl.ac.uk

In Brief

Consumption of fatty foods is associated across species with inflammation, metabolic imbalance, and reduced lifespan. Woodcock et al. use *Drosophila* fed a lipid-rich diet to demonstrate that an evolutionarily conserved "scavenger receptor-JNK-type 1 cytokine" cassette in macrophages controls glucose metabolism and reduces lifespan via activation of the JAK-STAT pathway.

Article



chronic lipid-rich diet results in shortened life expectancy, loss of glucose homeostasis, and insulin insensitivity

Katie J. Woodcock et al. Immunity .2015



Lipid-Rich Diet Promotes Upd3 Production by Macrophages in *Drosophila*

Katie J. Woodcock et al. Immunity .2015



Macrophage-Derived Upd3 Controls Survival and Insulin Sensitivity in Lipid-Rich Diet

Katie J. Woodcock et al. Immunity .2015

SUMMARY

Lipid and aging:

- **1.** *Drosophila* overexpressing Snz has higher triglycerides (TAG) in the storage of lipid droplets (LDs), which is more resistant to starvation stress and longer survival time.
- 2. Under the condition of long-term high-fat diet, *Drosophila* macrophages mediate the destruction of glucose homeostasis and shorten life span by producing upd3.

长期高脂饮食条件下,果蝇巨噬细胞通过产生upd3介导葡萄糖稳态的破坏以及寿命缩短

高脂--高热量

HFD Feeding Regime

Bottles of flies were emptied and dated; then 5 days after emptying the vial, all flies were taken and placed in a new vial of NF and aged 5 more days. This population was then spilt into two populations, one on NF and one on the designated concentration of HFD, for either 2, 5, or 10 days. We used 30% HFD for 5 days for the majority of the experiments, since it gave strong and reproducible phenotypes.

在大部分实验组给果蝇喂食5d时间30%的高脂饮食, 因为这种方式喂养得到的表型更加明显和稳定。 (适度)高脂-等热量

Cell Metabolism

CellPress

Article

An isocaloric moderately high-fat diet extends lifespan in male rats and *Drosophila*

Dan Shi,^{1,3} TianShu Han,^{1,3} Xia Chu,¹ Huimin Lu,¹ Xue Yang,¹ TianQi Zi,¹ YanHe Zhao,¹ XinYue Wang,¹ ZhiPeng Liu,¹ JingQi Ruan,¹ Xin Liu,¹ Hua Ning,¹ MaoQing Wang,¹ Zhen Tian,¹ Wei Wei,¹ Yue Sun,¹ YinLing Li,¹ Rui Guo,¹ Yu Wang,¹ Fan Ling,¹ Yue Guan,¹ Da Shen,² YuCun Niu,^{1,*} Ying Li,^{1,*} and ChangHao Sun^{1,4,*}

¹National Key Discipline Laboratory, Department of Nutrition and Food Hygiene, School of Public Health, Harbin Medical University, Harbin, P.R. China

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*Correspondence: niuyucun@163.com (Y.N.), liying_helen@163.com (Y.L.), changhaosun2002@163.com (C.S.) https://doi.org/10.1016/j.cmet.2020.12.017





① IHF (isocaloric moderately high-fat) 等热量中等高脂肪饮食的实现



An isocaloric moderately high-fat diet

② IHF显著延长了大鼠的寿命,改善了整体健康



IHF prolongs the lifespan and healthspan of rats

Dan Shi et al. Cell Metabolism .2021

③ IHF通过下调脂肪酸合成,上调脂肪酸分解,从而降低游离脂肪酸,加速脂肪代谢



Dan Shi et al. Cell Metabolism .2021

④ 蛋白质组学确定 PPRC1 作为候选靶点



⑤ IHF 也可以延长果蝇的寿命


SUMMARY

Lipid and aging:

- **1.** *Drosophila* overexpressing Snz has higher triglycerides (TAG) in which is more resistant to starvation stress and longer survival ti
- 2. Under the condition of long-term high-fat diet, *Drosophila* macı glucose homeostasis and shorten life span by producing upd3.



3. Isocaloric moderately high-fat can significantly improve fatty acid metabolism and reduce the level of free fatty acids. The reduced free fatty acids can improve inflammation and stress response by up regulating PPRC1, and finally prolong lifespan.

等能量高脂肪饮食可以显著提高脂肪酸代谢,降低游离脂肪酸水平,而降低的游离脂肪酸通过上调PPRC1,改善炎症和应激反应,最终延长寿命

How does sugar metabolism influence aging?



Sugar-Induced Obesity and Insulin Resistance Are Uncoupled from Shortened Survival in Drosophila

Esther van Dam,^{1,2,7} Lucie A.G. van Leeuwen,^{1,2,7} Eliano dos Santos,^{1,2,7} Joel James,^{1,2,7} Lena Best,^{3,7} Claudia Lennicke,^{1,2} Alec J. Vincent,^{1,2} Georgios Marinos,³ Andrea Foley,^{1,2} Marcela Buricova,^{1,2} Joao B. Mokochinski,^{1,2} Holger B. Kramer,^{1,2} Wolfgang Lieb,⁴ Matthias Laudes,⁵ Andre Franke,⁶ Christoph Kaleta,³ and Helena M. Cochemé^{1,2,8,*} ¹MRC London Institute of Medical Sciences, Du Cane Road, London W12 0NN, UK ²Institute of Clinical Sciences, Imperial College London, Hammersmith Hospital Campus, Du Cane Road, London W12 0NN, UK ³Institute for Experimental Medicine, Kiel University, 24105 Kiel, Germany ⁴Institute of Epidemiology, Kiel University, 24105 Kiel, Germany ⁵Department of Internal Medicine I, University Hospital Schleswig-Holstein, 24105 Kiel, Germany ⁶Institute of Clinical Molecular Biology, Kiel University, 24105 Kiel, Germany ⁷These authors contributed equally ⁸Lead Contact ^{*}Correspondence: helena.cocheme@lms.mrc.ac.uk https://doi.org/10.1016/j.cmet.2020.02.016

1. How does sugar metabolism influence aging?

水分补充充分而有力地挽救了高糖饮食引起的寿命缩短



1. How does sugar metabolism influence aging?

高糖饮食与嘌呤分解代谢失调导致肾结石的小管功能障碍有关



SUMMARY

Lipid and aging:

- **1.** *Drosophila* overexpressing Snz has higher triglycerides (T which is more resistant to starvation stress and longer su
- 2. Under the condition of long-term high-fat diet, *Drosophil* glucose homeostasis and shorten life span by producing u
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Sugar and aging:

L. High sugar diet induces uric acid deposition and tubule dysfunction, and then affects life expectancy. 高糖饮食以依赖于水的方式调节尿酸的产生,加剧肾小管结石的形成,进而影响寿命

SUMMARY

Lipid and aging:

- **1.** *Drosophila* overexpressing Snz has higher triglycerides (TAG) in the storage of lipid droplets (LDs), which is more resistant to starvation stress and longer survival time.
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Sugar and aging:

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THANKS!